ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 1
JANUARY 1969
PAGES 1–88

Mechanistic Organic Photochemistry

By H. E. Zimmerman[*]

Organic photochemical reactions can be understood as transformations of the electronically excited states of the reactant molecules. By considering Lewis structure or molecular orbital representations of these excited states it is possible to outline the several possible reactions available in the case of a given reactant. A number of different types of photochemical transformations are now reasonably well understood. In these cases one finds the same common controlling feature, namely the tendency for an excited state species to follow mechanistic pathways of minimum energy and the requirement for continuous electron redistribution in following these pathways. These preferred transformations can often be selected by inspection of relative bond orders for different types of bonding, by comparison of the potential energy surfaces available to the excited state molecules, and by use of correlation diagrams. The reactions derive from both singlet and triplet states, and one of the more reliable methods now available for identifying excited states reacting is termed the "fingerprint method". Examples of the author's mechanistic approach are given both for ketone and for hydrocarbon photochemistry.

1. Introduction

In 1961 we noted[1] that, despite the high energy employed in photochemistry, the molecular transformations encountered are generally very selective. The excited state molecule seems to transform itself in such a way that electron localization is minimized. We suggested that by use of simple Lewis structure and molecular orbital representations, one could often predict and understand the reaction route chosen by the electronically excited state of reactant. Subsequent to this we investigated the applicability of our proposal to a number of photochemical reactions. The present article summarizes some of these findings.

2. Molecular Orbital and Resonance Methods of Representing Excited States

The carbonyl group is especially useful in illustrating the two most important types of electronic excitation, n–π* and π–π*. Figure 1 shows the atomic orbitals (AO's) available at the different atoms and is really a three dimensional Lewis structure.

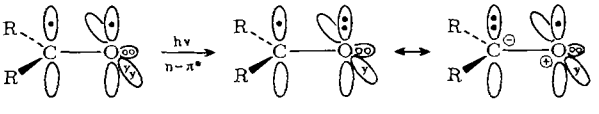


Fig. 1. Ground state *(1)* of carbonyl group. n-π* excited state resonance contributors *(2a)* and *(2b)*. ○ represents sp^n hybrid electrons; y's, p_y electrons; ●, π-system electrons. AO signifies atomic orbital representation.

In this representation there is a low energy sp^n hybrid orbital on oxygen coaxial with the sigma C–O bond and containing two electrons, a p_y non-bonding orbital containing two electrons in the ground state, and lastly a π-system deriving from interaction of two p_x orbitals.

n–π* excitation promotes a p_y electron to the π-system. In resonance terminology, two contributors result from our being able to write the promoted electrons as in the carbon or the oxygen p_x orbital. The molecular orbital equivalent picture (Fig. 2) differs only in that the two molecular orbitals (the

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[1] *H. E. Zimmerman*, Abstracts of the 17th National Organic Chemistry Symposium of the Amer. chem. Soc., Bloomington, Indiana, June 1961, p. 31.

MO's) derived from overlap of the two p_x orbitals are depicted explicitly. In the ground state the π MO is doubly occupied but the π^* MO is vacant. In the $n-\pi^*$ excited state, a p_y electron has been promoted to the antibonding (*i.e.* π^*) MO.

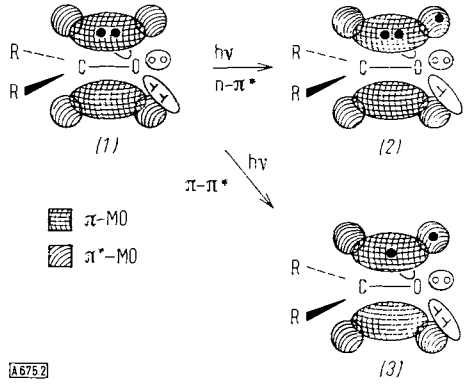


Fig. 2. Molecular orbital representation of $n-\pi^*$ and $\pi-\pi^*$ excitation of *(1)* to *(2)* and *(3)*, respectively.

The $n-\pi^*$ excited state results on excitation by ultraviolet light of *ca.* 300 nm (depending on exact structure) where there is a weak absorption band in ketones. A second excitation process may be seen to be possible, one in which a π-MO electron is promoted to the π^* orbital. This is termed $\pi-\pi^*$ and arises usually by irradiation at shorter wavelengths where there is the intense absorption band whose position follows *Woodward*'s rules. In two dimensions $n-\pi^*$ excitation can be represented as in Fig. 3.

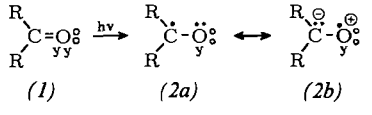
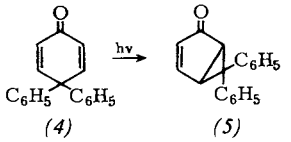


Fig. 3. Two dimensional representation of $n-\pi^*$ excitation.

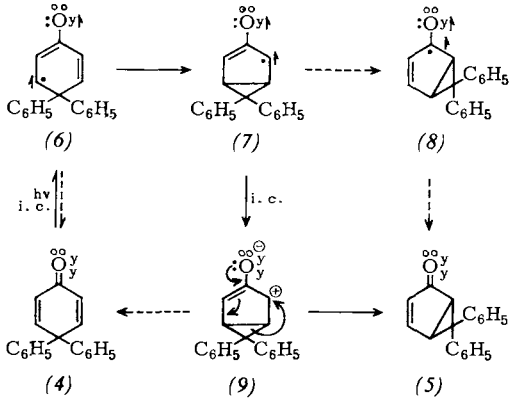
3. Cyclohexadienone Photochemistry

One of the most intriguing photochemical transformations is the "Type A"[2] rearrangement of cyclohexadienones. An example which has been of considerable interest to us is the case of 4,4-diphenylcyclohexadienone *(4)* which affords 6,6-diphenylbicyclo[3.1.0]hex-3-en-2-one *(5)*.



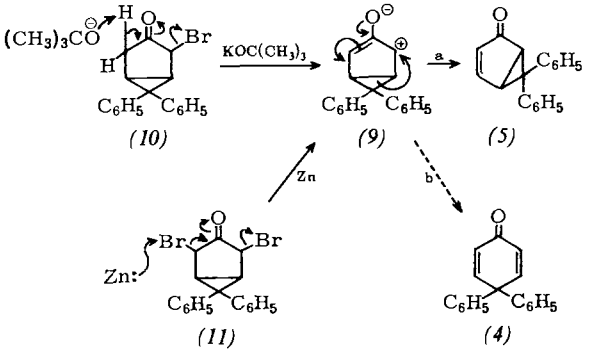
It was found that the reaction is unusually efficient with a quantum yield of 0.85 moles/Einstein[*]. Evidence was advanced that the reaction proceeds by way of the $n-\pi^*$ triplet excited state of the reactant, and this evidence is now summarized.

First of all, sensitization with acetophenone absorbing essentially all of the incident light gives the same quantum yield within experimental error (*i.e.* $\Phi = 0.81$). This finding can be reasonably interpreted to mean that both reactions involve the same excited state, the triplet (see Scheme 1).



Scheme 1. "Type A" rearrangement of 4,4-diphenylcyclohexadienone. The proposed mechanism of rearrangement is indicated by solid arrows. Potentially available pathways not utilized are shown by dashed arrows. The ground-state species are given in the bottom row, and above each ground-state species is drawn the corresponding $n-\pi^*$ excited state. Intersystem crossing occurs between *(4)* and *(6)*, and between *(7)* and *(9)*. The excitation energy gained on going from *(4)* → *(6)* is lost during the step *(7)* → *(9)*.

The evidence in favor of loss of electronic excitation prior to complete skeletal rearrangement is twofold. First, the triplet excited state *(8)* of 6,6-diphenylbicyclo[3.1.0]hex-3-en-2-one *(5)* exhibits behavior, when independently generated, which is not found in low conversion photolysis runs beginning with 4,4-diphenylcyclohexadienone *(4)*[3]. Secondly, the mesoionic zwitterion *(9)* has been independently generated in research by *Döpp*[4] and does indeed afford 6,6-diphenylbicyclo[3.1.0]hex-3-en-2-one *(5)* providing necessary evidence for the zwitterion being an intermediate in the photochemical rearrangements as postulated (see Scheme 2).



Scheme 2. "Photochemistry" without light (route b is not observed).

There are three interesting facets of the reaction *(4)* → *(5)*. One concerns the underlying reasons for the initial 3,5-bonding in the $n-\pi^*$ excited state of dienone. Reference to Fig. 4 shows the increased 3,5-bond

[2] a) *H. E. Zimmerman* and *D. I. Schuster*, J. Amer. chem. Soc. *83*, 4486 (1961); b) *84*, 4527 (1962).

[*] An Einstein is defined as 6.023×10^{23} quanta and corresponds to one "mole" of light.

[3] *H. E. Zimmerman* and *J. S. Swenton*, J. Amer. chem. Soc., *89*, 906 (1967).

[4] *H. E. Zimmerman, D. Döpp*, and *P. S. Huyffer*, J. Amer. chem. Soc. *88*, 5352 (1966).

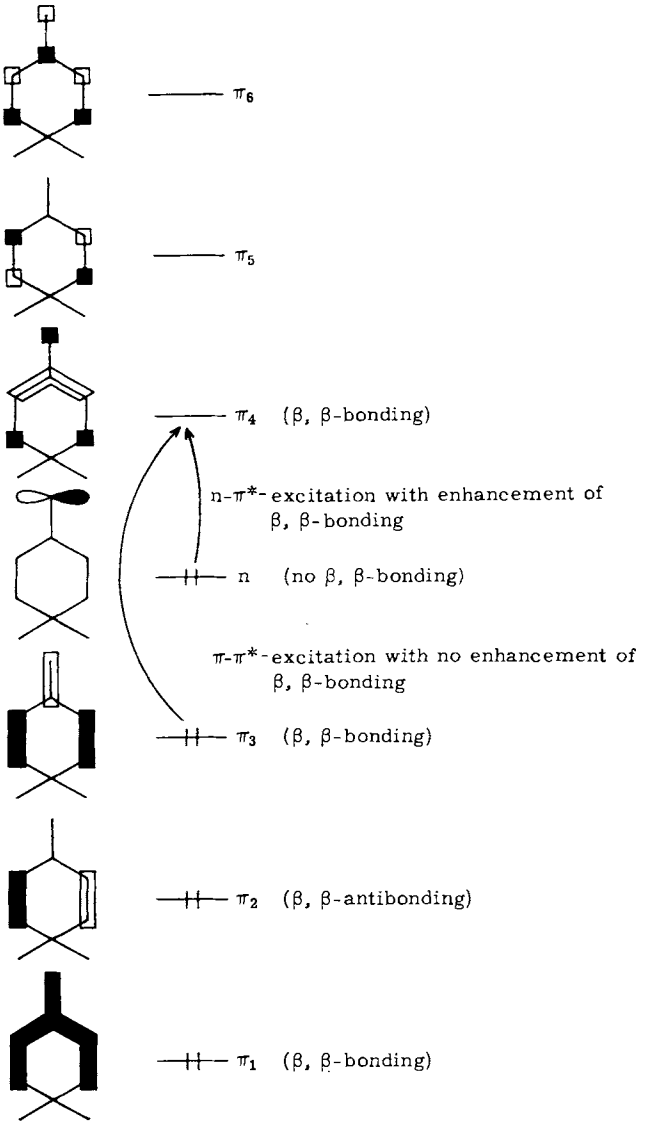
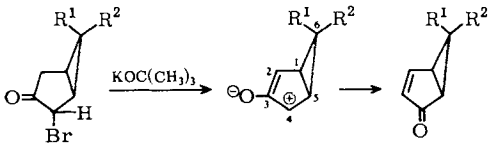


Fig. 4. Molecular orbital representation of n—π* and π—π* excitation processes for cyclohexadienones. ■, wave function positive. □, wave function negative.

order resulting on n–π* excitation [3]. The second point involves the question why the zwitterion *(9)* rearranges so efficiently to the bicyclic ketone *(5)* (process a in Scheme 2) rather than reverting to the dienone *(4)* (process b, Scheme 2). The latter process is one which an organic chemist might consider as a reasonable *a priori* possibility. The correlation diagram (Fig. 5) shows that reversion to the dienone *(4)* is forbidden by symmetry; without change in electron population an exceedingly high energy doubly excited state would result [3].

The third point of interest concerns the stereochemistry of the Type A rearrangement as observed [4a] in the non-photochemical approach to zwitterion *(9)*. When *(10a)* or *(10b)* – having two different aryl groups at C-6 – was allowed to react with potassium *tert*-butoxide, the group initially *exo* remained *exo* in the product and the *endo* group was still *endo* in the product. This finding has been confirmed indepen-



(10) *(9)* *(5)*

(a), $R^1 = C_6H_5$; $R^2 = p\text{-}BrC_6H_4$
(b), $R^1 = p\text{-}BrC_6H_4$; $R^2 = C_6H_5$

dently [4b]. Of two possible stereochemical courses for the reaction *(10)* → *(9)* → *(5)*, a pivot mechanism involving bond (C-1)–(C-6) breaking with pivoting about bond (C-5)–(C-6) and formation of bond (C-4) to (C-6) and a "slither" mechanism in which C-6 migrates from C-5 to C-4 and then from C-1 to C-5, only the latter occurs. The preferred process is equivalent to an inversion of configuration at C-6 with bond (C-1)–(C-6) breaking as (C-4)–(C-6) forms and with (C-5)–(C-6) remaining intact. This preference has been rationalized on two bases, one of which is touched upon briefly later in this article (see Section 8 and Fig. 15c).

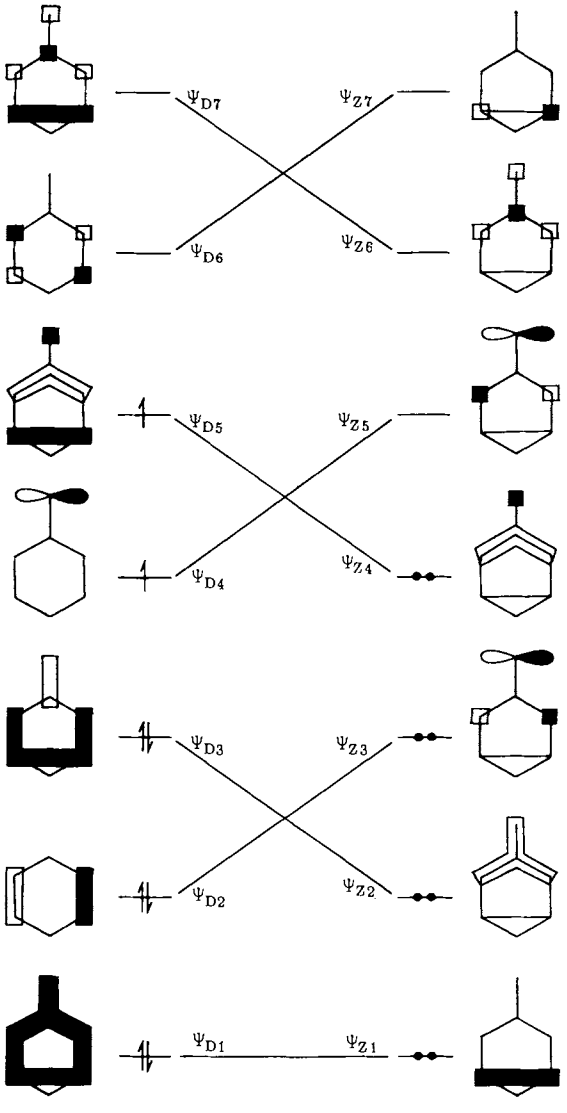
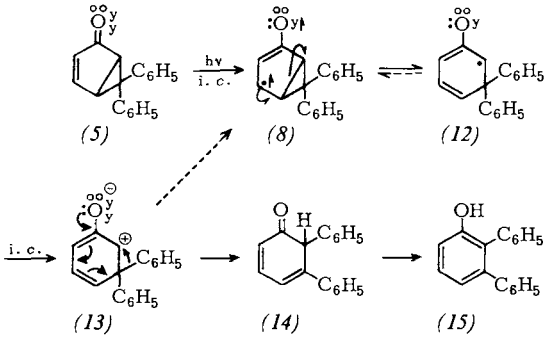


Fig. 5. MO correlation diagram for closure of dienone to 3,5-bridged species. ■, wave function positive; □, wave function negative. ↑ or ↓, electrons in levels occupied in dienone n—π* triplet. ●, electrons in levels occupied in ground state zwitterion. D, dienone. Z, zwitterion.

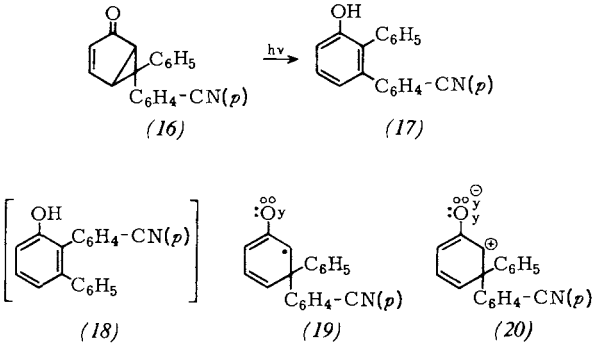
[4] a) *H. E. Zimmerman* and *D. S. Crumrine*, J. Amer. chem. Soc. *90*, 5612 (1968); b) *T. M. Brennan* and *R. K. Hill*, *ibid.* *90*, 5614 (1968).

A related rearrangement is the Type B transformation of bicyclo[3.1.0]hex-3-en-2-ones to phenols. Thus the bicyclic ketone *(5)* gives 2,3-diphenylphenol and some 3,4-diphenylphenol on irradiation. The mechanism proposed is given in Scheme 3. In agreement with



Scheme 3. Type B rearrangement of 6,6-diphenylbicyclo[3.1.0]hex-3-en-2-one. Electron demotion occurs between *(12)* and *(13)*. The dashed arrows indicate processes that have not been observed. Intersystem crossing takes place on going from *(5)* to *(8)* and from *(12)* to *(13)*.

the picture of the zwitterion *(13)* rearranging and not the diradical-like excited state *(12)*, it was found by *Grunewald*[5] that 6-*p*-cyanophenyl-6-phenylbicyclo-[3.1.0]hex-3-en-2-one *(16)* gives mainly 2-phenyl-3-*p*-cyanophenylphenol *(17)* but no *p*-cyanophenyl migration product (see Scheme 4).

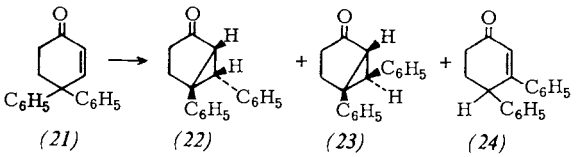


Scheme 4. Test for six-ring zwitterion in the reaction *(16)* → *(17)*. Whereas the cyanophenyl group would migrate in the biradical *(19)*, the phenyl group would migrate in the zwitterion *(20)*.

p-Cyanophenyl should migrate preferentially to an odd electron site while phenyl should migrate to an electron deficient center. The use of migratory aptitudes in photochemistry to determine the nature of the rearranging species is considered again later.

4. The Aryl Migration Reaction of 4,4-Diarylcyclohexenones

Irradiation of 4,4-diphenylcyclohexenone *(21)* leads to phenyl migration products (see Scheme 5). Since in the photolysis of 4,4-diphenylcyclohexadienone *(4)* (Type A transformation) such phenyl migration is an *a priori* possibility which does not occur, *Zimmerman* and *Wilson*[5a] suggested that removal of the second double bond enforces the phenyl migration and that the phenyl migration type rearrangement is less efficient than the dienone Type A process. This prediction was confirmed by quantum yield studies by *Zimmerman* and *Hancock*[6].



Quantum yields for unsensitized reaction:
Φ = 0.043 0.043 0.0003 0.0002

Quantum yields for reaction sensitized by propiophenone:
Φ = 0.040 0.039 0.0003 0.0002

Scheme 5. Examples of the fingerprint method applied to the irradiation of 4,4-diphenylcyclohexenone *(21)* to give *(22)*, *(23)*, and *(24)*.

The quantum yield measurements were obtained by inverse isotope dilution. This method has the advantage of great sensitivity so that reactions can be run to conversions as low as 1% with even relatively low quantum yields; this allows one to be certain that products are not competing for light.

Inspection of the quantum yields (see Scheme 5) with and without sensitization shows that the same distribution of efficiencies is obtained on direct irradiation as in the sensitized ones where one is dealing with preformed triplet excited state. The product and quantum yields distribution can be used as a "fingerprint", and the direct irradiations have the same fingerprint as those beginning with the triplet. This "fingerprint method" of demonstrating the intervention of triplet excited states is one of the more reliable tests available to the photochemist, and in the present case it shows that the direct irradiation of 4,4-diphenylcyclohexenone *(21)* leads to products by way of the triplet excited state.

A second aspect is of interest, namely the high stereoselectivity favoring formation of the *trans* isomer *(22)*[*] of 5,6-diphenylbicyclo[3.1.0]hexan-2-one by a factor of 140:1 over *cis (23)*. This stereochemical preference is not just a matter of mutual avoidance of two phenyl groups due to van der Waals forces, since in the *trans* isomer the *endo*-phenyl-five-ring interaction is just as severe as the phenyl-phenyl hindrance in the *cis*. This stereochemistry seems to arise from a 2,4-bonding to form the three-membered ring concerted with phenyl migration from C-4 to C-3 with inversion of configuration at C-4 (see Fig. 6).

In this process there is a disrotatory motion about bonds (C-1)–(C-2) and (C-4)–(C-5) to form the new internal three-ring bond; the net effect is one phenyl above the new three ring and one below.

It is generally insufficient merely to look at relative quantum yields in order to compare the facility with which two reactions proceed. Actually, one needs the

[5] *H. E. Zimmerman* and *J. O. Grunewald*, J. Amer. chem. Soc. *89*, 3353 (1967).

[5a] *H. E. Zimmerman* and *J. W. Wilson*, J. Amer. chem. Soc. *86*, 4036 (1964).

[6] *H. E. Zimmerman* and *K. G. Hancock*, J. Amer. chem. Soc. *90*, 3749 (1968).

[*] *trans* with respect to the phenyl groups on the three-membered ring.

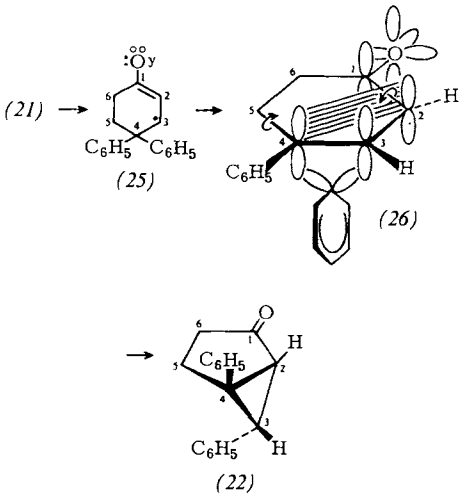


Fig. 6. The stereochemical course of aryl migration during the reaction *(21)* → *(22)* with inversion of configuration at C-4 (cyclohexane numbering).

rate at which the excited state reacts. One can obtain the rates of triplet state rearrangements from Stern-Volmer plots (see Fig. 8) by a method discussed below. 4,4-Diphenylcyclohexenone provides an example (note Fig. 7). Here the triplet rate was found to be $k_r = 3.8 \times 10^7$ sec^{-1} [6]. Although this is a very fast reaction

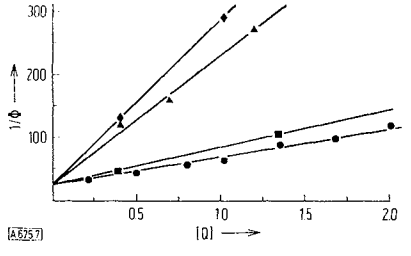


Fig. 7. Stern-Volmer plots of the reciprocal of the quantum yield $^1/_\Phi$ against the quencher concentration [Q] (mole/l). Variation of quenching rate with triplet energy of quencher for 4,4-diphenylcyclohexenone *(21)*. Quenchers: –◆– cyclohexadiene. –▲–, dimethylhexadiene. –■– 1,3-pentadiene. –●–, naphthalene.

compared to the ground state rate constants, it is slow compared to the lower limit of $k_r \geq 10^{10}$ sec^{-1} found for the rearrangement of the triplet excited state of 4,4-diphenylcyclohexadienone *(6)*. Thus the phenyl migration reaction does appear to follow a higher energy pathway than the Type A rearrangement of dienones. Yet the rearrangement of the triplet of *(21)* is faster than the Type A rearrangement of 4-alkylcyclohexenones such as *(44)*; and it has been proposed that this rearrangement fortuitously effects the same skeletal change as the Type A dienone rearrangement without having a similar low energy pathway. The relative efficiencies and rates of the three types of rearrangement are summarized in Table 1.

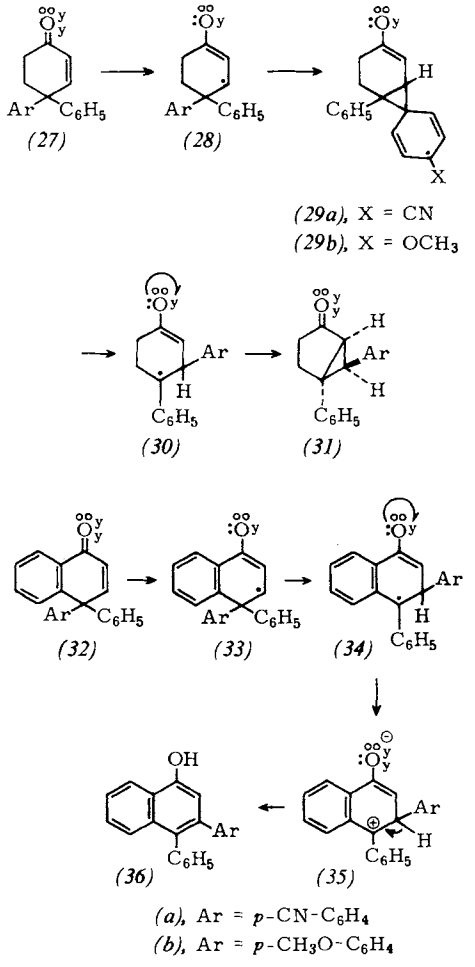
Very recently evidence has been obtained by *Elser* [6a] that the reaction in Scheme 5 has an appreciable activation energy (*ca.* 10 kcal/mole) for excited state rearrangement and that the activation process has a "normal" frequency factor (about $10^{14.5}$). This suggests that the potential energy surfaces surrounding the excited states may be similar to ground state surfaces.

[6a] *H. E. Zimmerman* and *W. R. Elser*, J. Amer. chem. Soc., in press.

Table 1. Efficiencies and rates of triplet rearrangements of cyclohexenones and cyclohexadienones.

Reactant	Type rearrangement	Quantum yield	k_r (sec^{-1})
4,4-diphenylcyclohexadienone *(4)*	Type A	0.85	$\geq 10^{10}$ sec^{-1}
4,4-diphenylcyclohexenone *(21)*	Phenyl migration	0.043	3.8×10^7
4a-methyl-2,3,4,4a,9,10-hexahydro-2-phenanthrone	Type A	0.00084	2.9×10^5

Also of interest in connection with the photochemistry of cyclohexenones is the matter of migratory aptitudes. In both the rearrangements of 4,4-diarylcyclohexenones, such as *(27)* [7], and 4,4-diaryl-1,4-dihydronaphthalenones, *e.g.* *(32)* [8], it has been found that cyanophenyl migrates with greater efficiency than phenyl. This tells us that the β-carbon (*i.e.* C-3) of the electronically excited enone moiety is not electron deficient, since phenyl migrates preferentially to positive centers. Additionally, when the competition is between phenyl and anisyl, we find that it is anisyl whose migration is preferred [7,9]. This result tells us that the β-carbon cannot be heavily electron rich in the excited state



Scheme 6. Migratory aptitudes.

[7] *H. E. Zimmerman, R. D. Rieke*, and *J. R. Scheffer*, J. Amer. chem. Soc. *89*, 2033 (1967).

[8] *H. E. Zimmerman, R. C. Hahn, H. Morrison*, and *M. C. Wani*, J. Amer. chem. Soc. *87*, 1138 (1965).

[9] *H. E. Zimmerman, R. Nasielski*, and *A. Guimanini*, unpublished.

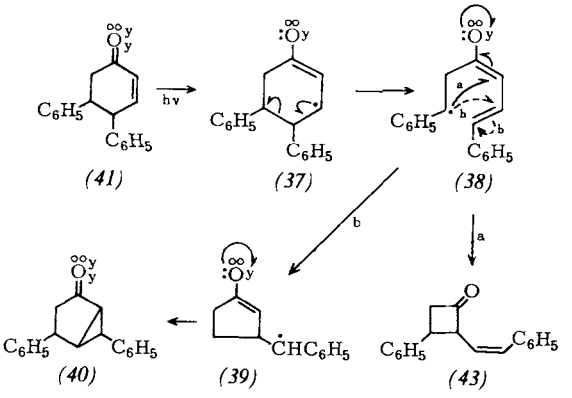
either, since anisyl would not elect to migrate to a negative center in preference to phenyl. One further point is that one might have attempted to explain the preferential migration of cyanophenyl over phenyl by the rationale that migration is to a positive center but that stabilization by the group remaining behind and not migrating is the controlling factor. However, in such a case anisyl would remain behind and this is not observed. The conclusion is that the excited state rearrangement can be pictured as a migration to an odd electron center (see Scheme 6).

Also recently evidence has been uncovered showing that not only the quantum yield for the reaction of 4,4-diarylcyclohexenones is increased by introduction of a *p*-cyano group but also the rate of triplet rearrangement is enhanced (by a factor of *ca.* 12)[9a]. The *p*-cyano group, however, does not appreciably affect the rate of excited state decay; this suggests that rearrangement and decay processes have little in common.

5. The Type A Rearrangement of Cyclohexenones

A second type of enone transformation is known. Skeletally, this is of the Type A variety; however, mechanistically it is quite different from the Type A dienone rearrangements. An example of the Type A enone rearrangement is the photochemical transformation of 4,5-diphenylcyclohexenone *(41)* to afford 4,6-diphenylbicyclo[3.1.0]hexan-2-one *(40)* along with 2-(*cis*-styryl)-3-phenylcyclobutanone *(43)*[10]. Although the same product *(40)* would arise by the phenyl migration mechanism discussed in the previous section, the mechanism of the rearrangement was established as Type A by following a C-14 label originally placed at C-3 in the 4,5-diphenylcyclohexenone *(41)*; the label was found at C-4 (cyclohexane numbering) to the extent of 98.5% showing a heavy predominance of a Type A skeletal transformation. Since 1.5% of the C-14 label originally at C-3 did remain at C-3 (cyclohexane numbering), it was concluded that a phenyl migration mechanism of the type discussed in the previous section occurred as a minor reaction (see Scheme 7).

It was mentioned that 2-(*cis*-styryl)-3-phenylcyclobutanone *(43)* was a product of the reaction as well. (The intermediate *(38)* in Scheme 7 is just the bridged version of the same biradical *(38)* shown in Scheme 8

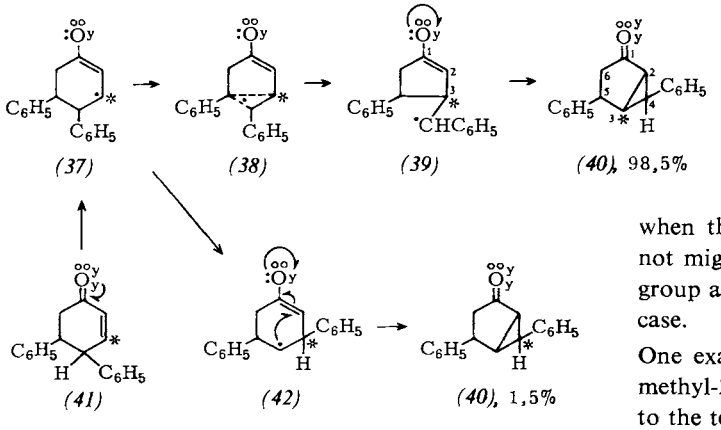


Scheme 8. Mechanism of cyclobutanone formation [10].

as open for simplicity.) The alternative mode of reaction in which the benzylic radical in *(38)* attacks C-2 rather than C-3 can be seen to afford the observed cyclobutane product *(43)*.

It may be noted in Scheme 7 that the phenyl migration route leads to intermediate species *(42)* in which there is an odd electron localized on C-4, a carbon not bearing a phenyl group. This contrasts with the situation in the rearrangement of 4,4-diphenylcyclohexenone where after phenyl migration any free valence on C-4 is stabilized by a phenyl located at this carbon and not migrating. As a consequence one can understand phenyl migration being preferred in the photolysis of 4,4-diphenylcyclohexenone *(21)* while the Type A enone rearrangement is preferred in the case of 4,5-diphenylcyclohexenone *(41)*.

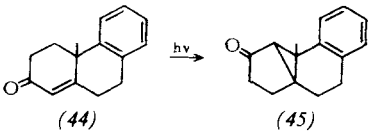
It appears that the Type A rearrangement of cyclohexenones takes precedence over the phenyl migration



Scheme 7. Competitive pathways for 4,5-diphenylcyclohexenone rearrangement [10]. Upper row, Type A route. Lower row, phenyl migration. *C, ^{14}C label.

when there is insufficient stabilization by the group not migrating in the aryl migration; with one phenyl group and one alkyl group at C-4 this seems to be the case.

One example of interest is the rearrangement of 4a-methyl-2,3,4,4a,9,10-hexahydro-2-phenanthrone *(44)* to the tetracyclic product *(45)*[11]. In this case the reaction was shown to proceed by way of the triplet



(1)

[9a] *H. E. Zimmerman* and *N. Lewin*, J. Amer. chem. Soc., in press.

[10] a) *H. E. Zimmerman* and *D. J. Sam*, J. Amer. chem. Soc. *88*, 4114 (1966); b) *ibid. 88*, 4905 (1966).

excited state since the quantum yield on acetophenone sensitization ($\Phi = 0.00086$) is the same within experimental error as that on direct irradiation ($\Phi = 0.00084$) [11]. This is a case of fingerprint identification with "only one finger" employed and is not totally satisfactory since it is conceivable that the singlet and triplet might accidentally rearrange with the same efficiency. Quenching experiments proved useful in dispelling any doubt. These are represented in Fig. 8 where the reciprocal of quantum yield is plotted *versus* the concentration of naphthalene and di-*tert*-butylnitroxyl quenchers [11]. The rationale for the Stern-Volmer plot can be seen in equation (2).

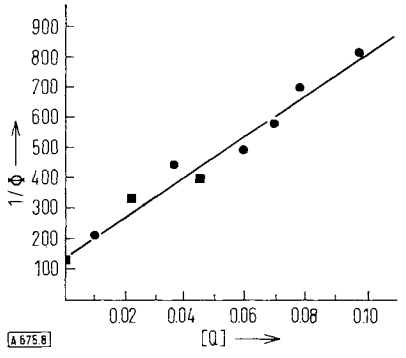


Fig. 8. Stern-Volmer plot of reciprocal of quantum yield *versus* quencher concentration. Quenchers: —■—, naphthalene. —•—, di-*tert*-butylnitroxyl.

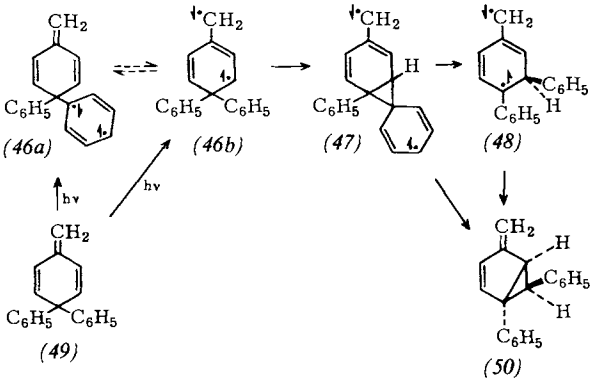
$$\frac{1}{\Phi} = \frac{\overbrace{k_r[T] + k_d[T] + k_q[Q][T]}^{\text{all triplet processes}}}{\underbrace{k_r[T]}_{\substack{\text{only triplet processes}\\ \text{leading to product}}}} = \frac{k_r + k_d}{k_r} + \frac{k_q}{k_r}[Q] \quad (2)$$

In equation (2), [T] is the concentration of triplet excited state, [Q] is the concentration of triplet quencher, and k_d is the rate constant for triplet deactivation. Equation (2) results from the definition of quantum yield, namely the ratio of the rate of product formation from an excited state to the sum of all possible rates of excited state disappearance. It can be seen that the reciprocal of quantum yield then is linear with the concentration of quencher, and that the slope of this plot is equal to the rate constant for quenching divided by the rate constant for triplet rearrangement. Where quenching is controlled by diffusion, one can substitute the known rate constants for diffusion into equation (2) for k_q and then, knowing the slope, solve for k_r.

6. Methylene Analogs of Dienones and Enones

Because the photochemistry of the dienones and enones studied was postulated to be characteristic of $n-\pi^*$ excited states and to derive from a π-system having one extra electron, it seemed of interest to look at systems lacking non-bonding electrons and therefore having only $\pi-\pi^*$ excited states. One example studied was the methylene analog *(49)* of 4,4-diphenylcyclohexadienone *(4)* [12].

When 1-methylene-4,4-diphenyl-2,5-cyclohexadiene *(49)* was irradiated, the initial product was the bicyclic product *(50)*. The reaction quite clearly involves phenyl migration rather than a Type A rearrangement and hence contrasts with the behavior of 4,4-disubstituted cyclohexadienones. When a high energy photosensitizer is used, there is virtually no reaction, although the triene *(49)* quenches the benzophenone-benzhydrol reaction. The quenching of the benzophenone-benzhydrol reaction shows that triplet energy transfer from benzophenone to *(49)* is effective. The lack of product from *(49)* under these conditions shows that the triene triplet is unreactive. The rearrangement on direct irradiation then must result from the singlet excited state (see Scheme 9) [12].



Scheme 9. Rearrangement of 1-methylene-4,4-diphenyl-2,5-cyclohexadiene *(49)*.

One especially interesting aspect of the photochemistry observed is the failure of the triplet, or singlet for that matter, of *(49)* to bond between C-3 and C-5; such bonding is common and facile for the corresponding dienones. However, in the case of the dienones *(4)* such bonding is expected for the $n-\pi^*$ excited states on the basis of a high positive bond order between C-3 and C-5. In contrast, for the $\pi-\pi^*$ excited state of the triene *(49)* the bond order is zero in the Hückel approximation. Hence the lack of such bonding and of a Type A rearrangement is not unreasonable.

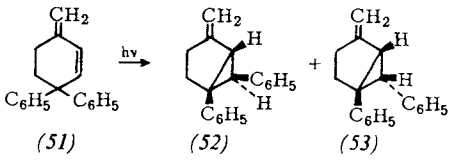
Another case of interest is the methylene analog *(51)* of 4,4-diphenylcyclohexenone *(21)* [13]. Here, irradiation of 1-methylene-4,4-diphenyl-2-cyclohexene *(51)* leads to phenyl migration and to formation of the two stereoisomers of 2-methylene-5,6-diphenylbicyclo-[3.1.0]hexane *(53)* (major product) and *(52)* (minor product). Again the reaction is found to be a singlet one; and the triplet, once formed, is unreactive.

The mechanism envisaged is very similar to that of triene *(49)*. We note that the stereochemistry is the

[11] a) *H. E. Zimmerman, R. G. Lewis, J. J. McCullough, A. Padwa, S. Staley,* and *M. Semmelhack,* J. Amer. chem. Soc. *88*, 159 (1966); b) *ibid. 88*, 1965 (1966).

[12] *H. E. Zimmerman, P. Hackett, D. F. Juers,* and *B. Schröder,* J. Amer. chem. Soc. *89*, 5973 (1967).

[13] *H. E. Zimmerman* and *G. E. Samuelson,* J. Amer. chem. Soc. *89*, 5971 (1967).

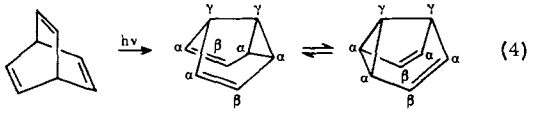


(51) (52) (53) (3)

same as that of the 4,4-diarylcyclohexenones, *e.g. (21)*, with the *trans*-product being preferred, giving weight to the view that this stereochemical course is general.

7. Further π–π^* Photochemistry

An especially intriguing photochemical reaction is the transformation of barrelene *(54)* to semibullvalene *(55)*. Since acetone sensitization is necessary for the reaction, we can conclude that a triplet excited state of barrelene is the rearranging species [14].

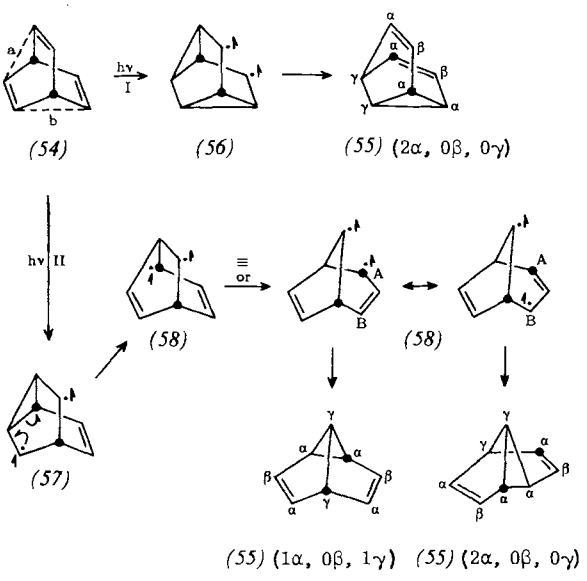


(54) (55a) (55b) (4)

Two fundamentally different mechanisms seemed possible for this transformation (see Scheme 10). A method of differentiating between these was available [15] which depended on the fact that semibullvalene undergoes exceedingly rapid valence tautomerism as shown in eq. (4) and as a consequence shows only three peaks in the NMR, those due to the *alpha*, *beta*, and *gamma* type hydrogen atoms (see eq. (4) for labeling) [14].

By photolysis of barrelene in which the vinyl hydrogen atoms were replaced by deuterium it was possible to follow the disposition of the remaining, bridgehead hydrogen atoms after irradiation. The labeling expected for the two mechanisms is seen in Scheme 10. Mechanism I predicts that the two hydrogen atoms will be located at *alpha* positions and that only this peak will be seen in the product NMR spectrum. Mechanism II predicts a distribution of 75% *alpha*, 0% *beta*, and 25% *gamma* hydrogen atoms; and it is this which is observed experimentally [15]. This prediction, however, is dependent on the triplet biradical *(58)* being a discrete intermediate with finite lifetime and thus symmetrical; the symmetrical allylic biradical *(58)* would bond at either allylic position with equal probability [*]. That the allylic biradical should have an appreciable lifetime is not surprising since it must arise from a triplet and would seem likely itself to be a triplet with intersystem crossing being necessary before collapse to product is possible.

In an attempt to understand the preference for Mechanism II, three-dimensional Hückel theory was utilized on barrelene, semibullvalene, and on each of the intermediate species utilized in the two mechanisms [15]. Thus the ground state and first excited state energies of reactant and each molecular species along the reaction coordinate of each mechanism was obtained. For geometries in between those of biradical species



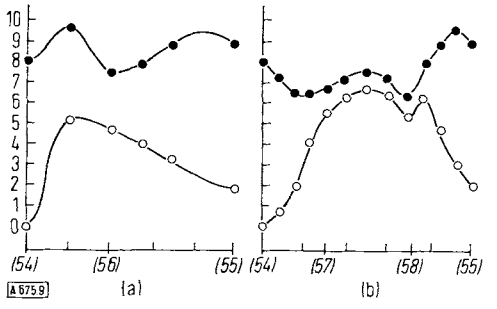
(54) (56) (55) (2α, 0β, 0γ)

(57) (58) (58)

(55) (1α, 0β, 1γ) (55) (2α, 0β, 0γ)

Scheme 10. Possible mechanisms for the barrelene *(54)* to semibullvalene *(55)* interconversion • signifies H label; deuterium elsewhere.

which can be written explicitly, the geometry was taken to be intermediate. From such calculations one obtains cross-sections of potential energy surfaces for the ground and excited states. These are depicted in Figs. 9a and 9b.



Figures 9a, 9b. Potential energy *vs* reaction coordinate for mechanisms I and II, respectively. –o–, ground state curve. –•–, excited state curve.

Mechanism I (Fig. 9a) leads on excitation to a species requiring quite an appreciable activation energy to bridge concertedly to give biradical *(56)*. On the other hand, the ground and excited state surfaces for mechanism II (Fig. 9b) are such that the vertically excited molecule (*i.e.* excited without change in geometry) is on a slope and has enough vibrational energy to surmount the barrier leading to the main excited-state minimum. This minimum is positioned above an electronic ground state minimum which leads preferentially to the product semibullvalene rather than back to barrelene. In agreement with this view is the failure to observe any barrelene from the irradiation of semibullvalene.

Although these three dimensional calculations are approximate and mainly of qualitative use, they present a starting point for considering the photochemical reactivity of molecules undergoing complex transformations.

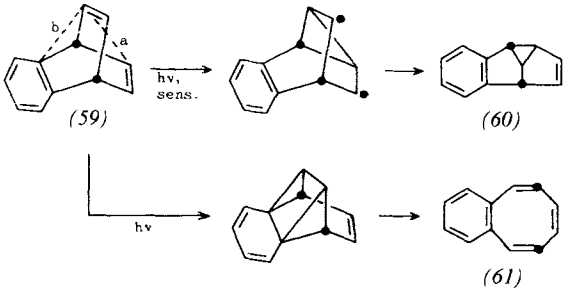
[14] *H. E. Zimmerman* and *G. L. Grunewald*, J. Amer. chem. Soc. *88*, 183 (1966).

[15] *H. E. Zimmerman, R. W. Binkley, R. S. Givens*, and *M. A. Sherwin*, J. Amer. chem. Soc. *89*, 3932 (1967).

[*] This assumed negligible secondary isotope effects.

In connection with the barrelene *(54)* to semibullvalene *(55)* conversion, it is of interest that semibullvalene has very recently been shown by *Iwamura*[15a] to be formed in the photolysis of cyclooctatetraene at −50 °C. Our photochemical finding is paralleled by the elegant thermal conversion of octamethylcyclooctatetraene to octamethylsemibullvalene reported by *Criegee*[15b].

A recent development is the finding[15c] that benzobarrelene *(59)* on sensitization gives the same reaction as barrelene. However, in the present instance, the same product *(60)* can in principle arise from initial vinyl-vinyl bridging (process a) or benzo-vinyl bridging (process b). Labeling experiments[15c] show that vinyl-vinyl bonding is preferred for the triplet. However, in unsensitized runs benzocyclooctene *(61)* is formed from the singlet by a route involving initial benzo-vinyl bonding.



8. The Occurrence of Möbius Systems in Organic Chemistry and Use of this Concept in Photochemistry

One concept which has been of great utility in organic chemistry is the Hückel rule which specifies that for ground state cyclic π-electron systems, $4n+2$ electrons afford a system with appreciable delocalization stabilization and these systems are the aromatic ones; the $4n$ systems are said to be "anti-aromatic". The preceding statement is correct only when these cyclic systems are made up of a set of atomic or hybrid orbitals in such a way that there is no sign inversion (or an even number of sign inversions)[*].

However, there are systems in organic chemistry which have a single sign inversion (or an odd number of sign inversions). In an intriguing article[16], *Heilbronner* noted that it might be possible to synthesize a Möbius molecule in which twisting of the π system along the molecule would lead to eventual overlap of what was the top portion of the π system with the bottom; this is depicted schematically in Fig. 10. Additionally, *Heilbronner* gave an algebraic formula describing the molecular orbital energies of such a molecule.

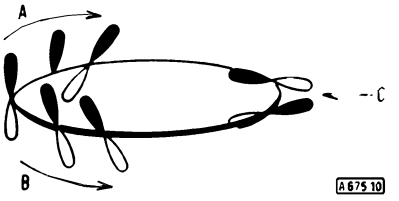


Fig. 10. *Heilbronner*'s Möbius polyene concept. A: plus lobes tilting inward. B: minus lobes tilting inward. C: sign inversion.

We suggested subsequently that it might be useful to focus attention on the presence or absence of a sign discontinuity in a molecule. In this we disregard the precise geometry and concern ourselves only with finding molecules that have such a single sign inversion in a cyclic array of orbitals which may include s orbitals as well as p.

The reason for this is that the secular determinant, the final molecular orbital energies, and also the form of molecular orbitals are not directly aware of geometry but are responsive only to the extent of overlap of such a cyclic array of orbitals in the Hückel approximation. We can term such systems "Möbius-like species", whether they are ground state or transition state molecules. Hence they are Möbius-like more in the mathematical sense than geometrically.

One point worth repeating here is that the cyclic array of orbitals one considers is the group of orbitals set up for purposes of definition and called the "basis set"; this should not be confused with groups of the same orbitals taken in combinations to form molecular orbitals.

We find that molecules composed of a single cycle of orbitals then fall into two categories: those of the Hückel variety and those of the Möbius variety. The Hückel type will always have zero or an even number of sign inversions; the Möbius type will have one or an odd number of sign inversions, depending on just how the basis set of atomic orbitals is arbitrarily chosen.

The reason for considering these two types of orbital systems is that there is a general and consistent pattern of molecular orbitals formed by each of the two. For the Hückel system this is most easily seen by using the mnemonic device of *Frost*[17] in which one draws a circle of radius $|2\beta|$ (see Fig. 11a). The polygon with the same geometry as the cyclic array of orbitals is inscribed with one vertex down. The center of the circle is taken as the energy of an electron isolated in a single orbital of the set and not allowed to distribute itself; we take this energy as our convenient but arbitrary zero. Corresponding to the vertical displacement of each intersection of the polygon with the circle there is a molecular orbital of that energy which results from quantum mechanical mixing of the individual orbitals. *Frost*'s mnemonic is a convenient way of geometrically paraphrasing *Hückel*'s original formula.

[15a] *H. E. Zimmerman* and *H. Iwamura*, J. Amer. chem. Soc. *90*, 4763 (1968).

[15b] *R. Criegee* and *R. Askani*, Angew. Chem. *80*, 531 (1968); Angew. Chem. internat. Edit. *7*, 537 (1968).

[15c] *H. E. Zimmerman, R. S. Givens*, and *R. M. Pagni*, J. Amer. chem. Soc. *90*, 6096 (1968).

[*] The set of orbitals discussed is the arbitrary, definitional set (*i.e.* the so-called "basis set") prior to mixing to give molecular orbitals. The sign refers to the wavefunction and is unrelated to formal charge.

[16] *E. Heilbronner*, Tetrahedron Letters *1964*, 1923.

[17] *A. Frost* and *B. Musulin*, J. chem. Physics *21*, 572 (1953).

If the orbitals are parallel p orbitals and at normal π bonding distances, then the value of $|2\beta|$, the radius of the circle, will be twice the normal resonance integral between two p orbitals of a π system and the MO's given by the mnemonic are those of the organic, cyclic systems. However, if the orbitals are those of a cyclic transition state or of a molecule with different overlap, the value of $|\beta|$ will vary proportionally with this overlap.

The array of molecular orbitals will be the same qualitatively but will be more compressed or expanded depending on the size of the circle. When the overlap is not equal everywhere or when some orbitals are s rather than p, then the simple picture gives only a qualitative approximation to the MO distribution.

Now, for systems with a single sign inversion (or an odd number) in a single cyclic array of orbitals the MO energies can be obtained by a mnemonic device proposed by the present author [18, 19, 19a] which gives exact solutions to the Heilbronner formula for Möbius systems. The author's device differs from the Frost-Hückel mnemonic only in inscribing the polygon with one *side* down in the circle. Also, the device is applicable to Möbius systems which are Möbius-like in the sense of merely having a single sign inversion while not geometrically resembling a Möbius system in a simple [*] manner [18, 19, 19a]. For convenience we term such systems comprised of three orbitals in a cyclic array as "Möbius cyclopropenyl", those with four orbitals as "Möbius cyclobutadiene", *etc.* These are given in Fig. 11b. Again it must be recognized that the radius of the circle is twice the resonance integral for adjacent orbitals of the species considered. As noted by *Heilbronner*, Möbius cyclic polyenes are twisted and $|\beta|$ will be a smaller quantity than the usual $|\beta_0|$. In our work we have noted that the circle radius must be adjusted for differing overlap.

Inspection of Fig. 11a shows that the bonding MO's of the Hückel systems will be filled with $4n+2$ electrons; this is no surprise. We find, on the contrary, that the bonding MO's of the Möbius systems are filled with $4n$ electrons, and this is interesting. For the first excited states in the one electron approximation, where an electron is promoted from the highest occupied to the lowest vacant MO, one finds just the reverse. Here in excited state chemistry, it is the $4n$ electron systems which have the lower electronic energy in molecules with Hückel-like orbital overlap; and the $4n+2$ electron systems which are of lower energy in molecules with Möbius-like overlap [18].

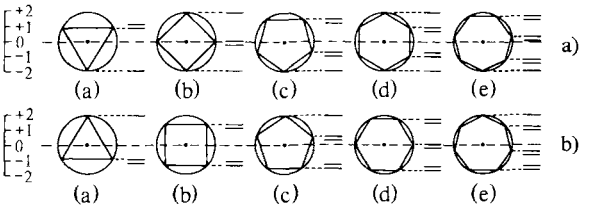


Fig. 11a. Device by *Frost* for obtaining MO energies of Hückel systems (energy units of $|\beta|$). (a): Hückel cyclopropenyl. (b): Hückel cyclobutadiene. (c): Hückel cyclopentadienyl. (d): Hückel benzene. (e): Hückel cycloheptatrienyl.

Fig. 11b. Device by *Zimmerman* for obtaining molecular orbital energies of Möbius systems (energy units of $|\beta|$) [18, 19, 19a]. (a) Möbius cyclopropenyl. (b): Möbius cyclobutadiene. (c): Möbius cyclopentadienyl. (d): Möbius benzene. (e): Möbius cycloheptatrienyl.

One application of this theory to photochemistry is in the photochemical cyclization of butadiene and hexatrienes to give cyclobutenes and cyclohexadienes, respectively. In the case of the butadiene-cyclobutadiene reaction, overlap of the top lobes at C-1 and C-4 of butadiene leads at an intermediate stage along the reaction coordinate to a species which is approximately isoelectronic with Hückel cyclobutadiene (*i.e.* no sign inversions or an even number depending on choice of the basis set of p orbitals); this closure has been termed disrotatory [20]. The intermediate species is depicted in Fig. 12a. The MO's are given by the drawing (b) in Fig. 11a.

Alternatively, different stereochemistry results by overlap of the top lobe at one end of the butadiene molecule with the bottom lobe of the other end. At some point along the reaction coordinate one has a cyclic array of orbitals with one (or an odd number) of sign inversions and with overlap between the terminal orbitals not too different in degree from that between the other adjacent orbitals. This is then a Möbius-like system; it is depicted in Fig. 12b, and the distribution of MO's is given by the drawing (b) in Fig. 11b [*].

With the MO's available for the two alternative partially closed species, we may draw a correlation diagram [21] (Fig. 13). For this one does have to know the placement of the butadiene MO's; however, additionally it is only necessary to connect molecular orbitals of reactant with those of the intermediate species with the same ordering. This mode of drawing the correlation diagram is then an alternative to the use of symmetry [20, 22].

It is seen that for the disrotatory (Hückel) closure, the highest bonding MO becomes antibonding in the reaction while this is not true in the conrotatory (Möbius) reaction. Therefore, for a ground state reaction, Hückel closure will lead to a doubly excited state of product and is said to be "forbidden" (actually in the thermal reaction one would be considering the reverse

[18] *H. E. Zimmerman*, J. Amer. chem. Soc. *88*, 1564 (1966); *88*, 1566 (1966).

[19] *H. E. Zimmerman*, Science (Washington) *153*, 837 (1966).

[19a] *H. E. Zimmerman*, Photochem. and Photobiol. *7*, 519 (1968).

[*] However, one can consider such systems to be Möbius in the geometric sense by considering the overlap of two adjacent orbitals as the attachment of two adjacent strips of surface with the plus and minus lobes of an orbital representing an upper or lower side of the strip. s-Orbitals are then considered as having only one side, plus or minus.

[20] a) *R. B. Woodward* and *R. Hoffmann*, J. Amer. chem. Soc. *87*, 395 (1965); b) *87*, 2511 (1965); c) *R. Hoffmann* and *R. B. Woodward*, *ibid.* *87*, 2046 (1965); d) *87*, 4389 (1965).

[*] A minor point is that due to the twisting and lessened overlap in these species, the radius of the circle used in Figs. 11a and 11b will be less than the usual $2|\beta_0|$. We assume as an approximation that the amount of twisting and lessened overlap is similar for the two species.

[21] *E.g. C. A. Coulson*: Valence. Oxford University Press, London 1952, pp. 93, 100, 101.

[22] *H. C. Longuet-Higgins* and *E. W. Abrahamson*, J. Amer. chem. Soc. *87*, 2046 (1965).

process of cyclobutenes opening to butadienes). For the photochemical process, study of the correlation diagram in Fig. 13 shows that the excited state process

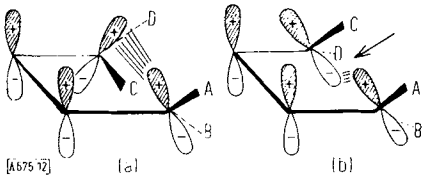


Fig. 12a. Disrotatory (Hückel-like) closure of butadiene.

Fig. 12b. Conrotatory (Möbius-like) closure of butadiene; sign inversion occurs at the site indicated by the arrow.

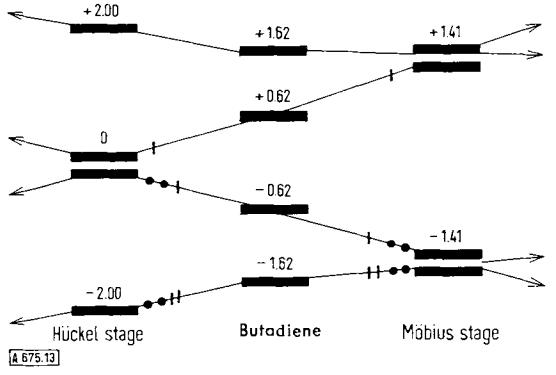


Fig. 13. Correlation diagrams for two types of butadiene closure.

which is favored is the Hückel one. These conclusions derive both from consideration of the energy of the system at the Hückel *versus* the Möbius stage as well as by consideration of the number of the antibonding electrons in the product compared to the reactant if no change in configuration (*i.e.* electron assignment) occurs in the reaction.

A few other examples of the utility of the concept are of interest. The hexatriene closure to cyclohexadiene is shown in Fig. 14. Additionally, in Fig. 15 we see

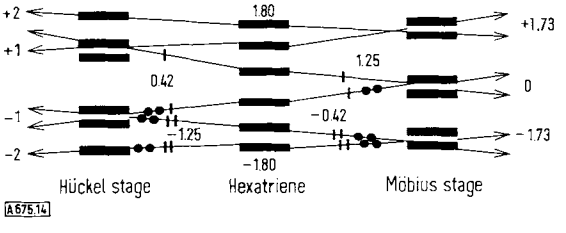


Fig. 14. Correlation diagrams for two types of hexatriene closure.

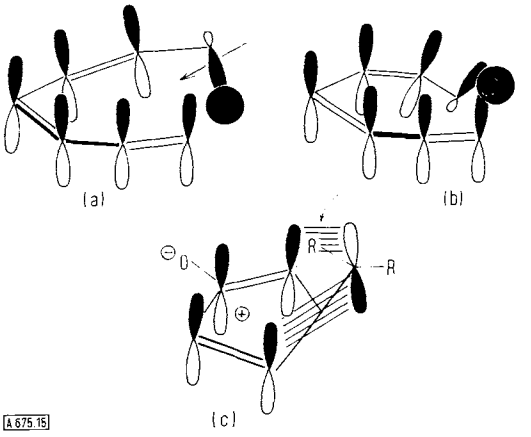


Fig. 15a. 1,7-Antarafacial hydrogen transfer; a Möbius system thus favoring the $4n$ electron ground state process (sign change indicated by arrow).

Fig. 15b. 1,7-Suprafacial hydrogen transfer, a Hückel system favoring the $4n$ electron redistribution in the excited state (no sign change).

Fig. 15c. The partially rearranged Zwitterion of the Type A rearrangement. One sign inversion and a Möbius system favored for the $4n$ electron redistribution process in the ground state; ■, positive orbital sign. □, negative orbital sign.

application to the two alternative 1,7-hydrogen migrations, suprafacial and antarafacial, as well as to the Type A dienone transformation.

9. Conclusion

The preceding discussion makes it clear that photochemistry is amenable to mechanistic discussion. It seems that many solution photochemical reactions follow pathways dictated by energetic considerations, tending to minimize molecular energy in the reaction process. It appears that quite often the excited state molecule rearrangement begins but that the excited state of product is not formed; rather electronic excitation is lost before this geometry is reached. The present article has summarized some of the recent results of the author's research with an attempt to focus attention on different types of findings and approaches.

Support of our research by NIH Grant GM07487 and the National Science Foundation is greatly appreciated.

Received: April 16, 1968 [A 675 IE]
German version: Angew. Chem. *81*, 45 (1969)

Hereditary DNA Alterations[**]

By Ernst Freese[*]

Mutations and recombinations are hereditary alterations of DNA, which is found mainly in the chromosomes of cells. They can occur spontaneously and they can be induced by high energy radiation or by chemicals. This article considers the developments following the discovery of the DNA structure that have led to a molecular explanation of point mutations, of large chromosome alterations, and of recombination. In conclusion, consequences for human society are drawn from the knowledge gained.

1. Introduction

The discovery of the DNA structure by *Watson* and *Crick* in 1953, based on the experimental results of *Wilkins*, *Chargaff*, and others, has rendered feasible an investigation of mutation and recombination in molecular terms.

At that time it was known that most hereditary information is carried by chromosomes which consist of DNA, RNA, and protein. Different sites of a chromosome determine different phenotypic properties, as was revealed by *Morgan* [1] and his school by crosses of *Drosophila* mutants. These investigators found that some of the hereditary properties segregated not randomly, as expected from Mendel's laws, but more frequently remained associated. The closeness of genetic linkage between different phenotypic properties was determined by the frequency with which recombinants of the parental properties were found in the offspring. The resulting "linkage map" of many different markers turned out one-dimensional. The reciprocal recombinants between different parental markers occurred with equal frequency, which *Morgan* ascribed to reciprocal "crossing over". By a subsequent cytological examination of salivary gland chromosomes of *Drosophila*, which consist of about 2000 parallel chromosome strands, it proved possible to identify the sites determining different phenotypic properties by bands on the chromosome. In this way a one-to-one correspondence has been established between the genetic linkage map and the cytological map (see Fig. 1).

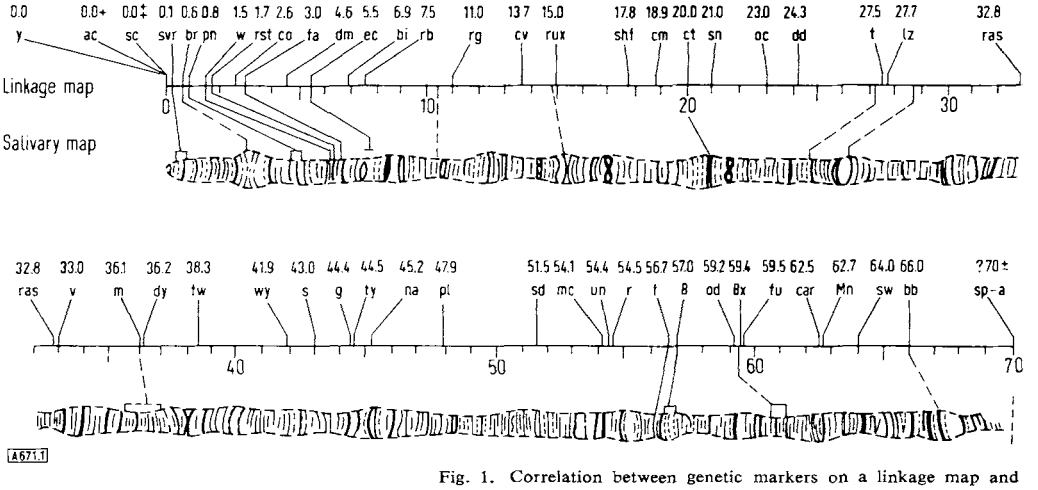


Fig. 1. Correlation between genetic markers on a linkage map and bonds on a salivary gland chromosome of *Drosophila melanogaster* [1a].

However, chromosome alterations could arise not only by the recombination of information present in two homologous chromosomes, but also by mutation, *i.e.* a hereditary alteration of information within one chromosome. Spontaneous mutations were clearly identified by *Bauer* [2] and the first X-ray induced ones by *Muller* [3].

The unit within a chromosome which determines the functional property of a particular phenotype was called a gene. Following the isolation of biochemical

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[**] Presented at the American Chemical Society Symposium on the history of DNA, San Francisco, California, March 31 to April 3, 1968.

[1] *T. H. Morgan*, Amer. Naturalist *1910*, 44.

[1a] Redrawn after *C. B. Bridges*, J. Heredity *26*, 60 (1935).

[2] *E. Bauer*, Bibl. Gen. IV, 1924.

[3] *H. J. Muller*, Science (Washington) *66*, 382 (1927).

mutants, *Beadle* and *Tatum*[4] postulated that one gene controls the information of one enzyme. Since genes were assumed to be complex molecules that were arranged along the chromosome strand like beads on a string, it was automatically postulated that the gene was not only the smallest functional unit but also the smallest mutational and recombinational unit.

The structure of DNA suggested that a functional unit should contain many nucleotide pairs and rendered unlikely the concept of the trinity of the gene. This concept was indeed soon disproved by *Benzer*[5] who showed that mutations could arise at many different genetic sites within a functional unit and that they could be separated by recombination (see Fig. 2). The concept gene should therefore be restricted to a functional unit.

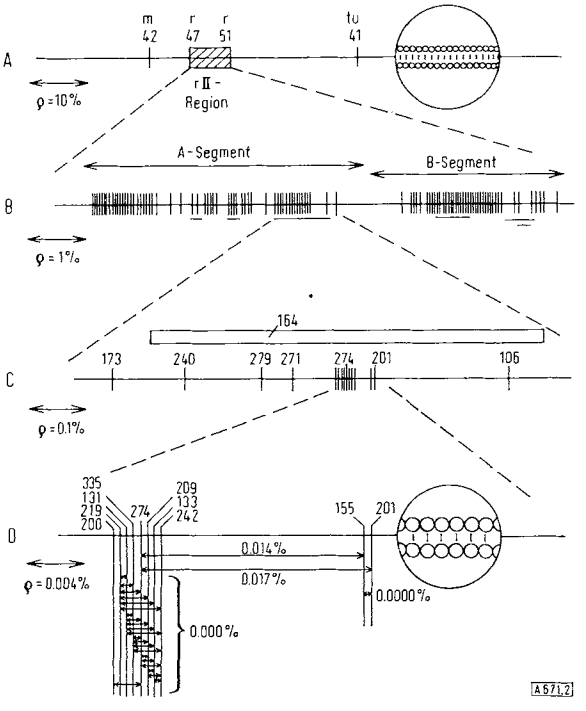


Fig. 2. Genetic fine structure determination within the genetic region determining the "r_{II}" functional property of bacteriophage T4. B, C, and D represent successive magnifications of limited areas. The circles represent nucleotides (magnification in A: × 750, in D: × 7.5). p = recombination frequency. m, tu, and r designate "minute plaque", "turbid plaque", and "rapid lysis" mutants [5a].

However, even the functional definition of a gene is ambiguous. If the final product, derived from a DNA region, is a protein, one could define a gene as exactly that base sequence that is eventually translated into a complete polypeptide. But if the final product is transfer- or ribosomal-RNA, the corresponding gene should carry that information. Finally, in the case of an operator or promoter region, which controls the transcription of adjacent DNA into messenger RNA, a gene could refer to this region which itself is not transcribed into any product. The concept gene, therefore, is imprecise but it is useful until more detailed information is available about the kind of functional unit one is concerned with.

Another loose term is used in the description of the extent of mutations. In order to distinguish small from large hereditary alterations one defines as a "point mutation" a mutation which is limited to a point by all tests that happen to have been performed: cytological, recombination, or functional tests, or the sequence analyses of mutational proteins or eventually of mutational RNA. Ideally, one would like to identify a point mutation as an alteration of a single nucleotide pair in DNA, but since a sequence analysis of DNA is at present impossible, the identification of a point mutation as the change of a single nucleotide pair can be obtained only more or less indirectly, although in some cases quite convincingly. The antipode to point mutations are large chromosomal alterations which involve simultaneously many nucleotide pairs.

2. Point Mutations

In order to understand the nature of point mutations it was necessary to find agents which induce such mutations exclusively and which react with nucleic acids in a known manner. The first promising agent was 5-bromouracil, an analog of thymine, which was known to be incorporated into DNA and which *Litman* and *Pardee*[6] had used to induce mutations in bacteriophage T4. *Benzer* and *Freese*[7] showed, by fine-structure recombination experiments, that such mutations behaved genetically as point mutations and that their distribution pattern differed from that of spontaneous mutations. Subsequently *Freese*[8] found other mutagenic base analogs, *e.g.* 2-aminopurine, and explained the mutation induction by mistakes in base pairing during or following the incorporation of the base analogs into DNA.

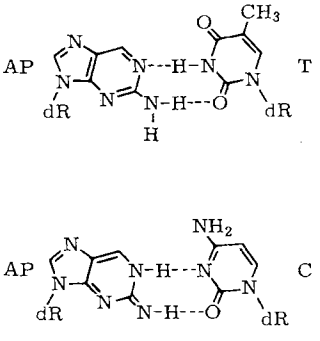


Fig. 3. Normal base pairing between 2-aminopurine (AP) and thymine (T); rare base pairing of 2-aminopurine with cytosine (C).

In Fig. 3 is illustrated the base pairing of 2-aminopurine, whose incorporation into DNA has been demonstrated. 2-Aminopurine apparently can pair normally (by two hydrogen bonds) with thymine and occasionally with cytosine; for the rare pairing it perhaps forms first one hydrogen bond to cytosine, thus inducing a tautomeric shift which permits formation of the second hydrogen bond. In the case of 5-bromouracil, again a tautomeric shift was assumed to allow the pairing of this base with guanine in place of its normal partner adenine. It has so far not been possible to measure the frequencies of the tautomeric forms.

[4] *G. W. Beadle* and *E. L. Tatum*, Proc. nat. Acad. Sci. USA *27*, 499 (1941).

[5] *S. Benzer*, Proc. nat. Acad. Sci. USA *41*, 344 (1955).

[5a] *S. Benzer*, Brookhaven Sympos. Biology *8*, 3 (1955).

[6] *R. M. Litman* and *A. B. Pardee*, Nature (London) *178*, 562 (1956).

[7] *S. Benzer* and *E. Freese*, Proc. nat. Acad. Sci. USA *44*, 112 (1958).

[8] *E. Freese*, J. molecular Biol. *1*, 87 (1959).

Alternatively, *Lawley* and *Brookes*[9] have proposed that it may be the ionized form of the base analogs which undergoes the pairing mistake. The frequency of ionized bases, however, would seem to be too high to explain the mutagenic effect without any further assumptions.

Whatever the detailed reason for the pairing mistake may be, base analogs should be able to induce "base pair transitions"

Adenine ⟷ Guanine
Thymine ⟷ Cytosine

in both directions, owing to mistakes in incorporation or in replication, as illustrated in Fig. 4[8,10]. The induction of transitions in both directions has been proved by the fact that mutants induced by a base

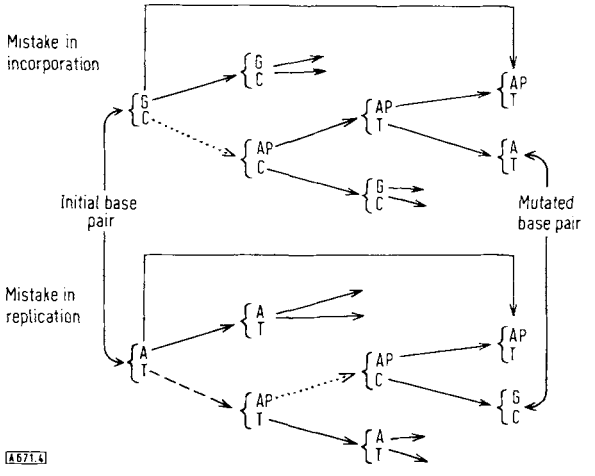


Fig. 4. Induction of base pair changes by mistakes in incorporation or replication of 2-aminopurine. The final altered base pair duplicates as such in the absence of the base analog (G = guanine, C = cytosine, AP = 2-aminopurine, A = adenine, T = thymine).

analog can also be induced to revert to the original phenotype. Nevertheless, each base analog tends to induce mutations preferentially in one direction[10]. After several DNA duplications the base pair change is established and duplicates as such indefinitely, even after the base analog has been removed.

Whereas the previous mutations were all induced *in vivo*, *Mundry* and *Gierer*[11] reported the *in vitro* induction of mutations in tobacco mosaic virus RNA by nitrous acid. Again, it was possible to explain this induction by base pairing of the deaminated cytosine and adenine with the wrong complementary base and to postulate that deaminated guanine should not be mutagenic[12], as has been verified by *Vielmetter* and *Schuster*[13] (see Fig. 5).

At about the same time, ethylating agents, which were long known to be mutagenic, were found to mutate T4 phages[14] and to react mainly with the N-7 of

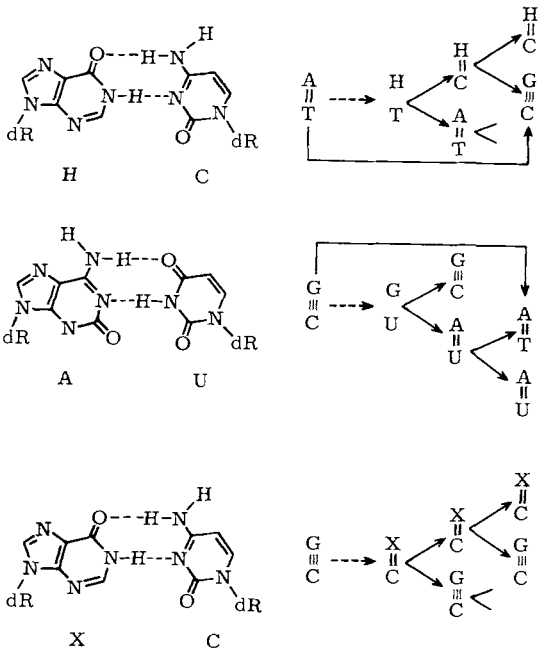


Fig. 5. Base pair changes induced by nitrous acid deamination of bases (H = hypoxanthine, X = xanthine; for other symbols see Fig. 4).

guanine, inducing base pair transitions from GC to AT[15–17] (see Fig. 6). But alkylating agents react also with cytosine and adenine and they induce inactivating DNA alterations, as will be discussed later (for reviews, see refs.[18,19]). The most specific mutagenic

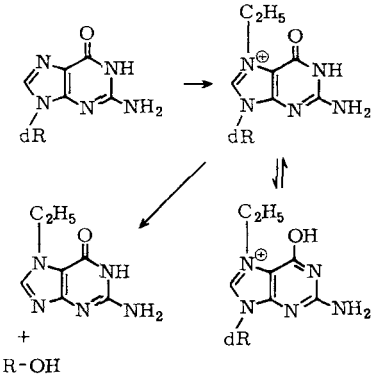


Fig. 6. Reactions of alkylated guanine leading first to "mutagenic" DNA alterations (base alterations) and later to "inactivating" DNA alterations (base removal).

agent found so far is hydroxylamine (or its *o*-methyl derivative, methoxyamine)[20,21]. It induces exclusively point mutations and reacts exclusively with cytosine, if it is used under conditions under which no radicals can be formed by reaction with oxygen.

[9] *P. D. Lawley* and *P. Brookes*, J. molecular Biol. *4*, 217 (1962).
[10] *E. Freese*, Proc. nat. Acad. Sci. USA *45*, 622 (1959).
[11] *K. W. Mundry* and *A. Gierer*, Z. Vererb.-Lehre *89*, 614 (1958).
[12] *E. Freese*, Brookhaven Sympos. Biology *12*, 63 (1959).
[13] *W. Vielmetter* and *H. Schuster*, Biochem. biophysic. Res. Commun. *2*, 324 (1960).
[14] *A. Loveless*, Proc. Roy. Soc. (London), Ser. B *150*, 486, 497 (1959).
[15] *P. Brookes* and *P. D. Lawley*, J. chem. Soc. (London) *1960*, 539.
[16] *E. Bautz* and *E. Freese*, Proc. nat. Acad. Sci. USA *46*, 1585 (1960).
[17] *D. R. Krieg*, Genetics *48*, 561 (1963).
[18] *P. Brookes* and *P. D. Lawley*, J. cellular comparat. Physiol. *64*, Suppl. I, 111 (1964).
[19] *E. Freese* and *E. B. Freese*, Radiat. Res. (Suppl.) *6*, 97 (1966).
[20] *E. Freese*, *E. B. Freese*, and *E. Bautz*, J. molecular. Biol. *3*, 133 (1961).
[21] *E. Freese*, *E. Bautz*, and *E. B. Freese*, Proc. nat. Acad. Sci. USA *47*, 845 (1961).

This can best be achieved in the presence of 1 M or more hydroxylamine and 0.05 M pyrophosphate (pH = 6.5)[22]. Hydroxylamine produces 4-hydroxyaminocytosine or 6-hydroxyamino-5,6-dihydrocytosine or 4,6-bis(hydroxyamino)-5,6-dihydrocytosine, their relative frequency depending on the substitution of C-5. The substituted cytosines apparently pair mostly with adenine thus producing base pair changes from GC to AT (for a review, see ref.[23]).

The explanation of induced mutations by pairing mistakes of base analogs agreed well with the original proposal by *Watson* and *Crick*[24] that spontaneous mutations might arise by pairing mistakes of the normal bases in their tautomeric forms. If all point mutations would arise by such pairing mistakes, only base pair transitions should occur. This simple picture was clearly ruled out by *Freese*[10], who observed in phage T4 that practically all mutants induced by the above base analogs could also be induced to revert by these base analogs, whereas only 14 % of the spontaneous mutations and hardly any of the proflavin (3,6-diaminoacridine) induced mutations responded in this way. Most of the spontaneous mutations, therefore, had to be caused by some other base pair changes. *Freese* assumed as the most likely changes the replacement of a purine by a pyrimidine

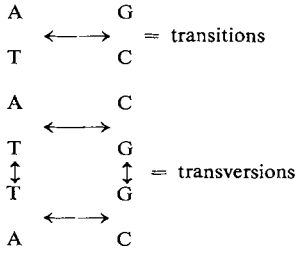


Fig. 7. The two types of base pair substitutions.

and *vice versa*, which he called "transversions" (see Fig. 7). The existence of transversions was strengthened by the fact that treatment (by low pH or ethyl ethanesulfonate), which removed a few guanine bases from DNA, induced the reversion of mutants that could not be induced to revert by any agent inducing only base transitions[25]. Figure 8 explains the induction of different base pair changes by depurination.

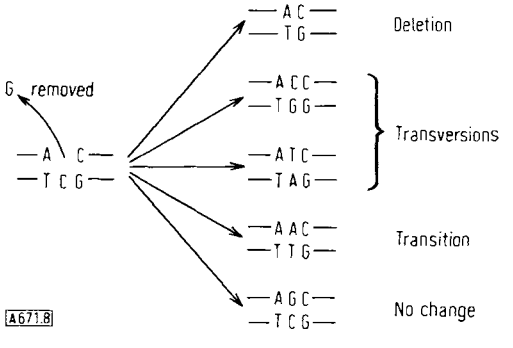


Fig. 8. Base pair changes induced by base removal from DNA.

An alternative model explaining non-transition mutants was soon proposed by *Brenner et al.*[26]. Stimulated by *Lerman*'s[27] observation of proflavine intercalation between DNA bases, they suggested that proflavine induces deletions or insertions of bases. In support of this assumption, *Crick et al.*[28] observed the division of proflavine-induced mutations into two classes (+ and −) with respect to their ability to restore the r_{II} function in double mutants. They consequently proposed the frame shift hypothesis, according to which a deletion shifts the reading frame for the translation of the nucleic acid code to the left and an insertion to the right of the original frame.

At this stage it was clear that only a correlation of amino acid changes in proteins and mutations in DNA could settle which of the above DNA alterations of the non-transition type actually occurred. On the one hand, *Yanofsky*[29] found that an amino acid at a certain position of tryptophan synthetase could be changed by single step mutations into four different amino acids. Since experiments on the cell-free synthesis of proteins had shown that each amino acid is coded by three bases, single base pair transitions altering the same amino acid could occur on three different nucleotide sites in DNA. Hence at least one of the four observed amino acid changes had to be due to a transversion. Similar data have been obtained by *Weigert* and *Garen*[30]. By the analysis of amino acid changes, *Yanofsky et al.*[31] have even shown that a particular bacterial strain spontaneously produces a very high frequency of transversions from AT → CG. On the other hand, *Terzaghi et al.*[32] have proved that proflavine-induced mutations do shift the reading frame by which the message of DNA is translated into the lysozyme protein of phage T4 (see Fig. 9). These results clearly show that proflavine induces deletions and insertions of one or a few DNA bases. All pos-

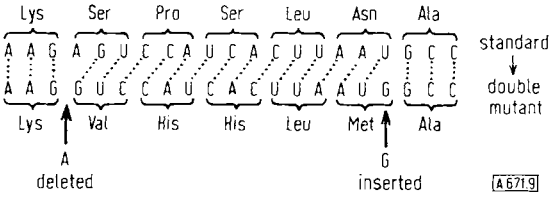


Fig. 9. Shift of reading frame resulting from deletion and insertion of one base pair in phage T4 DNA and the consequence for the amino acid sequence in the lysozyme protein.

[22] *E. Freese* and *E. B. Freese*, Biochemistry *4*, 2419 (1965).

[23] *J. H. Phillips* and *D. M. Brown* in *J. N. Davidson* and *W. E. Cohn*: Progress in Nucleic Acid Research and Molecular Biology. Academic Press, New York 1967, Vol. 7, p. 349.

[24] *J. D. Watson* and *F. H. C. Crick*, Cold Spring Harbor Sympos. quantitat. Biol. *18*, 123 (1953).

[25] *E. B. Freese*, Proc. nat. Acad. Sci. USA *47*, 540 (1961).

[26] *S. Brenner, L. Barnett, F. H. C. Crick*, and *A. Orgel*, J. molecular Biol. *3*, 121 (1961).

[27] *L. S. Lerman*, J. molecular Biol. *3*, 18 (1961).

[28] *F. H. C. Crick, L. Barnett, S. Brenner*, and *R. J. Watts-Tobin*, Nature (London) *192*, 1227 (1961).

[29] *C. Yanofsky*, Biochem. biophysic. Res. Commun. *18*, 898 (1965).

[30] *M. G. Weigert* and *A. Garen*, Nature (London) *206*, 992 (1965).

[31] *C. Yanofsky, C. E. Cox*, and *V. Horn*, Proc. nat. Acad. Sci. USA *55*, 274 (1966).

[32] *E. Terzaghi, Y. Okada, G. Streisinger, J. Emrich, M. Inouye*, and *A. Tsugita*, Proc. nat. Acad. Sci. USA *56*, 500 (1966).

sible types of base pair changes can therefore be produced: transitions, transversions, deletions, and insertions. Presumably, inversions and reiterations of a base sequence also exist, but they have not yet been proved experimentally.

All these base pair changes cannot only be induced, but they also arise spontaneously. Which of them occur with the highest frequency depends on the organism. In this connection, an interesting observation has been made by *Speyer* [33], who has shown that the frequency of spontaneous mutations is controlled, at least to some extent, by DNA polymerase. A temperature-sensitive phage mutant, producing an altered polymerase, showed a greatly increased frequency of spontaneous mutations.

This result raised the question of whether DNA replication actually depends on the accurate pairing, by hydrogen bonding, between the old and new DNA bases or whether the replicating enzymes might have enough specificity in themselves to mate always guanine with cytosine and adenine with thymine [33]. This problem was investigated by examining whether mutagenically altered bases would increase the frequency of mutations by the same amount in the presence of the mutant polymerase as for the normal polymerase [34]. If the polymerase would ensure the correct duplication, by actually recognizing the bases, at least some of the altered bases might be recognized differently by the mutant enzyme. No such difference was found. The authors postulated, therefore, that complementary bases pair by hydrogen bonding and that the DNA polymerase recognizes the correct structure, position, and angle of the sugar phosphate moiety of the incoming nucleotide triphosphate. The mutant polymerase presumably accepts more deviations from the correct conformation than the normal polymerase.

Drake [34a] has recently discovered another phage mutant which produces both spontaneous and 5-bromouracil induced mutations at a reduced rate. It is not known whether the more discriminating mutant polymerase can recognize bases directly or whether it recognizes the slight changes in position of the deoxyribose phosphate group that are caused in the incoming nucleotide by an alteration of the base structure.

In different organisms, spontaneous mutations arise by different molecular mechanisms and involve different base specificities. Their frequency determines the rate at which an organism can evolve by creating new base sequences. But many base pair changes in DNA do not alter the phenotypic properties of the organism, because the amino acid code is degenerate, because some amino acid changes do not alter the enzymatic properties of a protein, or because some DNA regions are not utilized. This explains why bacteria which have surprisingly similar properties and biochemical pathways have such different GC/AT base ratios [35, 36]. Their base ratio apparently has shifted slowly, the rate depending on the organism. But only those bacteria survived for which the phenotypic properties were not significantly changed or which could utilize a phenotypic change to adapt to a new ecological niche [37, 38].

3. Large Chromosomal Alterations

If we next want to understand how large chromosome alterations come about, we should know how DNA is built into the structure of a chromosome. For example, DNA molecules carrying different information conceivably could be arranged as side chains to a main chromosomal stem. But we know from genetic experiments by *Pritchard* [39] and many others that mutations within a gene are located on the same information tape as distant outside markers for other functions. Consequently, chromosome models have been proposed in which DNA molecules are one-dimensionally arranged in a long strand and covalently held together by peptide units that are connected always to one of the two strands [40,41]. Chromosomes of higher organisms could carry several identical information tapes in parallel, as suggested by the finding of chromatid and subchromatid strands in chromosomes. At the time of these proposals, DNA molecules were measured to have a molecular weight of no more than 10 million. *Davison* [42] later showed that DNA was subject to shear during its isolation and that carefully isolated DNA molecules were very much longer, with no limit being apparent. Nevertheless, measurements of the unwinding time of rotating DNA [43, 44] have shown that in larger chromosomes swivel points must exist in the information tape, at least during the duplication of DNA. It is unknown whether the interruptions in the double strand are all produced by a DNAase or whether peptide links exist. In any case, DNA itself seems to make up the major portion of the information tape. Hence, any chromosome-breaking agent that can affect DNA presumably causes the breaks owing to its alteration of DNA.

The effect of different agents on chromosomes can be cytologically detected quite early by gaps in or exchanges between the substrands of a chromosome (chromatids or subchromatids); the exchanges apparently occur because broken chromosome ends are "sticky" and tend to attach to other sticky ends [45]. These chromosome aberrations later produce chromosome breaks or other large alterations and thus mutations if the cell can still duplicate.

[33] *F. Speyer*, Biochem. biophysic. Res. Commun. *21*, 6 (1965).

[34] *E. B. Freese* and *E. Freese*, Proc. nat. Acad. Sci. USA *57*, 650 (1967).

[34a] *J. Drake*, personal communication.

[35] *N. Sueoka*, Proc. nat. Acad. Sci. USA *45*, 1480 (1959).

[36] *R. Rolfe* and *M. Meselson*, Proc. nat. Acad. Sci. USA *45*, 653 (1959).

[37] *E. Freese*, J. theoret. Biol. *3*, 82 (1962).

[38] *N. Sueoka*, Proc. nat. Acad. Sci. USA *48*, 582 (1962).

[39] *R. M. Pritchard*, Heredity *9*, 343 (1955).

[40] *E. Freese*, Cold Spring Harbor Sympos. quantitat. Biol. *23*, 13 (1958).

[41] *J. H. Taylor*, Proc. 10th int. Congr. Genetics, Montreal *1*, 63 (1958).

[42] *P. F. Davison*, Proc. nat. Acad. Sci. USA *45*, 1560 (1959).

[43] *E. B. Freese* and *E. Freese*, Biochemistry *2*, 707 (1963).

[44] *P. F. Davison*, J. molecular Biol. *22*, 97 (1966).

[45] *B. A. Kihlman*: Actions of Chemicals on Dividing Cells. Prentice-Hall, Englewood Cliffs, N.J. 1966.

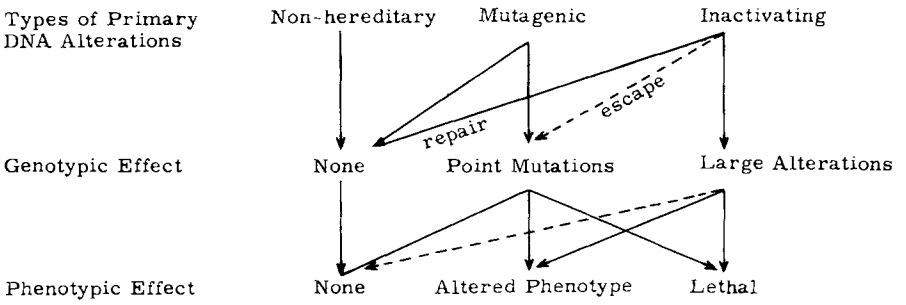


Fig. 12. Primary DNA alterations and their genotypic and phenotypic effects.

The biological effect of these agents on DNA can be measured directly by the inactivation of transforming DNA (Fig. 10a) and by the rate at which (point) mutations are induced (Fig. 10b). More specifically, one can distinguish between "mutagenic" and "inactivating" DNA alterations by measuring the frequency of linked mutations per lethal hit [19]. This is illustrated in Fig. 11: "Mutagenic DNA alterations," induced, *e.g.* by 1 M hydroxylamine, produce point mutations, as indicated by fluorescent colonies in this test; these DNA alterations do not prevent DNA duplication and therefore cannot induce chromosome breaks. In contrast, inactivating DNA alterations, induced *e.g.* by H_2O_2, inactivate transforming DNA, as measured by the number of lethal hits [equal to $-\ln$ (surviving fraction)], but they induce hardly any point mutations; these DNA alterations apparently prevent normal DNA duplication.

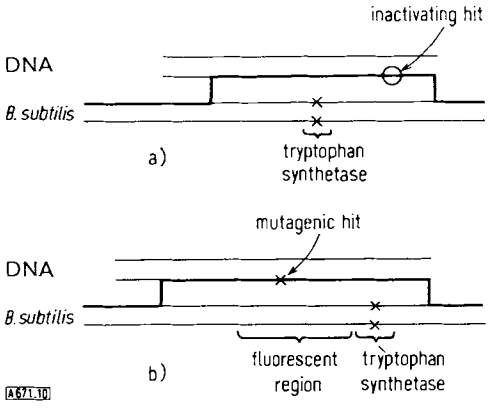


Fig. 10. Measurement of "inactivating" and "mutagenic" DNA alterations in transforming DNA of *B. subtilis*. a) Inactivation caused by an alteration of the gene for tryptophan synthetase. b) Mutation caused by a mutagenic alteration of the DNA region that is linked to the tryptophan synthetase gene and whose functional inactivity causes fluorescent colonies, if the plates contain only suboptimal (derepressing) amounts of indole.

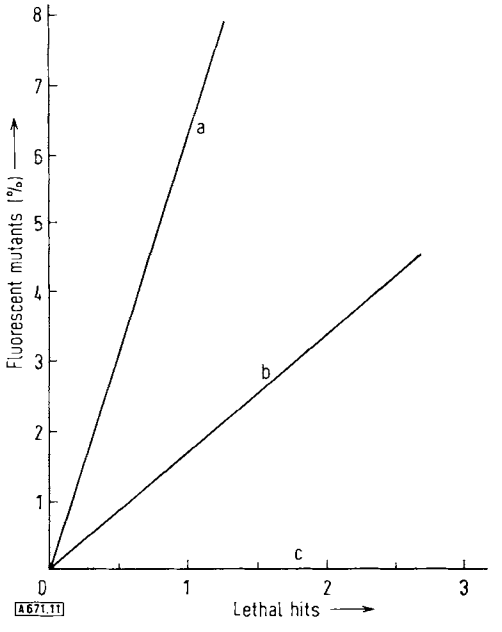


Fig. 11. Measurement of point mutagenic *versus* inactivating effect of different chemicals on transforming DNA. The mutagenic effect is determined by the frequency of fluorescent colonies, whereas lethal hits are equal to $-\ln$ survival of the tryptophan marker.

a) 1 M hydroxylamine in 0.05 M pyrophosphate, pH = 7.5, 70 °C. b) 0.1 M nitrous acid, pH = 4.2, 37 °C. c) 0.01 M hydroxylamine or 0.001 M H_2O_2 or 0.001 M disuccinyl proxide or pH = 4.2 alone or UV radiation.

Fig. 12 summarizes the possible genotypic and phenotypic effects of different primary DNA alterations. Some alterationhave no effect, either because they do not affect DNA replis cation (*e.g.* methylation) or because they are repaired. The different types (of inactivating DNA alterations are summarized in Fig. 13 for a review, see ref. [19]). The relative frequency with which the different possible genotypic or phenotypic effects are produced depends on the type of the primary DNA alteration and on the organism,

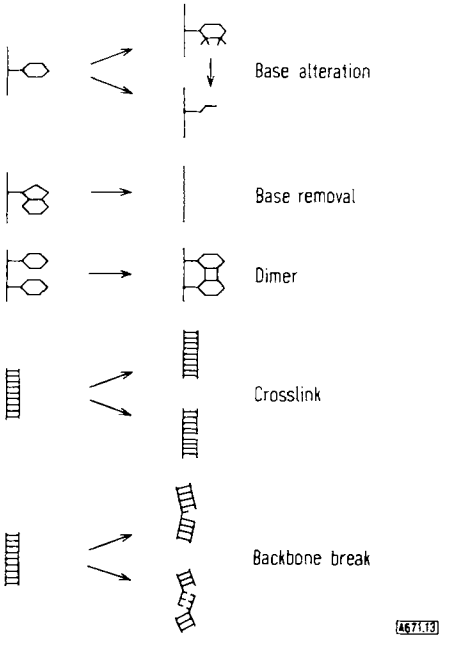


Fig. 13. Types of inactivating DNA alterations.

X-rays were the first agents for which the induction of mutations and chromosome breaks was proved by *Muller* [3]; X-rays also inactivate transforming DNA [46]. All these effects are greatly increased in the presence of oxygen [47] (for a review, see ref. [45]), hence DNA is altered not only directly by ionizing hits but also indirectly by oxidizing radicals. Many other radical-producing agents, *e.g.* peroxides and nitroso compounds and autooxidizable substances such as hydroxylamines, hydrazines, and phenols, are now known to induce chromosome breaks and to inactivate DNA (for a review, see ref. [19]).

[46] *R. M. Drew*, Radiation Res. *3*, 116 (1955).

[47] *J. M. Thoday* and *J. Read*, Nature (London) *160*, 608 (1947).

The chemical reactions of OH radicals with DNA and its components have been examined most extensively. OH radicals saturate the double bonds between C-5 and C-6 of pyrimidines [48,49] (see Fig. 14). Less frequently OH radicals remove all four bases from DNA and thus cause the back-

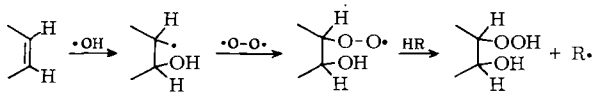


Fig. 14. Opening of 5,6 double bond of pyrimidines by OH radicals. The hydroxy-hydroperoxy-pyrimidine is relatively stable for thymine and reacts further for cytosine.

bone breakage of the sugar phosphate bonds by β-elimination, as has been analyzed by the use of oligodeoxyadenylic acid [50] (see Fig. 15). All of the above radical reactions represent inactivating DNA alterations, because the point mutagenic effect of radicals is negligible.

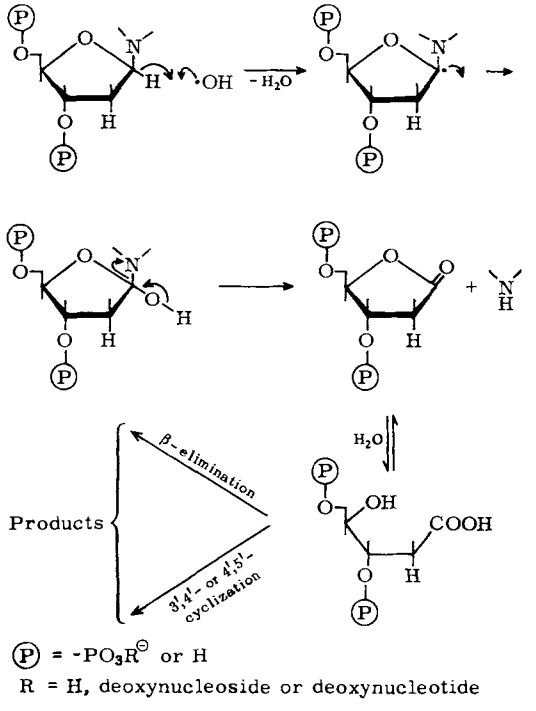


Fig. 15. Mechanisms of DNA backbone breakage by OH radicals.

Another important class of chromosome breaking agents consists of the alkylating agents of which nitrogen mustard was first discovered to induce mutations by *Auerbach* and *Robson* [52]. Other well known alkylating agents are alkylsulfates, epoxides, ethyleneimines, lactones, and diazo compounds, which are liberated at alkaline pH by *N*-alkylnitroso compounds (for review, see ref. [45]). They have in common the tendency to attack nucleophilic groups.

Brookes and *Lawley* [15] have shown, *e.g.*, that alkyl sulfates react with guanine, adenine, and cytosine, preferentially alkylating the N-7 position of guanine. When the ethylation of DNA is immediately followed by DNA duplication, many point mutations arise, apparently by base pairing mistakes of the alkylated guanine (see Fig. 6). But the alkylated guanine bases soon separate from DNA, leading to inactivating DNA alterations and backbone breaks whose number increases with the time of incubation after DNA treatment [14,16,17]. In addition to the bases, the phosphates are also alkylated with the same frequency and the intermediate triesters are occasionally hydrolyzed by the splitting of the sugar phosphate backbone [51,53].

The removal of purines, which can also be accomplished by exposure to low pH or to high temperatures, occasionally produces crosslinks in double stranded DNA (see Fig. 13). Such crosslinks within and between DNA double helices can also be produced by UV light, nitrous acid, and, in especially high frequency, by bifunctional alkylating agents (see refs. [19,45]).

Many of the above agents which induce inactivating DNA alterations cause chromosome aberrations and breakage [45]. They also induce mutations that result from large chromosome alterations, as has been shown by special genetic methods [54].

Some agents seemingly are exceptions to this correlation between chromosome breaking agents and inactivating alterations of DNA. This discrepancy results either from activating or from protective mechanisms of the cell, as will be illustrated by a few examples.

Certain carbamates produce chromosome breaks, as *Oehlkers* [55] has discovered for urethan, whereas they do not inactivate transforming DNA [56]. But they can be *N*-hydroxylated by enzymes present in many organisms [57], and the *N*-hydroxycarbamates do indeed inactivate DNA [58,59], and induce chromosome breaks [60]. Carbamates seem to undergo, therefore, a series of reactions in the cell, which eventually produce radicals which react with DNA. Aromatic amines behave similarly.

Ascorbic acid or H_2O_2 rapidly inactivate DNA [61,62], but they usually do not induce chromosome breaks [63,64]. They are, however, natural metabolites or nutrients which are utilized by enzymes inside the cell; *e.g.* H_2O_2 is rapidly broken down by catalase or peroxidase. Such compounds presumably do not often get close enough to the chromosomes, which are much of the time protected by the nuclear membrane, but they can become effective if the cellular metabolism is altered. For example, H_2O_2 induces chromosome breaks in certain tissue cultures in which the concentration of catalase is greatly reduced [63].

[48] *J. Weiss*: Les Peroxydes Organique en Radiobiologie. Masson, Paris 1958.

[49] *R. Latarjet, B. Ekert*, and *D. Demerseman*, Radiation Res. (Suppl.) *3*, 247 (1963).

[50] *H. J. Rhaese* and *E. Freese*, Biochim. biophysica Acta *155*, 476 (1968).

[51] *H. J. Rhaese* and *E. Freese*, in preparation.

[52] *C. Auerbach* and *J. M. Robson*, Nature (London) *157*, 302 (1946).

[53] *P. Alexander* and *K. A. Stacey*, Ann. New York Acad. Sci. *68*, 1225 (1958).

[54] *B. B. Webber* and *F. J. De Serres*, Proc. nat. Acad. Sci. USA *53*, 430 (1965).

[55] *F. Oehlkers*, Z. Vererb.-Lehre *81*, 313 (1943).

[56] *E. B. Freese*, Genetics *51*, 953 (1965).

[57] *E. Boyland* and *R. Nery*, Biochem. J. *94*, 198 (1965).

[58] *E. B. Freese, J. Gerson, H. J. Rhaese*, and *E. Freese*, Mutation Res. *4*, 517 (1967).

[59] *R. De Giovanni-Donnelly, S. M. Kolbye*, and *J. A. Dipaolo*, Mutation Res. *4*, 543 (1967).

[60] *E. Borenfreund, M. Krim*, and *A. Bendlich*, J. nat. Cancer Inst. *32*, 667 (1964).

[61] *A. Zamenhof, H. E. Alexander*, and *G. Leidy*, J. exp. Medicine *98*, 373 (1953).

[62] *K. Berneis*, Helv. chim. Acta *46*, 57 (1963).

[63] *J. Schöneich*, Mutation Res. *4*, 385 (1967).

[64] *R. F. J. Whithers* in *Z. Landa*: Mechanism of Mutation and Inducing Factors. Academia, Praha 1966, p. 359.

Other protective mechanisms are represented in Fig. 16.

Structural:	Cell membrane, only certain molecules can enter
	Nuclear membrane, protects during DNA replication
	Condensation of DNA into chromosomes, avoids tearing of DNA during segregation
	Precision of chromosomal segregation
Enzymic:	Destruction of dangerous chemicals
	Specificity of nucleotide kinases and replicases, avoids incorporation of wrong nucleotides
	Excision of wrong bases + repair
	Repair of single strand lesions by copying of complementary strand and sealing of gap
	Repair of double strand breaks by stickiness and joining of broken ends
	Maintenance of pH, ion concentration, *etc.*

Fig. 16. Cellular protection against DNA alterations.

Particularly interesting is the ability of certain enzymes to repair damaged DNA. The first molecular explanation of this phenomenon has been obtained both by *Setlov* and *Carrier* [65] and by *Boyce* and *Howard-Flanders* [66]. They discovered that thymine dimers, produced in one DNA strand by ultraviolet irradiation, can be excised and the excised region can be repaired; the repair apparently involves copying the information of the unexcised complementary strand [67]. In the meantime, it has become clear that other DNA lesions, *e.g.* a cut induced by alkylating agents, can also be repaired. Some of the repair enzymes are also used in recombination [68] and probably in normal DNA replication in which the gaps of randomly produced swivel points have to be closed.

In addition to agents which chemically alter DNA and thereby prevent its normal duplication, several nucleosides which inhibit DNA synthesis also induce large chromosomal alterations. They are, *e.g.* cytosine-arabinoside, 5-fluorodeoxyuridine, and adenosine deoxyriboside [45].

Fig. 17 finally gives a brief summary of different general causes of mutations.

Physical:	Mechanical tearing apart of DNA
	Cutting by ionizing radiation or ^{32}P decay
	Non-disjunction of chromosomes
Chemical:	Alteration or removal of DNA bases
	Incorporation of altered bases
	Intercalation of oligocyclic aromatic compounds
	Alteration of DNA backbone
Enzymic:	Production of chemicals affecting DNA
	Mistakes of the DNA replicating system
	Alteration of the DNA replicating system
	Mistakes in recombination

Fig. 17. Causes of mutations.

4. Recombination

When two genetic markers are distantly located on homologous chromosomes, recombination between them appears to involve one reciprocal exchange between the two chromosomes. However, by using closely linked genetic markers, one finds that recombination involves several nonreciprocal recombinational acts within a region of "intimate" or "effective" pairing [69, 70].

The events taking place at the molecular level remained obscure until *Meselson* [71] showed in bacteriophage λ that recombination involves the breakage and rejoining of DNA double strands. This process apparently requires several enzymes that can break, chew away, and repair single DNA strands, because *Clark* and *Margulies* [72] have found several types of mutants that are unable to undergo recombination.

The recombination process occurs usually between homologous portions of DNA, requiring the specific pairing of an extended DNA region. The nonreciprocality of recombination in small dimensions may therefore involve a cut of DNA on the left side of the pairing region for one chromosome and on the right side for the other chromosome, followed by excision of part of the DNA and repair along the pairing partner. But the details of this process are still unclear.

Recombination does not only occur spontaneously, but its frequency can be increased by several agents, all of which induce inactivating DNA alterations. It can also occur between non-homologous chromosomes, when the end of a broken chromosome pairs with that of another chromosome. Again, the molecular events accompanying this repair are unknown.

Recombination is involved even in the production of spontaneous mutations. The frequency of mutations of the deletion type greatly increases in the chromosome area in which recombination occurs [73]. The induction of deletions or insertions by proflavine also occurs especially frequently in recombining organisms such as bacteriophages. These mutations may arise by mistakes in the repair processes which accompany recombination. Consequently, a distinction between mutation and recombination is sometimes hard to make for small dimensions of DNA.

5. Applications

New mutagenic agents have been beneficial to mankind in various ways. They have been employed in the fermentation industry to isolate more efficiently fermenting strains [74]. This approach could be greatly extended by the use of multiple and regulatory mutants, to obtain strains which accumulate just about

[65] *R. B. Setlow* and *W. L. Carrier*, Proc. nat. Acad. Sci. USA *51*, 226 (1964).

[66] *R. P. Boyce* and *P. Howard-Flanders*, Proc. nat. Acad. Sci. USA *51*, 293 (1964).

[67] *E. B. Freese* and *E. Freese*, Genetics *54*, 1056 (1966).

[68] *P. Howard-Flanders* and *R. P. Boyce*, Radiation Res. (Suppl.) *6*, 156 (1966).

[69] *E. Freese*, Z. Vererb.-Lehre *88*, 388 (1957).

[70] *R. M. Pritchard*, Genet. Res. *1*, 1 (1960).

[71] *M. Meselson*, J. Molecular Biol. *9*, 734 (1964).

[72] *A. J. Clark* and *A. D. Margulies*, Proc. nat. Acad. Sci. USA *53*, 451 (1965).

[73] *G. E. Magni*, J. cellular. comparat. Physiol. *64*, Suppl. *1*, 1965 (1964).

[74] *H. J. Peppler*: Microbial Technology. Reinhold, New York 1967.

any desirable metabolite or enzyme. In agriculture, new types of wheat have been isolated, by mutagenic treatment with alkylating agents [75], but so far most new strains of plants or animals are still produced by the classical method of breeding.

Several findings have been employed in medicine. For example iododeoxyuridine is successfully employed against Herpes simplex in the eye. Neoplastic diseases are treated by cytosine arabinoside, fluorodeoxyuridine, hydroxyurea, methotrexate, or other agents which inhibit DNA synthesis; or they are exposed to agents inactivating DNA, such as alkylating agents or methylhydrazine [76].

But we have also learned to be more careful with many compounds in our environment. Certain dyes were readily discovered as carcinogens. The chromosome breaking and carcinogenic effects of X-rays, other ionizing radiations, and radioactive particles are now widely recognized and protective measures have been taken. A similar educational and legislative effort will have to be undertaken before all people will be satisfactorily protected against mutagenic chemicals.

Knowing the chemical and biological action of certain compounds, we can now predict which other chemicals, containing the same reactive groups, are potentially harmful to DNA and chromosomes. For example, all hydrazines are potentially hazardous; they are especially dangerous when they carry lipophilic groups enabling them to enter cells. Such agents are still used as antidepressants [77], all of which inactivate DNA [78], and they apparently are employed as rocket fuels [79]. Also, many carbamates are used as pharmaceutica, herbicides, insecticides, and in varnishes; some of them can probably be converted into chromosome-breaking *N*-hydroxycarbamates by the same or similar enzymes that convert urethan to *N*-hydroxyurethan. Several carbamate herbicides are known to induce chromosome breaks in plants [80]. We cannot be sure which of these compounds are activated or inactivated by enzymes in humans. It is even possible that different humans differ in this respect. However, we should not wait for decades of statistical evaluation, but start now to reduce our exposure to potential mutagens, until they have been proved harmless. If the possibility of cancer does not seem threatening enough to everyone, young people at least owe this precaution to their future children, who should not be doomed to miserable lives, caused by new hereditary defects.

Received: July 22, 1968 [A 671 IE]
German version: Angew. Chem. *81*, 1 (1969)

[75] *Å. Gustafsson* in *S. J. Geerts*: Genetics Today. Pergamon, Oxford 1965, p. 307.

[76] *P. Calabresi* and *A. D. Welch* in *L. S. Goodman* and *A. Gilman*: The Pharmacological Basis of Therapeutics. Macmillan, New York 1966, p. 1345.

[77] *M. E. Jarvik*, see [76], p. 159.

[78] *E. Freese, S. Sklarow*, and *E. B. Freese*, Mutation Res. *5*, 343 (1968).

[79] *S. A. Greene*, US-Pat. 3117415 (1964).

[80] *L. J. Audus*: The Physiology and Biochemistry of Herbicides. Academic Press, London 1964.

New Methods of Preparative Organic Chemistry [**]

Reactions of Isocyanide Dihalides and their Derivatives

By E. Kühle
in collaboration with B. Anders, E. Klauke, H. Tarnow, and G. Zumach[*]

The readily obtainable isocyanide dichlorides can be used as starting materials for the preparation of many types of substances. Exchange reactions yield numerous derivatives of formic and carbonic acids, while heterocyclic products have been obtained by reaction with bifunctional partners. The present article deals not only with reactions that are known from the literature but also with the author's own work, some of which has not been published before.

1. Introduction

In our review of "Syntheses of Isocyanide Dihalides" [1] [***], we mentioned the relationship of these compounds to isocyanates, isothiocyanates, and carbodiimides, as well as to phosgene and thiophosgene. This relationship makes it easy to understand the reactions of the isocyanide dichlorides.

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509 Leverkusen (Germany)

[**] Earlier articles in this series have been published in five volumes by Verlag Chemie, Weinheim/Bergstr. An English edition has also been published.

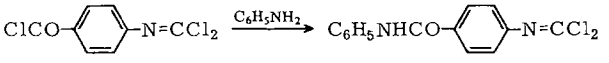
[***] The isocyanide dichlorides should, strictly speaking, be named as imidoyl chlorides, *i.e.* as *N*-substituted chloroformimidoyl chlorides.

[1] *E. Kühle, B. Anders*, and *G. Zumach*, Angew. Chem. *79*, 663 (1967); Angew. Chem. internat. Edit. *6*, 649 (1967).

The reactivities of isocyanide dichlorides increase from the alkyl and cycloalkyl, through the aryl, to the acyl isocyanide dichlorides. Whereas many reactions of the aliphatic and aromatic members can be carried out in aqueous media, the acyl isocyanide dichlorides are readily hydrolyzed, and their reactions must therefore be carried out in non-aqueous media.

The alkyl and aryl isocyanide dichlorides react less readily than acyl chlorides, whereas acyl isocyanide dichlorides react at least as readily. α-Chlorinated aliphatic isocyanide dichlorides form a special case, since their α-chloro atom generally reacts first in nucleophilic substitutions [2].

We have studied the difference in the behavior of acyl chlorides and isocyanide dichlorides, using derivatives that also contain a chlorocarbonyl grouping. For example, 4-chlorocarbonylphenyl isocyanide dichloride (4-dichloromethyleneaminobenzoyl chloride) *(1)* reacts with aniline to form the substitution product *(2)*.



(1) *(2)*

(2) m.p. = 187 °C

In the aliphatic series, *Reusche* [3] showed that the reaction of chlorocarbonyl isocyanide dichloride *(3)* with an equimolar quantity of ethanol leads selectively to ethoxycarbonyl isocyanide dichloride *(4)*.

$$\underset{(3)}{ClCO{-}N{=}CCl_2} \xrightarrow{C_2H_5OH} \underset{(4)\ \text{b.p.} = 68\,^\circ\text{C}/20\ \text{torr}}{H_5C_2OCO{-}N{=}CCl_2}$$

According to *Oertel* [4], *(3)* reacts with epoxides in the presence of a catalytic quantity of aluminum chloride to form β-chloroethoxycarbonyl isocyanide dichlorides, *e.g. (5)* in the case of ethylene oxide.

$$\underset{(3)}{} \xrightarrow[AlCl_3]{\text{ethylene oxide}} \underset{(5)}{ClCH_2CH_2O{-}CO{-}N{=}CCl_2}$$

Cyanogen chloride can be split off from many isocyanide dichlorides; this tendency is particularly strong in chlorosulfenyl isocyanide dichloride (thiocyanogen trichloride) [5], which reacts as sulfur dichloride in many reactions.

Apart from a few reactions of isocyanide difluorides, the following discussion will be confined to reactions of isocyanide dichlorides; the isocyanide dibromides, which are more difficult to obtain, and of which only a few have been described in the literature, will be ignored.

[2] *H. Holtschmidt*, Angew. Chem. *74*, 848 (1962); Angew. Chem. internat. Edit. *1*, 633 (1962).

[3] *W. Reusche*, unpublished.

[4] *G. Oertel*, DAS 1249515 (Nov. 24, 1964), Farbenfabriken Bayer AG.

[5] *R. G. R. Beacon* and *R. S. Irwin*, J. chem. Soc. (London) *1960*, 5079.

If one of the geminal chlorine atoms in an isocyanide dichloride is replaced by another group, the reactivity of the remaining chlorine atom generally decreases. This difference in the reactivity of the two chlorine atoms can be used for selective substitutions.

2. Replacement of the Two Chlorine Atoms by Oxygen, Sulfur, or Imino Groups, and Isocyanide Formation

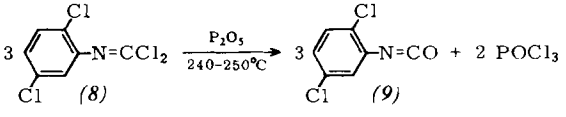
2.1. Isocyanates

The conversion of an isocyanide dichloride into an isocyanate has been studied by *Sell* and *Zierold* [6] with phenyl isocyanide dichloride *(6)*, which reacts exothermally with silver oxide to form phenyl isocyanate *(7)*.

$$\underset{(6)}{C_6H_5{-}N{=}CCl_2} \xrightarrow{Ag_2O} \underset{(7)}{C_6H_5{-}N{=}C{=}O}$$

In our attempts to convert isocyanide dichlorides into isocyanates, we also used the isocyanide dichloride as an acylating agent and allowed it to react with an acid anhydride. In addition to acyl chlorides, this reaction leads in principle to isocyanates; however, the yields are unsatisfactory (mostly because of secondary reactions).

After heating 2,5-dichlorophenyl isocyanide dichloride *(8)* with phosphorus pentoxide at 240–250 °C, we were able to distil off dichlorophenyl isocyanate *(9)* in a 55% yield.



(8) *(9)*

Arlt [7] recently discovered a very simple and very productive method for the preparation of isocyanates, in which isocyanide dichlorides are treated at room temperature with very strong acids, such as chlorosulfuric or dichlorophosphoric acid, and subsequently distilled. Aliphatic and aromatic isocyanates are readily obtainable by this method.

$$R{-}N{=}CCl_2 + HOSO_2Cl \xrightarrow[-HCl]{} [R{-}N{=}CCl{-}OSO_2Cl] \xrightarrow[-SO_2Cl_2]{} RN{=}C{=}O$$

Mukaiyama et al. [8] utilized the ease of dehydration of benzaldoxime *(10)* to convert phenyl isocyanide dichloride *(6)* into phenyl isocyanate *(7)*.

$$\underset{(6)}{C_6H_5{-}N{=}CCl_2} + \underset{(10)}{C_6H_5{-}CH{=}NOH} \rightarrow \underset{(7)}{C_6H_5{-}N{=}C{=}O} + C_6H_5CN + 2\,HCl$$

Kirsanov et al. [9] obtained a phosphorylated isocyanate *(12)* by reaction of a dialkyloxyphosphoryl isocyanide dichloride *(11)* with anhydrous formic acid. This method has the advantage that all by-products are gaseous.

[6] *E. Sell* and *G. Zierold*, Ber. dtsch. chem. Ges. *7*, 1228 (1874).

[7] *D. Arlt*, German Pat. Appl. F 52867 IVb/12 o (July 6, 1967), Farbenfabriken Bayer AG.

[8] *T. Mukaiyama et al.*, Bull. chem. Soc. Japan *35*, 1104 (1962).

[9] *A. V. Kirsanov*, *G. I. Derkač*, and *N. I. Liptuga*, Ž. obšč. Chim. *34*, 2812 (1964).

$$(AlkO)_2P(O)-N=CCl_2 \xrightarrow{HCOOH} (AlkO)_2P(O)-N=C=O + CO + 2\,HCl$$
(11) *(12)*

The reaction of phenyl isocyanide dichloride *(6)* with ethanol, in which hydrogen chloride and chloroethane are split off to form *N*-phenylethylurethane *(13)*, was also reported by *Sell* and *Zierold*[6].

$$C_6H_5-N=CCl_2 \xrightarrow[-HCl\ -C_2H_5Cl]{C_2H_5OH} C_6H_5-NH-COOC_2H_5$$
(6) *(13)*

This reaction probably proceeds *via* ethyl *N*-phenylchloroformimidate, which readily loses chloroethane, the loss being catalyzed by hydrogen chloride[8,10]. The resulting isocyanate then reacts with the excess of ethanol to form the urethane.

2.2. Isothiocyanates

Whereas nearly all isocyanates can be prepared by phosgenation of primary amines, there is no general synthesis for isothiocyanates, apart from the reaction of primary amines with the expensive thiophosgene. It is therefore fortunate that isothiocyanates can be obtained in good yields from isocyanide dichlorides by two mutually complementary methods.

Sell and *Zierold*[6] obtained phenyl isothiocyanate in quantitative yield by treatment of phenyl isocyanide dichloride with hydrogen sulfide at room temperature. According to *Petrov et al.*[11], however, this method cannot be used with aliphatic isocyanide dichlorides. We found that even in the case of phenyl isocyanide dichloride, the isothiocyanate is formed only at about 100 °C.

The action of sulfur on 4-chlorophenyl isocyanide dichloride at 250 °C leads to the elimination of sulfur dichloride and formation of 4-chlorophenyl isothiocyanate in moderate yield[12].

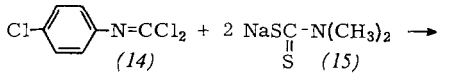
2.2.1. The Sodium Sulfide Method[13,14]

Aliphatic and aromatic isocyanide dichlorides react with sodium or ammonium sulfide in aqueous acetone to give high yields (>80 %) of the corresponding isothiocyanates:

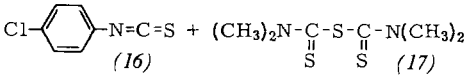
$$R-N=CCl_2 + Na_2S \rightarrow R-N=C=S + 2\,NaCl$$

This reaction can be used only for the preparation of isothiocyanates that do not react with water under the reaction conditions (20–50 °C). Thus the acylated isocyanide dichlorides derived from carboxylic acids, sulfonic acids, and phosphoric acids cannot be converted in this way into the reactive isothiocyanates. The method also fails with isocyanide dichlorides containing a functional group that reacts with water (*e.g.* COCl, NCO).

Isothiocyanates are sometimes also formed by the action of thiolates such as *(15)* on isocyanide dichlorides (cf. Section 4.3). Thus the reaction of 4-chlorophenyl isocyanide dichloride *(14)* and 2 moles of sodium dimethyldithiocarbamate *(15)* yields 4-chlorophenyl isothiocyanate *(16)* together with tetramethylthiuram monosulfide *(17)*.



(14) *(15)*



(16) *(17)*

Chloromethyl isocyanide dichloride *(18)* reacts similarly with 3 moles of *(15)* to give isothiocyanatomethyl dimethyldithiocarbamate *(19)* in a yield of more than 90% [15].

$$ClCH_2N=CCl_2 + 3\,(15) \rightarrow (CH_3)_2NCS-S-CH_2-N=C=S + (17)$$
(18) *(19)*

By the reaction of potassium *N*-*p*-toluenesulfonyldithiocarbonimidate with phenyl isocyanide dichloride, we obtained phenyl isothiocyanate and the first sulfonyl isothiocyanate. This reaction has been developed into a method for the preparation of sulfonyl isothiocyanates from *N*-sulfonyldithiocarbonimidates and phosgene[16].

2.2.2. The Phosphorus Pentasulfide Process[17]

By analogy with the reaction of isocyanide dichlorides and phosphorus pentoxide to form isocyanates (cf. Section 2.1), the isothiocyanates should be obtainable by reaction of isocyanide dichlorides with phosphorus pentasulfide. This reaction does in fact proceed in high yields when the reactants are heated in inert solvents (boiling toluene or chlorobenzene):

$$3\,R-N=CCl_2 + P_2S_5 \rightarrow 3\,R-N=C=S + 2\,PSCl_3$$

This process, which is carried out in anhydrous media, can be used even with readily hydrolyzable acyl isocyanide dichlorides (*e.g.* tetrameric cyanogen chloride) and aliphatic or aromatic isocyanide dichlorides containing a group that reacts with water (*e.g.* COCl or NCO) (yields >80 %).

Higher temperatures (*e.g.* boiling dichlorobenzene) are generally necessary for highly chlorinated groups R, and the method sometimes even fails.

1-Perchloronaphthyl isocyanide dichloride *(20)* reacts with excess phosphorus pentasulfide at 180 °C to form the isothiocyanate *(21)*. In this case the sodium sulfide method gives the naphthothiazole derivatives *(22)* and *(23)* [18].

[10] *F. Lengfeld* and *J. Stieglitz*, Amer. chem. J. *16*, 70 (1894).

[11] *K. A. Petrov* and *A. A. Nejmysheva*, Ž. obšč. Chim. *29*, 2165 (1959).

[12] With more highly chlorinated aromatic compounds, sulfur is incorporated in a cyclization reaction leading to 2-chlorobenzothiazoles (*E. Roos*, unpublished).

[13] *E. Kühle*, German Pat. 1167331 (Feb. 11, 1961), Farbenfabriken Bayer AG.

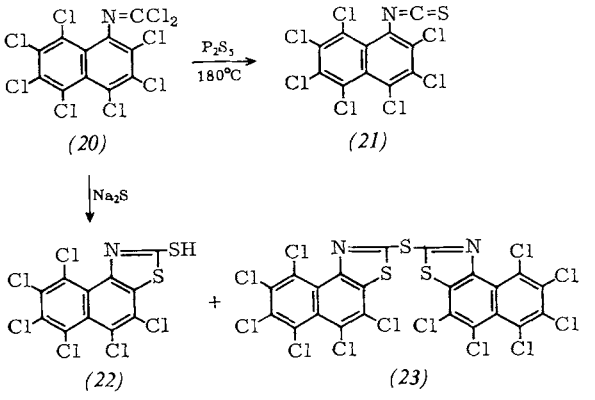
[14] *E. Kühle*, German Pat. 1192189 (Mar. 10, 1962), Farbenfabriken Bayer AG.

[15] This compound is effective as a leaf fungicide in plant protection (experiments by *F. Grewe*, Leverkusen).

[16] *K. Dickoré* and *E. Kühle*, Angew. Chem. *77*, 429 (1965); Angew. Chem. internat. Edit. *4*, 430 (1965).

[17] *E. Kühle* and *K. Sasse*, German Pat. 1174772 (July 20, 1962), Farbenfabriken Bayer AG.

[18] *G. Beck*, unpublished.



(20) (21) (22) (23)

(21) m.p. = 121–122 °C
(22) m.p. = 267–269 °C
(23) m.p. = 358–359 °C (decomp.)

2.3. Carbodiimides

The hydrochlorides of primary amines can be converted into carbodiimides by "iminophosgenation" The amines must be used in the form of these rather inert salts because the free bases react further with isocyanide dichlorides under these conditions, generally with direct formation of guanidines (cf. Section 4.1).

The synthesis of the carbodiimides proceeds as follows:

$$R{-}N{=}CCl_2 + H_2NR^1 \cdot HCl \xrightarrow[-3\ HCl]{} R{-}N{=}C{=}N{-}R^1$$

and is carried out between 170 and 180 °C (dichlorobenzene solution) in the case of alkyl or aryl isocyanide dichlorides[19]. Temperatures of 120–130 °C (chlorobenzene solution) are sufficient for sulfonyl isocyanide dichlorides[20].

Carbodiimides can also be obtained from isocyanide dichlorides *via* the chloroformamidines. For example, the reactions of *(6)* and *(14)* with 2 moles of *n*-propylamine at 20–30 °C lead directly to the carbodiimides *(24)* and *(25)*[20a].

$C_6H_5{-}N{=}C{=}N{-}C_3H_7$ *(24)* b.p. = 120–122 °C/11 torr
4-$ClC_6H_4{-}N{=}C{=}N{-}C_3H_7$ *(25)* b.p. = 98–102 °C/0.5 torr

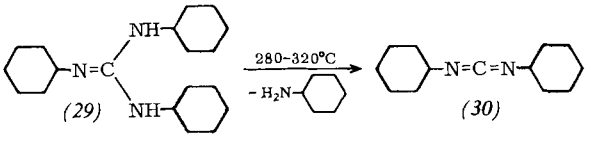
This reaction can also be carried out with acyl isocyanide dichlorides; however, the isocyanide dichlorides of carboxylic acids give the desired carbodiimides only with aliphatic amines in which the amino group is attached to a tertiary carbon atom[21]. 4-Chlorobenzoyl isocyanide dichloride reacts with *tert*-butylamine at room temperature in a molar ratio of 1:1 in the presence of triethylamine to give the stable *N*-(4-chlorobenzoyl)-*N'*-*tert*-butylcarbodiimide *(26)*.

4-$ClC_6H_4{-}CO{-}N{=}C{=}N{-}C(CH_3)_2$
(26) b.p. = 135–137 °C/0.05 torr

Derkač et al.[22] have obtained phosphorylated carbodiimides such as *(27)* and *(28)* from phosphorylated isocyanide dichlorides and anilines.

$(C_3H_7O)_2P(O){-}N{=}C{=}N{-}C_6H_5$ *(27)*
$(C_6H_5O)_2P(O){-}N{=}C{=}N{-}C_6H_4{-}Br(p)$ *(28)*

Carbodiimides can also be obtained from isocyanide dichlorides *via* guanidines. N^1,N^2,N^3-Tricyclohexylguanidine *(29)*, which can be obtained from cyclohexyl isocyanide dichloride and cyclohexylamine, loses one mole of cyclohexylamine at 280–320 °C to form dicyclohexylcarbodiimide *(30)*.



(29) (30)

2.4. Isocyanides

Traces of isocyanides can often be detected by their odor in nucleophilic exchange of isocyanide dichlorides; they are undoubtedly formed in side reactions in which the isocyanide dichlorides act as oxidizing agents. The formation of methyl isocyanide *(32)* was detected by *Petrov et al.*[11] in the reaction of methyl isocyanide dichloride *(31)* with iodide, the intermediate methyl isocyanide diiodide immediately decomposing into *(32)* and iodine.

$$\underset{(31)}{CH_3{-}N{=}CCl_2} \xrightarrow{HI} [CH_3N{=}CI_2] \rightarrow \underset{(32)}{CH_3{-}N{\equiv}C} + I_2$$

By analogy with the reaction of isothiocyanates with triethylphosphine[23], we were able to convert isocyanide dichlorides into isocyanides by treatment with trialkyl- or triarylphosphines at high temperatures[24]. For example *(6)* gives phenyl isocyanide *(33)* in this reaction.

$$\underset{(6)}{C_6H_5{-}C{=}NCl_2} + P(C_6H_5)_3 \xrightarrow[-Cl_2P(C_6H_5)_3]{60-100\,^\circ C} \underset{(33)}{C_6H_5N{\equiv}C}$$

Our observations so far indicate that this method is unsuccessful in the case of acyl isocyanide dichlorides.

3. Nucleophilic Substitution of a Chlorine Atom

3.1. Chloroformamidines

Chloroformamidines are readily obtained by reaction of isocyanide dichlorides with primary or secondary amines in a molar ratio of 1:1. Twice the required

[19] *E. Kühle*, German Pat. 1149712 (Nov. 14, 1961), Farbenfabriken Bayer AG.

[20] *B. Anders* and *E. Kühle*, Angew. Chem. *77*, 430 (1965); Angew. Chem. internat. Edit. *4*, 430 (1965); cf. also *R. Neidlein* and *E. Heukelbach*, Arch. Pharmaz. *299*, 944 (1966).

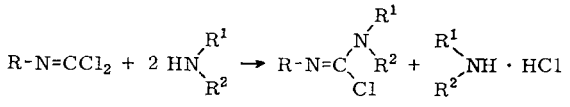
[20a] Cf. also *M. Seefelder* and *G. Neubauer*, German Pat. 1125914 (Sept. 14, 1960) Badische Anilin- und Soda-Fabrik.

[21] *P. Schnegg*, Dissertation, Universität München, 1965.

[22] *G. I. Derkač et al.*, Ž. obšč. Chim. *36*, 461 (1966).

[23] *A. W. Hofmann*, Ber. dtsch. chem. Ges. *3*, 766 (1870).

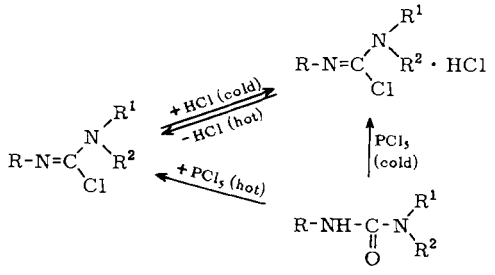
[24] *H. Malz* and *E. Kühle*, German Pat. 1158501 (May 23, 1962), Farbenfabriken Bayer AG.



quantity of amine should preferably be used, in order to bind the hydrogen chloride liberated [25].

Where the amine is expensive, a corresponding quantity of a tertiary amine may be used to bind the hydrogen chloride. The reaction, which occurs even at room temperature, proceeds only with strongly basic amines in the cases of aliphatic and aromatic isocyanide dichlorides. Higher temperatures must be used for aromatic amines; in addition to unreacted starting material, guanidines are obtained directly in this case by replacement of both chlorine atoms [6].

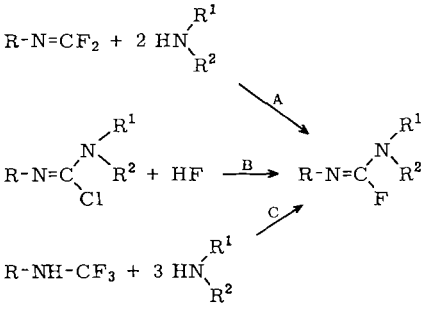
Most chloroformamidines add on hydrogen chloride in the cold to form salts, which readily lose hydrogen chloride again above their melting points.



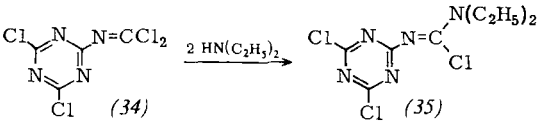
The chloroformamidinium chlorides ("urea dichlorides") are also formed in good yields on reaction of substituted ureas with phosphorus pentachloride in the cold [26], while at higher temperatures, simultaneous elimination of HCl leads directly to the free chloroformamidines [27].

The fluoroformamidines can be obtained in three ways [28]. As in the case of the isocyanide dichlorides, a fluorine atom in the isocyanide difluoride may be replaced by an amine residue (path A). Secondly, treatment of chloroformamidines with anhydrous hydrofluoric acid leads to chlorine-fluorine exchange and formation of fluoroformamidines (path B). Finally, the *N*-trifluoromethylamines, which are described in Section 6.1, can be converted into fluoroformamidines by reaction with 3 moles of an amine (path C).

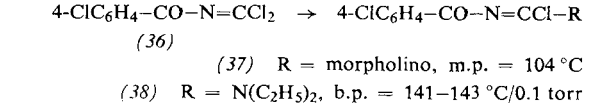
Acyl isocyanide dichlorides can also be converted selectively into acylated chloroformamidines by reaction with amines.



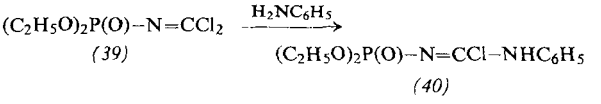
Thus "tetrameric cyanogen chloride" *(34)*, which may be formally regarded as an acyl isocyanide dichloride, reacts in good yields with primary and secondary amines even at −15 °C [29,30]. An example is the formation of N^1,N^1-diethyl-N^2-dichlorotriazinylchloroformamidine *(35)*.



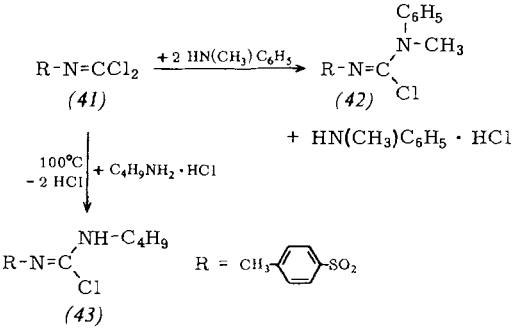
Acyl isocyanide dichlorides derived from carboxylic acids react in a similar manner with amines to form acylated chloroformamidines. For example, we have synthesized *(37)* and *(38)* in good yields from *(36)*.



In the phosphoryl isocyanide dichloride series, *Derkač et al.* [22] described the synthesis of the phosphorylated chloroformamidine *(40)* from diethoxyphosphoryl isocyanide dichloride *(39)* and aniline.



Finally, *Neidlein et al.* [31] converted sulfonyl isocyanide dichlorides, *e.g. (41)*, into sulfonated chloroformamidines, *e.g. (42)*, by reaction with 2 moles of a secondary aromatic amine.



Sulfonylated chloroformamidines such as *(43)* can also be obtained by heating sulfonyl isocyanide dichlorides with hydrochlorides of primary amines at 100 °C.

Only 2 moles of hydrogen chloride are liberated at this temperature the third mole being lost only at 120–130 °C to form a carbodiimide (cf. Section 2.3).

3.2. Esters of Chloroformimidic Acid

Lengfeld et al. [10] obtained ethyl *N*-phenylchloroformimidate *(44)* by reaction of phenyl isocyanide dichloride *(6)* with sodium ethoxide in a molar ratio of 1:1.

[25] *E. Kühle* and *L. Eue*, German Pat. 1211163 (May 16, 1959), Farbenfabriken Bayer AG.

[26] *R. Wegler, E. Kühle*, and *L. Eue*, German Pat. 1129161 (Jan. 19, 1960), Farbenfabriken Bayer AG.

[27] *D. L. Smathers*, US-Pat. 3084192 (Apr. 14, 1959), DuPont.

[28] *E. Kühle, E. Klauke*, and *L. Eue*, German Pat. 1153743 (Aug. 12, 1961), Farbenfabriken Bayer AG.

[29] Geigy AG, Belg. Pat. 604736 (June 7, 1961).

[30] *Y. Kodama, T. Sekiba*, and *M. Kato*, J. Soc. org. synth. Chem., Japan *22*, 749 (1964).

[31] *R. Neidlein* and *W. Haussmann*, Tetrahedron Letters *1966*, 2217.

$C_6H_5-N=CCl_2 + NaOC_2H_5 \rightarrow C_6H_5-N=CCl-OC_2H_5$
(6) (44)

This reaction can also be used with aliphatic isocyanide dichlorides; the compound *(45)*, for example, is obtained in this way.

$CH_3-(CH_2)_3-CH(C_2H_5)-CH_2-N=CCl-OCH_3$

(45) b.p. = 100–101 °C/11 torr

In the case of aryl isocyanide dichlorides we use an inert, water-immiscible solvent such as chlorobenzene and an aqueous-alcoholic alkali solution[32]. This modified procedure has the advantage that owing to the presence of two phases, the excess of water-soluble alcohol can no longer react with the chloroformimidate during subsequent treatment of the reaction mixture at high temperatures, but is removed beforehand by the aqueous phase.

The reaction of *(6)* with ethylene oxide in the presence of triethylamine at 95–100 °C leads, not to β-chloroethyl *N*-phenylchloroformimidate *(46)*, but by a Chapman rearrangement to the isomeric carbamoyl chloride *(47)*[33].

$C_6H_5-N=CCl_2$ (6) + H_2C-CH_2 (O)

$\xrightarrow{(C_2H_5)_3N}$ $C_6H_5-N=C(Cl)-OCH_2-CH_2Cl$ *(46)*

$\xrightarrow{\rho}$ $C_6H_5-N(CH_2-CH_2Cl)-COCl$ *(47)*

Phenols, like alcohols, also react in equimolar quantities with isocyanide dichlorides to give aryl chloroformimidates, *e.g. (48)*[34]. It has been found that the best results are obtained in this case with sodium phenoxides in a polar solvent such as dioxane.

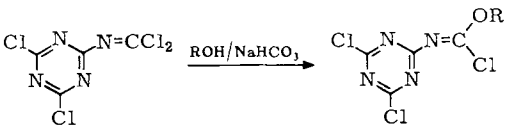
$C_6H_5-N=CCl_2$ (6) + 4-$ClC_6H_5ONa \rightarrow C_6H_5-N=CCl-OC_6H_4Cl(p)$ *(48)*

Though these compounds are sufficiently stable to be distilled, they sometimes undergo Chapman rearrangement at extreme temperatures. For example, phenyl *N*-phenylchloroformimidate *(49)* isomerizes at 330 °C to give diphenylcarbamoyl chloride *(50)*

$C_6H_5-N=CCl-OC_6H_5 \rightarrow (C_6H_5)_2N-COCl$

(49) b.p. = 170–180 °C/10 torr *(50)* m.p. = 82–84 °C

"Tetrameric cyanogen chloride" *(34)* has been converted into the *N*-(dichlorotriazinyl)chloroformimidates *(51)* and *(52)* by reaction with lower aliphatic alcohols in the presence of sodium hydrogen carbonate[35].



(34) *(51)*, R = CH_3; *(52)*, R = C_2H_5

Alimov et al.[36] obtained ethyl *N*-(diethoxyphosphoryl)-chloroformimidate *(53)* by reaction of diethoxyphosphoryl isocyanide dichloride *(39)* with ethanol in the presence of triethylamine.

$(C_2H_5O)_2P(O)-N=CCl_2$ (39) + $HOC_2H_5 \xrightarrow{(C_2H_5)_3N} (C_2H_5O)_2P(O)-N=CCl-OC_2H_5$ *(53)*

3.3. Thioesters of Chloroformimidic Acids

A few thio analogs of the chloroformimidates, such as *(54)*, have been described, and can be prepared *e.g.* from isocyanide dichlorides and thiolates[37].

4 $ClC_6H_4-N=CCl_2$ (14) + $NaS-C_6Cl_5 \xrightarrow[\text{acetone}]{} 4\text{-}ClC_6H_4-N=CCl-SC_6Cl_5$ *(54)*

This selective chlorine exchange does not always proceed in a uniform manner with acyl thiolates such as dithiocarbamates, xanthates, and dithiophosphates.

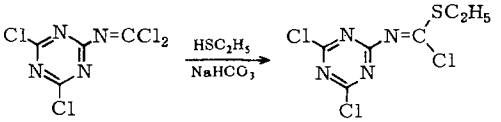
The best methods of obtaining thioesters of chloroformimidic acids are the addition of sulfenyl chlorides to isocyanides (path A) and the reaction of sulfenyl chlorides with monosubstituted formamides in the presence of thionyl chloride (path B)[38].

$R-N\equiv C + ClSR^1 \rightarrow RN=CCl-SR^1$ path A

$R-NH-CHO \xrightarrow[SOCl_2]{R^1SCl} RN=CCl-SR^1$ path B

The acyl isocyanide dichloride "tetrameric cyanogen chloride" *(34)* has been converted into the thioester *(55)* by reaction with alkanethiols in the presence of sodium hydrogen carbonate[39].

Alimov et al.[36, 40] have also obtained a phosphorylated thiochloroformimidate *(56)* by the reaction of di-



(34) *(55)*

[32] *E. Kühle*, German Pat. 1126380 (Oct. 14, 1960), Farbenfabriken Bayer AG.

[33] *V. S. Etlis, A. P. Sinekov*, and *M. E. Sergeva*, Ž. org. Chim. *2*, 1684 (1966).

[34] *A. Hantzsch* and *L. Mai*, Ber. dtsch. chem. Ges. *28*, 977 (1895).

[35] *Y. Kodama* and *T. Sekiba*, J. Soc. org. synth. Chem., Japan *21*, 788 (1963).

[36] *P. I. Alimov* and *L. N. Levkova*, Izvest. Akad. Nauk SSSR, Div. of Chem. Science *1964*, 1889.

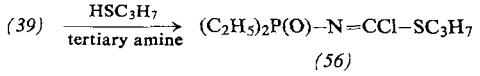
[37] *E. Enders, E. Kühle*, and *H. Malz*, German Pat. 1154089 (Nov. 10, 1960), Farbenfabriken Bayer AG.

[38] *E. Kühle*, Angew. Chem. *74*, 861 (1962); Angew. Chem. internat. Edit. *1*, 647 (1962).

[39] *Y. Kodama*, J. Soc. org. synth. Chem., Japan *23*, 57 (1965).

[40] *P. I. Alimov* and *L. N. Levkova*, Izvest. Akad. Nauk SSSR, Div. of Chem. Science *1965*, 1298.

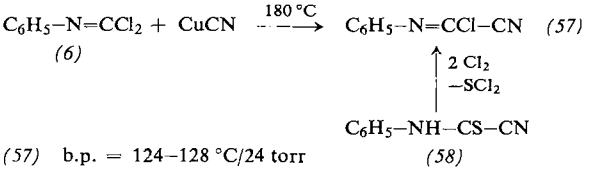
ethoxyphosphoryl isocyanide dichloride *(39)* with propanethiol in the presence of a tertiary amine.



(39) $\xrightarrow[\text{tertiary amine}]{HSC_3H_7}$ $(C_2H_5)_2P(O)-N=CCl-SC_3H_7$ *(56)*

3.4. Cyanoformimidoyl Chlorides

Isocyanide dichlorides and copper(I) cyanide react when heated in equimolar quantities in a high-boiling solvent such as dichlorobenzene to give cyanoformimidoyl chlorides such as *(57)* [41]. These compounds are also obtainable by chlorination of adducts such as *(58)* [42]



$C_6H_5-N=CCl_2$ + CuCN $\xrightarrow{180\,°C}$ $C_6H_5-N=CCl-CN$ *(57)*

(6)

$\uparrow$ 2 Cl_2, $-SCl_2$

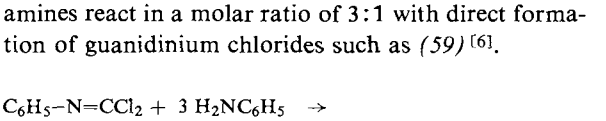
$C_6H_5-NH-CS-CN$

(57) b.p. = 124–128 °C/24 torr *(58)*

4. Nucleophilic Substitution of Both Chlorine Atoms by Similar Groups

4.1. Guanidines

Trisubstituted, tetrasubstituted, and pentasubstituted guanidines can be prepared from isocyanide dichlorides and amines. Isocyanide dichlorides and aromatic amines react in a molar ratio of 3:1 with direct formation of guanidinium chlorides such as *(59)* [6].



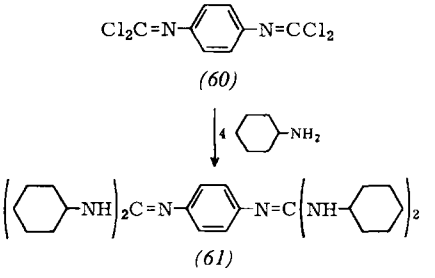
$C_6H_5-N=CCl_2$ + 3 $H_2NC_6H_5$ $\rightarrow$

(6) $C_6H_5-N=C(NHC_6H_5)_2 \cdot HCl$ + $C_6H_5NH_2 \cdot HCl$

(59)

This guanidine synthesis proceeds particularly smoothly and uniformly in aqueous alkaline media at or slightly above room temperature; the guanidines are then formed directly as the free bases [43].

Tetrasubstituted guanidines are better prepared from chloroformamidines (cf. Section 3.1), which can be converted specifically into unsymmetrically substituted guanidines with primary or secondary amines.



$Cl_2C=N-C_6H_4-N=CCl_2$

(60)

$\downarrow$ 4 $C_6H_5-NH_2$

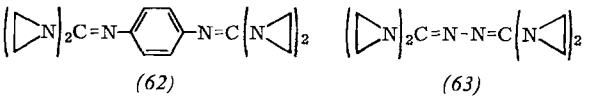
$(C_6H_5-NH)_2C=N-C_6H_4-N=C(NH-C_6H_5)_2$

(61)

(61) m.p. = 168–171 °C

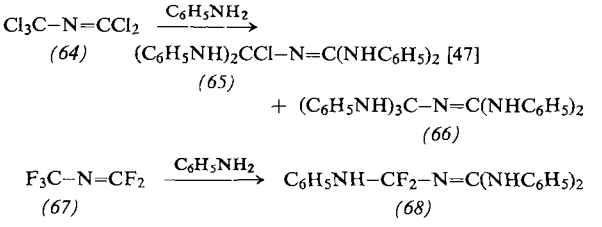
Diguanidines such as *(61)* can be obtained from bis-isocyanide dichlorides and 4 moles of an amine

Diguanidines based on ethyleneimine, *e.g. (62)* and *(63)*, have been synthesized by several research groups because of their possible action as cytostatic or chemical sterilizing agents [44, 45].



(62) *(63)*

Trichloromethyl isocyanide dichloride *(64)* and trifluoromethyl isocyanide difluoride *(67)* gave guanidine derivatives having additional amine functions in the molecule; the reactions with aniline yield the compounds *(65)* and *(66)* [11] or *(68)* respectively [46].



$Cl_3C-N=CCl_2$ $\xrightarrow{C_6H_5NH_2}$

(64) $(C_6H_5NH)_2CCl-N=C(NHC_6H_5)_2$ [47]

(65)

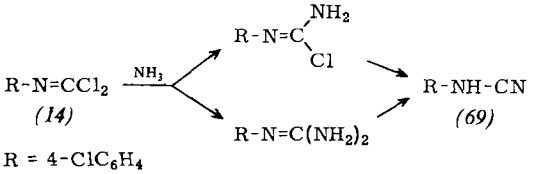
+ $(C_6H_5NH)_3C-N=C(NHC_6H_5)_2$

(66)

$F_3C-N=CF_2$ $\xrightarrow{C_6H_5NH_2}$ $C_6H_5NH-CF_2-N=C(NHC_6H_5)_2$

(67) *(68)*

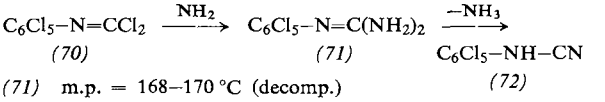
With ammonia as the amine component, the reaction of isocyanide dichlorides yields cyanamides, possibly *via* chloroformamidines or even guanidines. 4-Chlorophenyl cyanamide *(69)* is obtained in this way in a yield of more than 90 % from 4-chlorophenyl isocyanide dichloride *(14)* [48].



$R-N=CCl_2$ *(14)* $\xrightarrow{NH_3}$ $R-N=C(NH_2)Cl$ / $R-N=C(NH_2)_2$ $\rightarrow$ $R-NH-CN$ *(69)*

R = 4-ClC_6H_4

On reaction of pentachlorophenyl isocyanide dichloride *(70)* with ammonia, we were able to isolate the guanidine *(71)*; this product loses ammonia above its melting point to form the cyanamide *(72)*.



$C_6Cl_5-N=CCl_2$ $\xrightarrow{NH_3}$ $C_6Cl_5-N=C(NH_2)_2$ $\xrightarrow{-NH_3}$ $C_6Cl_5-NH-CN$

(70) *(71)* *(72)*

(71) m.p. = 168–170 °C (decomp.)

(72) m.p. = 280 °C

Acyl isocyanide dichlorides give acylated guanidines or cyanamides. Similarly, diaminoguanidines such as *(73)* and *(74)* are obtained from acyl isocyanide dichlorides and substituted hydrazines.

[41] *E. Kühle* and *B. Anders*, German Pat. 1224306 (June 18, 1965), Farbenfabriken Bayer AG.

[42] *E. Degener* and *H. Holtschmidt*, German Pat. 1224305 (April 14, 1965), Farbenfabriken Bayer AG.

[43] *B. Anders* and *E. Kühle*, German Pat. 1170931 (Sept. 14, 1962), Farbenfabriken Bayer AG.

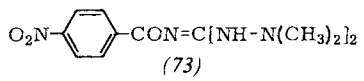
[44] *W. Gauss* and *E. Kühle*, Brit. Pat. 978089 (June 27, 1963), Farbenfabriken Bayer AG.

[45] *R. Neidlein* and *W. Haussmann*, Angew. Chem. *77*, 506 (1965); Angew. Chem. internat. Edit. *4*, 521 (1965).

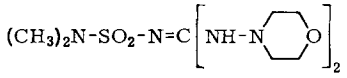
[46] *K. A. Petrov* and *A. A. Nejmysheva*, Ž. obšč. Chim. *29*, 2695 (1959).

[47] According to investigations by *H. Holtschmidt*, isomeric chloroformamidine derivatives are also formed.

[48] *E. Kühle* and *B. Anders*, DAS 1261498 (Aug. 31., 1964), Farbenfabriken Bayer AG.



(73)



(74)

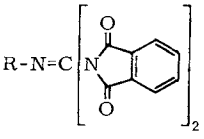
(73) m.p. = 147 °C; *(74)* m.p. = 205–208 °C

Diacylated and peracylated guanidine derivatives can also be obtained from isocyanide dichlorides. The reaction of isocyanide dichlorides such as *(75)* with sulfonamides, *e.g. (76)*, in a molar ratio of 1:2 in an inert solvent at 140–150 °C leads to loss of hydrogen chloride and direct formation of 1,3-disulfonylated guanidine *(77)*.

$$\underset{(75)}{C_4H_9N{=}CCl_2} + 2\,\underset{(76)}{H_2NSO_2{-}C_6H_4{-}CH_3(p)} \xrightarrow{-2\,HCl} C_4H_9{=}C[NHSO_2{-}C_6H_4{-}CH_2(p)]_2$$

(77) m.p. = 115–117 °C

The reaction of acylated isocyanide dichlorides with 2 moles of potassium phthalimide yields peracylated guanidines, such as *(78)* and *(79)*.



(78), R = CH_3SO_2- m.p.=210–214 °C

(79), R = $(C_2H_5O)_2\overset{\overset{O}{\|}}{P}$- m.p.=145–148 °C

4.2. Esters of Carbonimidic Acids

The action of sodium alkoxides or alcoholic alkali solution on isocyanide dichlorides leads to esters of carbonimidic acids, such as dimethyl *N*-phenylcarbonimidate *(80)* [49].

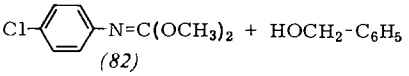
$$\underset{(6)}{C_6H_5{-}N{=}CCl_2} + 2\,NaOCH_3 \rightarrow \underset{(80)}{C_6H_5{-}N{=}C(OCH_3)_2}$$

With chloroformimidates (cf. Section 3.2) as starting materials, it is also possible in this way to obtain carbonimidates with different alkyl groups, *e.g. (81)*.

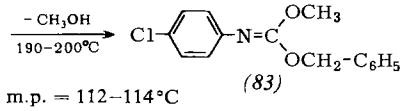
$$\underset{(44)}{C_6H_5{-}N{=}CCl{-}OC_2H_5} \xrightarrow{NaOCH_3} \underset{(81)}{C_6H_5{-}N{=}C(OCH_3){-}OC_2H_5}$$

b.p. = 120–123 °C/13 torr

Compounds of this type can sometimes also be obtained by partial transesterification of carbonimidates containing lower alkyl groups with a high-boiling alcohol at the boiling point. Thus, when heated in benzyl alcohol, the ester *(82)* loses methanol to form benzyl methyl *N*-(4-chlorophenyl)carbonimidate *(83)*.



(82)

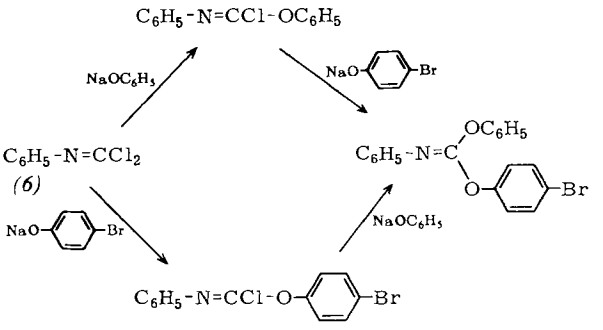


(83)

m.p. = 112–114 °C

[49] *W. R. Smith*, Amer. chem. J. *16*, 372 (1894).

In the series of diaryl esters, *Hantzsch et al.* [34] tried in the course of stereochemical studies to prepare unsymmetrically esterified carbonimidic acids. They found, however, that the compounds synthesized by two routes are identical.



According to *Dyson et al.* [50], phenyl isocyanide dichloride *(6)* also forms diaryl carbonimidates, *e.g. (84)*, when heated at 150 °C with free phenols.

$$\underset{(6)}{C_6H_5{-}N{=}CCl_2} \xrightarrow[-HCl]{HOC_6H_5} \underset{(84)}{C_6H_5{-}N{=}C(OC_6H_5)_2}$$

From a purely formal standpoint, the reactions of isocyanide dihalides with salts of acids in which an oxygen atom carries the negative charge should also be discussed here.

(a) Reaction with salts of phosphates [51].

$$R{-}N{=}CCl_2 + 2\,NaOP(O)(O\text{-}Alkyl)_2 \rightarrow R{-}N{=}C[OP(O)(OAlkyl)_2]_2$$

(b) Reaction with salts of sulfinic acids [52].

$$Br_2C{=}N{-}N{=}CBr_2 + 2\,C_6H_5{-}SO_2Na \xrightarrow{H_2O} (C_6H_5{-}SO_2)_2C{=}N{-}NH_2$$

4.3. Thioesters of Carbonimidic Acids

It was mentioned in Section 2.2.1 that isocyanide dichlorides react readily with thiolates to form isothiocyanates. The reaction of isocyanide dichlorides with 2 moles of a thiol or thiophenol, on the other hand, leads smoothly to thioesters of carbonimidic acids when carried out in strongly alkaline media, and particularly in aqueous alkali. The thioester *(85)*, for example, can be obtained in this way.

$$\underset{(6)}{C_6H_5{-}N{=}CCl_2} + 2\,HSC_4H_9 \xrightarrow{NaOH/H_2O} C_6H_5N{=}C(SC_4H_9)_2$$

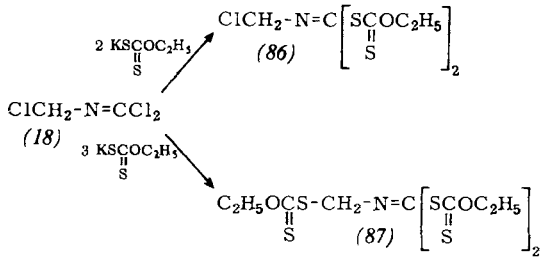
(85) b.p. = 205–210 °C/12 torr

Whereas the reaction of chloromethyl isocyanide dichloride *(18)* with 3 moles of sodium dimethyldithiocarbamate leads to the formation of tetramethylthiuram monosulfide *(17)* and the isothiocyanate *(19)* (cf. Section 2.2.1), *(18)* reacts

[50] *G. M. Dyson* and *T. Harrington*, J. chem. Soc. (London) *1942*, 150.

[51] Ihara Agriculture Chem. Comp., Jap. Pat. Appl. 24399/63 (Nov. 15, 1963).

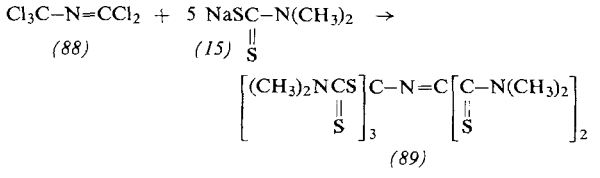
[52] *J. Diekmann*, J. org. Chemistry *28*, 2933 (1963).



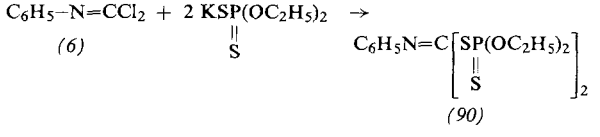
(86) b.p. = 100–103 °C (decomp.)/35 torr
(87) b.p. = 110 °C (decomp.)/10 torr

with 2 or 3 moles of potassium ethylxanthate to form the compounds *(86)* and *(87)* [53].

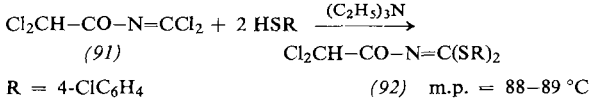
On reaction of trichloromethyl isocyanide dichloride *(88)* with 5 moles of sodium dimethyldithiocarbamate *(15)*, sulfur is eliminated with formation of the trisdithiocarbamate *(89)* [54].



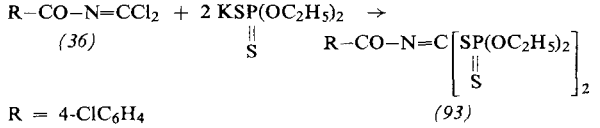
Aliphatic and aromatic isocyanide dichlorides, such as *(6)*, react with the salts of mono- or dithioesters of phosphoric acid to give bisthiophosphoryl compounds such as *(90)* [55, 56].



Thioesters of *N*-acylcarbonimidic acids, *e.g.* *(92)* have been synthesized by several research groups from acyl isocyanide dichlorides, *e.g.* *(91)*. The reactions generally proceed smoothly with thiols in the presence of a tertiary amine or with alkali metal thiolates. The same reaction occurs with sulfonyl and phosphoryl isocyanide dichlorides.



Triacylated esters such as *(93)* are obtained by reaction of acyl isocyanide dichlorides such as *(36)* with a mono- or dithiophosphate. The reaction products are mostly very viscous oils.



[53] *L. Eue, H. Hack, E. Kühle,* and *H. Holtschmidt,* German Pat. 1211164 (Feb. 5, 1964), Farbenfabriken Bayer AG.

[54] *E. Kühle, H. Holtschmidt, F. Grewe,* and *H. Kaspers,* Belg. Pat. 691561 (Dec. 23, 1965), Farbenfabriken Bayer AG.

[55] *H. Malz, E. Kühle,* and *O. Bayer,* German Pat. 1138389 (Oct. 17, 1959), Farbenfabriken Bayer AG.

[56] *H. Malz, H. Holtschmidt, E. Kühle,* and *O. Bayer,* German Pat. 1233852 (Jan. 26, 1962), Farbenfabriken Bayer AG.

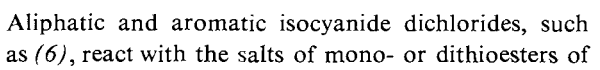
[57] *F. Sachs,* Ber. dtsch. chem. Ges. *33*, 959 (1900).

4.4. Imidomesoxalic Dinitriles

We have tried to use isocyanide dichlorides for the preparation of imidomesoxalic dinitriles, which can be obtained in special cases from aromatic nitroso compounds and malonic dinitrile [57]. Whereas the desired result could not be achieved by the action of alkali metal cyanides or hydrogen cyanide on isocyanide dichlorides, it was possible to react *e.g.* 4-chlorophenyl isocyanide dichloride *(14)* with copper(I) cyanide in a molar ratio of 1:2 at 150–180 °C. Instead of the expected 4-chloroimidomesoxalic dinitrile *(94)*, which is formed only in small quantities, the main product is a very stable, black copper complex, which we did not investigate further.

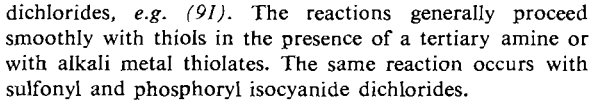
4-ClC_6H_4-N=$C(CN)_2$ *(94)* b.p. = 130–136 °C/11 torr, m.p. = 135–137 °C

Imidomesoxalic dinitriles such as *(95)* are obtained in moderate yields (up to about 30 %) from imidocyanoformyl chlorides (cf. Section 3.4) and copper cyanide.

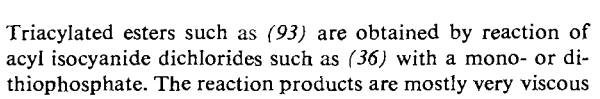


4.5. Carbonimidoylbisphosphonates

Isocyanide dichlorides react with trialkyl phosphites at room temperature in a sort of Arbusov reaction leading to elimination of chloroalkane and formation of carbonimidoylbisphosphonates such as *(96)* [55].



Chloromethyl isocyanide dichloride *(18)* reacts with 3 moles of triethylphosphite under the same conditions to form the triphosphonate *(97)* [56].

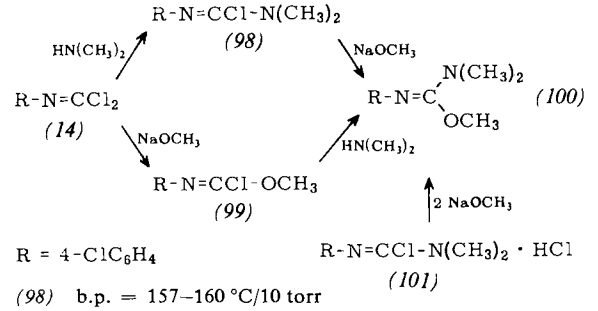


5. Replacement of the Chlorine Atoms by Two Different Nucleophilic Groups

The chloroformamidines (Section 3.1), chloroformimidates (Section 3.2), and thiochloroformimidates (Section 3.3) still contain one reactive chlorine atom, which can be replaced by any nucleophilic group. This route can be used for the preparation not only of the unsymmetrically substituted guanidines discussed in Section 4 but also of isoureas, isothioureas, and unsymmetrically substituted carbonimidates and thiocarbonimidates.

5.1. Isoureas

In contrast with the mono- and disubstituted isoureas, which can be prepared by the addition of alcohols to cyanamides and carbodiimides, the *N,N,N'*-trisubstituted isoureas are practically unobtainable except from isocyanide dichlorides. The isourea *(100)* may be obtained by reaction either of a chloroformamidine *(98)* with an alcohol or phenol, or of a chloroformimidate *(99)* with an amine.

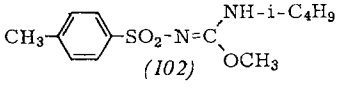


(98) b.p. = 157–160 °C/10 torr
(99) b.p. = 127–128 °C/11 torr
(100) b.p. = 147–149 °C/11 torr

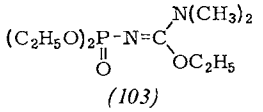
Neither method presents any difficulties, but using the chloroformimide method, we have carried out the reaction as a one-reactor process with aromatic isocyanide dichlorides. The isocyanide dichloride in an inert solvent was first allowed to react with aqueous-alcoholic sodium hydroxide solution, and the isourea was then obtained in good yields by reaction with amine [58, 59].

In a variant of this method, isoureas such as *(100)* are obtained by reaction of chloroformamidinium chlorides (obtainable from ureas and phosphorus pentachloride) such as *(101)* with 2 moles of sodium methoxide [60].

The *O*-arylisoureas are formed by the same principle [61]. In the case of acyl isocyanide dichlorides, the above reactions lead to *N*-acylated isoureas [examples: *(102)* and *(103)* [36]]. Both paths (*via* *N*-acylated chloroformamidines or *N*-acylchloroformimidates) are again possible.



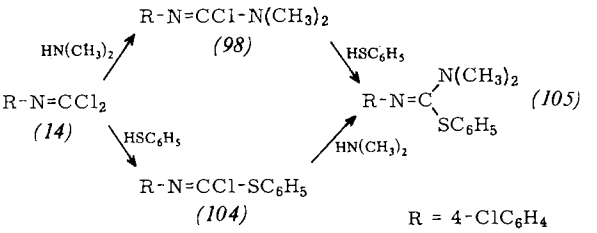
(102)



(103)

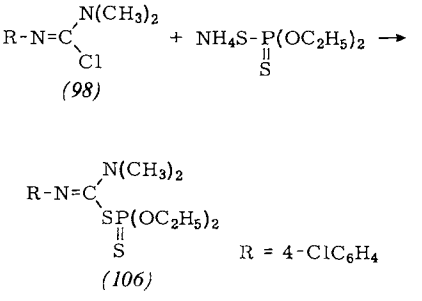
5.2. Isothioureas

Whereas *S*-alkylisothioureas in general can be prepared by alkylation of thioureas, *S*-arylisothioureas have so far been obtained only in special cases (by addition of thiophenols to cyanamide [62]). Isothioureas such as *(105)* can be readily prepared from isocyanide dichlorides *via* chloroformamidines (Section 3.1) or thiochloroformimidates (Section 3.3) in a process similar to the above isourea synthesis.



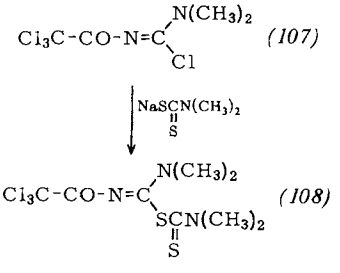
(104) b.p. = 167 °C/0.05 torr; m.p. = 66 °C
(105) m.p. = 57–59 °C

The reaction of chloroformamidines, *e.g.* *(98)*, with dithiophosphates yields *S*-phosphorylated isothioureas, *e.g.* *(106)* [55].



(106)

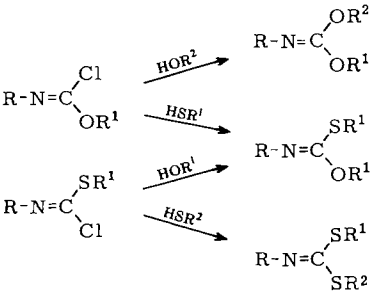
N^2-Trichloroacetyl-N^1,N^1-dimethylchloroformamidine *(107)* and sodium dimethyldithiocarbamate give the isothiourea *(108)*.



(108) m.p. = 102–105 °C

5.3. Carbonimidates and Thiocarbonimidates

The reactions of chloroformimidates (Section 3.2) or thiochloroformimidates (Section 3.3) with alcohols or thiols lead to esters and monothio- or dithioesters of the carbonimidic acid (cf. Sections 4.2 and 4.3).



[58] *E. Kühle* and *L. Eue*, German Pat. 1138039 (June 4, 1959), Farbenfabriken Bayer AG.

[59] The *O*-alkylisoureas are good alkylating agents, which react with urea formation even under mild conditions in the acidic and alkaline ranges.

[60] *E. Kühle* and *R. Wegler*, German Pat. 1219020 (Oct. 10, 1959), Farbenfabriken Bayer AG.

[61] *E. Kühle*, *L. Eue*, and *O. Bayer*, German Pat. 1137000 (Feb. 10, 1961), Farbenfabriken Bayer AG.

[62] *F. Arndt*, Liebigs Ann. Chem. *384*, 322 (1911).

Whereas isocyanates or isothiocyanates readily add on amines, alcohols, or thiols, isocyanide dihalides undergo nucleophilic substitution on reaction with these compounds (cf. Sections 3 to 5). The only compounds that have been successfully added to the N=C bond of isocyanide dihalides are hydrogen fluoride, some carbonyl fluorides, hydrazoic acid, diazomethane, and epoxides.

6.1. Addition of Hydrogen Fluoride

The most extensively studied of this group of additions is the addition of hydrogen fluoride to isocyanide dichlorides or difluorides. In the case of isocyanide dichlorides this reaction proceeds as an addition-elimination, in which hydrogen chloride is split off to form *N*-trifluoromethylamines. No intermediates containing chlorine could be isolated. Even when less than the theoretical quantity of hydrofluoric acid is used, the reaction yields only the trifluoromethylamine and unreacted starting material.

According to *Barr* and *Haszeldine*[63], the addition of hydrogen fluoride to trifluoromethyl isocyanide difluoride *(67)* leads to high yields of bis(trifluoromethyl)amine *(109)*.

$$\underset{(67)}{CF_3{-}N{=}CF_2} \xrightarrow{HF} \underset{(109)}{CF_3{-}NH{-}CF_3}$$

The reaction of an isocyanide dichloride with hydrofluoric acid was first studied by *Petrov et al.*[64] with phenyl isocyanide dichloride *(6)*; this reaction leads to low yields of *N*-trifluoromethylaniline *(110)* together with large quantities of a "polymer".

$$\underset{(6)}{C_6H_5{-}N{=}CCl_2} \xrightarrow[-2\ HCl]{3\ HF} \underset{(110)}{C_6H_5{-}NH{-}CF_3}$$

The authors also described the perfluorination of trichloromethyl isocyanide dichloride *(64)* to form *(109)*.

We have found that aromatic isocyanide dichlorides with negative ring substituents and isocyanide dichlorides with heterocyclic substituents (*e.g.* "tetrameric cyanogen chloride") can be converted into *N*-trifluoromethylamines by hydrofluoric acid in high yields and with practically no "polymer" formation[65]. Isocyanide dichlorides containing readily exchangeable chlorine (*e.g.* acyl chlorides) are converted into their fluorine analogs by this reaction.

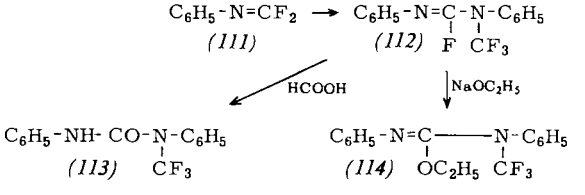
[63] *D. A. Barr* and *R. N. Haszeldine*, J. chem. Soc. (London) *1955*, 2532.

[64] *K. A. Petrov* and *A. A. Nejmysheva*, Ž. obšč. Chim. *29*, 2169 (1959).

[65] *E. Klauke* and *E. Kühle*, German Pat. 1170414 (May 15, 1962), Farbenfabriken Bayer AG.

The "polymer" formation reported by *Petrov*[64] for isocyanide difluorides is related to the addition of hydrofluoric acid. Our investigations indicate that this is a dimerization of the isocyanide difluoride, which proceeds rapidly under the action of heat or on catalysis by fluoro ions; an example is the formation of N^1,N^2-diphenyl-N^1-trifluoromethylfluoroformamidine *(112)*.

The structure of *(112)* has been confirmed by IR spectroscopy and by degradation reactions[66]. Thus *(112)* reacts with formic acid to give the urea *(113)*, while reaction with sodium ethoxide yields the isourea *(114)*.



(112) b.p. = 102 °C/0.1 torr
(113) m.p. = 102–103 °C
(114) b.p. = 95 °C/0.01 torr

Carbonyl difluoride also adds on to isocyanide difluorides. According to *Fawcett et al.*[67], the reaction of trifluoromethyl isocyanide difluoride *(67)* and carbonyl difluoride at 150 °C leads to bis(trifluoromethyl)carbamoyl fluoride *(115)*.

$$\underset{(67)}{CF_3{-}N{=}CF_2} \xrightarrow[150\,^\circ C]{COF_2} \underset{(115)}{(CF_3)_2N{-}COF}$$

Sheppard[68] described the addition of carbonyl difluoride to aromatic isocyanide difluoride, which leads in the presence of cesium fluoride to *N*-aryl-*N*-trifluoromethylcarbamoyl fluorides in yields of more than 80 %.

6.3. Addition of Hydrazoic Acid and Diazomethane

The first reported addition to isocyanide dichlorides was the reaction of phenyl isocyanide dichloride *(6)* with 2 moles of sodium azide[69], which leads to 5-azido-1-phenyltetrazole *(117)*, probably by substitution followed by addition to the intermediate diazide *(116)*.

The reaction of isocyanide dichlorides, *e.g.* *(6)*, with sodium azide in a molar ratio of 1:1 gives 1-aryl-5-chlorotetrazoles, *e.g.* *(118)*[70,71].

[66] This constitution was discussed earlier by *M. Hauptschein et al.*, J. org. Chemistry *23*, 323 (1958).

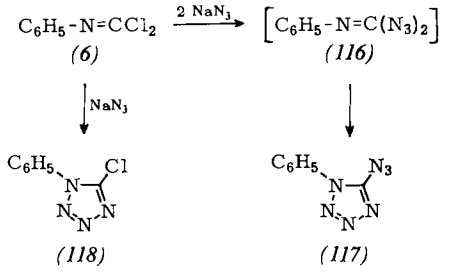
[67] *F. S. Fawcett*, *C. W. Tullock*, and *D. D. Coffman*, J. Amer. chem. Soc. *84*, 4275 (1962).

[68] *W. A. Sheppard*, J. Amer. chem. Soc. *87*, 4338 (1965).

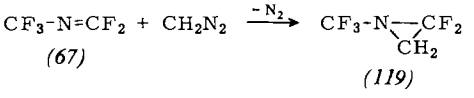
[69] *P. S. Pelkis* and *T. S. Dunajewska*, Mem. Inst. Chem., Akad. Sci. Ukr. SSR Inst. Microbiol. Epidemiol. *6*, 163 (1940); Chem. Abstr. *34*, 5829[9] (1940).

[70] *C. A. Maggiulli* and *R. E. Paine*, DAS 1251327 (Oct. 25, 1965), Eastman Kodak Comp.

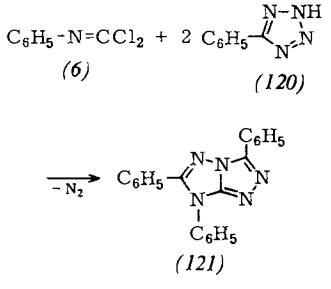
[71] *J. C. Kauer* and *W. A. Sheppard*, J. org. Chemistry *32*, 3580 (1967).



Diazomethane reacts with trifluoromethyl isocyanide difluoride *(67)* with liberation of nitrogen and formation of trifluoromethylaziridine *(119)* [72].



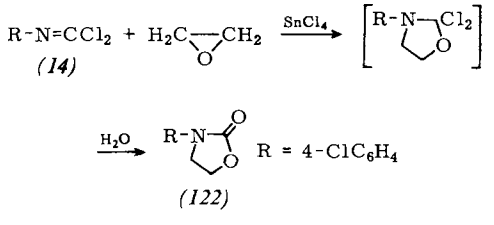
Finally, by analogy with a reaction described by *Huisgen* [73], we were able to react phenyl isocyanide dichloride *(6)* with 2 moles of 5-phenyltetrazole *(120)*. The products are nitrogen and 3,6,7-triphenyl-7*H*-*s*-triazolo-[4,3-*b*]-*s*-triazole *(121)*.



(121) m.p. = 286–288 °C

6.4. Addition of Epoxides

Oxazolidinones are obtained in moderate yields by the action of epoxides on isocyanide dichlorides in the presence of zinc chloride or tin tetrachloride followed by hydrolysis. For example, the reaction of 4-chlorophenyl isocyanide dichloride *(14)* with ethylene oxide yields oxazolidinone *(122)* [74].

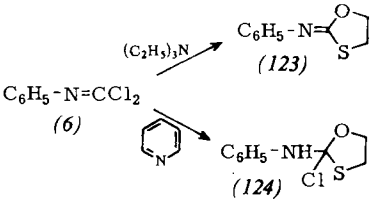


7. Ring Closure Reactions

Like phosgene and thiophosgene, the isocyanide dichlorides also enter into a wide range of ring closure reactions with bifunctional nucleophilic compounds.

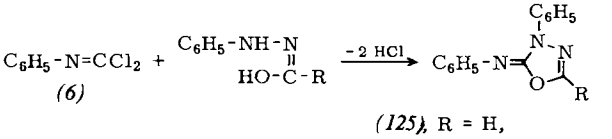
Some of the cyclizations can be carried out in aqueous alkaline media at room temperature, while others proceed only on heating in an inert solvent, possibly in the presence of a tertiary base.

Different reaction conditions sometimes lead to different cyclization products. Thus the reaction of phenyl isocyanide dichloride *(6)* with mercaptoethanol in the presence of triethylamine yields 2-phenylimido-1,3-oxathiolane *(123)*, while in the presence of pyridine the reaction gives 2-chloro-2-phenylamino-1,3-oxathiolane *(124)* [75].



7.1. Five-Membered Heterocycles

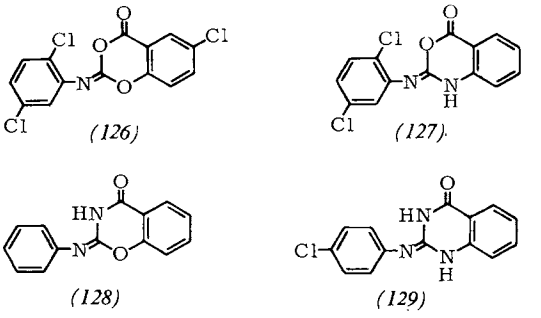
The five-membered heterocycles obtainable from isocyanide dichlorides have been very intensively studied. As early as 1893, *Freund et al.* [76] obtained the heterocyclic system *(125)* by reaction of phenyl isocyanide dichloride *(6)* with acylated phenylhydrazines. A selection of the heterocycles that can be obtained from isocyanide dichlorides is given in Table 1.



(125), R = H, CH_3, C_6H_5

7.2. Heterocycles with Six or More Ring Atoms

Higher membered heterocycles have so far only been prepared from isocyanide dichlorides in isolated cases. We have investigated the cyclization products formed on reaction of isocyanide dichlorides with salicylic and anthranilic acids and their amides. Each of the com-



(126) m.p. = 174–176 °C; *(127)* m.p. = 175–176 °C;
(128) m.p. = 218–219 °C; *(129)* m.p. = 237–239 °C

[72] *A. L. Logothetis*, J. org. Chemistry *29*, 3049 (1964).

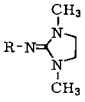
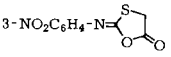
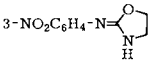
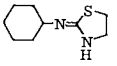
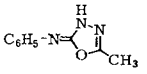
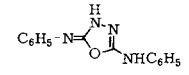
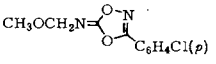
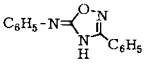
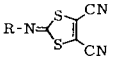
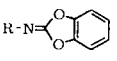
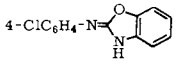
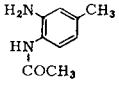
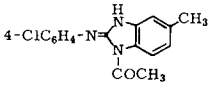
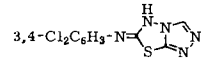
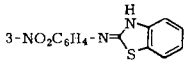
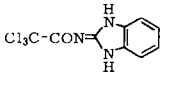
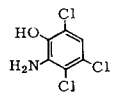
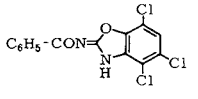
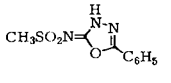
[73] *R. Huisgen, J. Sauer*, and *M. Seidel*, Chem. Ber. *93*, 2885 (1960).

[74] *R. Oda, T. Hamada, Y. Ito*, and *M. Okano*, Bull. Inst. chem. Res., Kyoto Univ. (Kagaku Kenkyusho Hokoku) *44*, 227 (1966).

[75] *V. S. Étlis, A. P. Sineokov*, and *G. A. Razuvaev*, Ž. obšč. Chim. *34*, 4090 (1964).

[76] *M. Freund* and *E. König*, Ber. dtsch. chem. Ges. *26*, 2869 (1893).

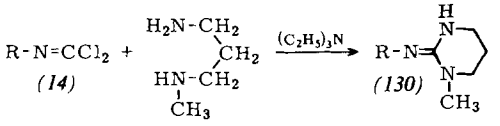
Table 1. Examples of five-membered heterocycles obtained from isocyanide dichlorides or acyl isocyanide dichlorides and bifunctional partners.

Reaction partners	Product	R	B.p. (°C/torr) (M.p. (°C))	Ref.
$HOCH_2-CH_2OH$		C_6H_5 [a] $(C_2H_5O)_2P(O)$ [a]	(73—75) 134—135/1	[77] [40]
$HOCH_2-CH_2SH$		C_6H_5 [b] C_6H_5CO [b] 3,4-$Cl_2C_6H_3-SO_2$ [b]	(67) (58) (127—129)	[75, 78] [81]
$HSCH_2-CH_2SH$		C_6H_5 [b] C_6H_5CO [b]	(43—44) (79)	[79] [81]
$(CH_3NH-CH_2-)_2$		3,4-$Cl_2C_6H_3$ [b] 4-$NO_2C_6H_4CO$ [b]	228—230/15 (155)	[78]
$HSCH_2-COOH$		[b]	(188—191)	[78]
$HOCH_2-CH_2NH_2$		[c]	(165—167)	
$HSCH_2-CH_2NH_2$		[b]	(164—165)	[78]
$CH_3CO-NHNH_2$		[c]	(166)	
$C_6H_5NHCO-NHNH_2$		[b]	(207—208)	[80]
4-$ClC_6H_4-CONHOH$		[c]	(156—157) (decomp.)	
$C_6H_5-C(NH_2)=NOH$		[c]	(151—153)	
		2,4-$Cl_2C_6H_3$ [c] 4-Cl-3-$NO_2C_6H_3CO$[c]	(142—145) (229—231)	
		c-C_6H_{11} [b] C_6H_5CO [b] $C_6H_5SO_2$ [b]	118/0.06 (113—115) (179—181)	[81]
	4-ClC_6H_4-N= 	[c]	(218—220)	[78]
	4-ClC_6H_4-N= 	[b]	(166—167)	[78]
	3,4-$Cl_2C_6H_3-N$= 	[c]	(292—294)	
	3-$NO_2C_6H_4-N$= 	[b]	(189)	[78]
	Cl_3C-CON= 	[b]	(271—273)	
	C_6H_5-CON= 	[b]	(219—221)	
$C_6H_5CO-NHNH_2$	CH_3SO_2N= 	[b]	(189—190)	[82]

[a] In benzene with ethanediol as the sodium salt. [b] In the presence of triethylamine or pyridine. [c] In aqueous alkali.

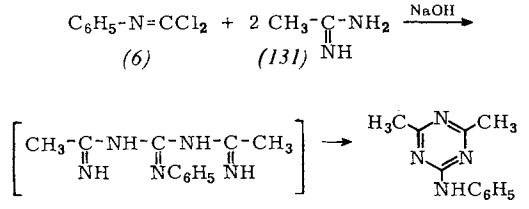
pounds *(126)–(129)* represents a member of this series [78,83].

Isocyanide dichlorides also give six-membered heterocycles, such as *(130)*, on reaction with 1,3-trimethylenediamines, 1,3-trimethylenedithiols, or 3-amino-1-propanols.



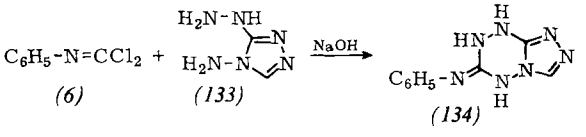
R = 4-ClC_6H_4 *(130)* m.p. = 68 °C

Symmetrical triazines are obtained, in analogy with earlier work in the triazine series [84], by cyclization of isocyanide dichlorides instead of phosgene with amidines in the presence of sodium hydroxide solution. For example, 2-anilino-4,6-dimethyl-*s*-triazine *(132)* is obtained in 87 % yield by this method.



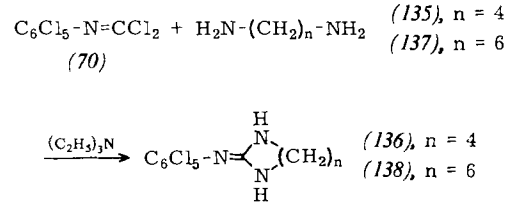
(132) m.p. = 125–126 °C *(132)*

Phenyl isocyanide dichloride reacts readily with 4-amino-3-hydrazino-1,2,4-triazole *(133)* to form the triazolotetrazine *(134)*.



(134) m.p. = 250 °C (decomp.)

Pentachlorophenyl isocyanide dichloride *(70)* reacts with 1,4-diaminobutane *(135)* and 1,6-diaminohexane as bifunctional partners to give seven-membered *(136)* and nine-membered heterocycles *(138)* respectively.



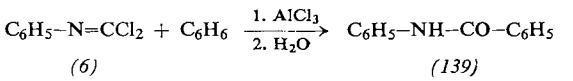
(136) m.p. = 245–246 °C

(138) m.p. = 218–220 °C (slow sintering from 160 °C)

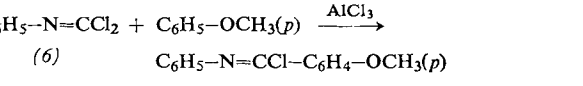
8. Other Reactions

8.1. Friedel-Crafts Reactions

The most extensively studied of the few known electrophilic substitutions of isocyanide dichlorides are the Friedel-Crafts reactions. *Dyson* and *Harrington* [50] were the first to report the reaction of phenyl isocyanide dichloride *(6)* with benzene in the presence of aluminum chloride to form benzanilide *(139)*.

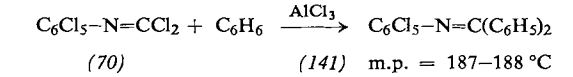


We have obtained several imidoyl chlorides, such as *(140)*, by the reaction of aromatic and cycloaliphatic isocyanide dichlorides with benzene or anisole.

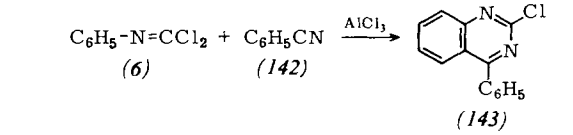


(140) b.p. = 159–163 °C/0.2 torr
m.p. = 70–71 °C

The second chlorine atom cannot generally be substituted even when an excess of aluminum chloride is used. The only known exception is pentachlorophenyl isocyanide dichloride *(70)*, which gives *N*-diphenylmethylenepentachlorophenylamine *(141)* in 55 % yield when heated for 30 minutes in benzene in the presence of aluminum chloride [85].



The reaction of benzonitrile *(142)* with phenyl isocyanide dichloride *(6)* in the presence of aluminum



(143) m.p. = 108–110 °C

[77] *T. Mukaiyama, T. Fujisawa*, and *T. Hyugaji*, Bull. chem. Soc. Japan *35*, 687 (1962).

[78] *B. Anders* and *E. Kühle*, Belg. Pat. 632578 (May 20, 1963), Farbenfabriken Bayer AG.

[79] *V. S. Étlis, A. B. Sineokov*, and *G. A. Razuvaev*, Ž. obšč. Chim. *34*, 4018 (1964).

[80] *K. Möckel* and *H. Gehlen*, Z. Chem. *4*, 388 (1964).

[81] *J. Burkhardt, R. Feinauer, E. Gulbins*, and *K. Hamann*, Chem. Ber. *99*, 1912 (1966).

[82] *R. Neidlein* and *W. Haussmann*, Arch. Pharmaz. *300*, 180 (1967).

[83] Heterocycles in which only one Cl atom of the $NCCl_2$ group is involved in the ring closure, together with an α-Cl atom, will not be discussed here; cf. *H. G. Schmelzer, E. Degener*, and *H. Holtschmidt*, Angew. Chem. *78*, 982 (1966); Angew. Chem. internat. Edit. *5*, 960 (1966).

[84] *A. Pinner*, Ber. dtsch. chem. Ges. *23*, 2919 (1890).

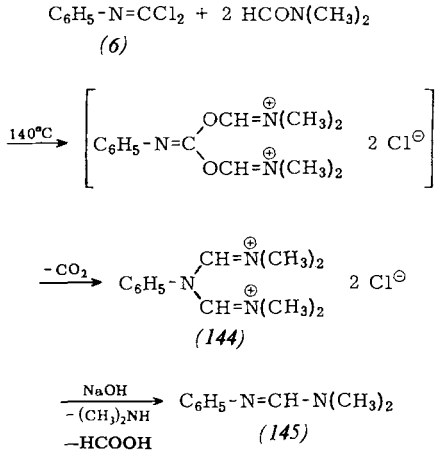
[85] *K. Findeisen*, unpublished.

chloride is similar to the Meerwein synthesis of quinazoline [86]. Cyclization takes place with formation of 2-chloro-4-phenylquinazoline *(143)* [87].

8.2. Reactions with Formamides

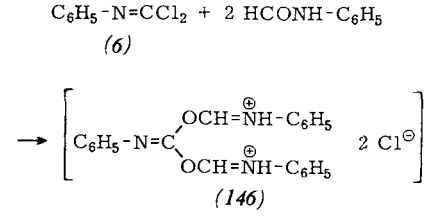
In analogy with the adducts formed from formamides and acid chlorides (*e.g.* phosgene, sulfonyl chlorides, phosphoryl chloride, thionyl chloride, cyanuryl chloride), isocyanide dichlorides react with mono- and disubstituted formamides to give adducts, which are converted into stable formamidines at high temperatures.

Thus phenyl isocyanide dichloride *(6)* and dimethylformamide (molar ratio 1:2) react exothermally at 140 °C with elimination of carbon dioxide and formation of a bisformamidinium chloride *(144)*, which loses dimethylamine on treatment with sodium hydroxide solution to form N^1,N^1-dimethyl-N^2-phenylformamidine *(145)* in 87 % yield.



(144) m.p. = 208–210 °C
(145) b.p. = 132–133 °C/13 torr

The reaction of phenyl isocyanide dichloride *(6)* with formanilide in a molar ratio of 1:2 is more complex. The first step is probably again the formation of a 1:2 adduct *(146)*, which is converted directly into N^1,N^2-diphenylformamidinium chloride *(147)* with liberation of carbon monoxide, carbon dioxide, and hydrogen chloride. Phenyl isocyanate and phenyl isocyanide have been detected as by-products, indicating a complex reaction that proceeds in several steps.



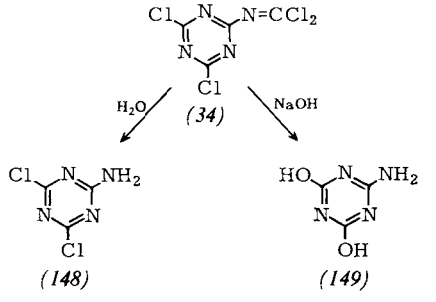
(147) m.p. = 248 °C (decomp.)

8.3. Conversion into Amines and Salts

The conversion of an isocyanide dichloride into an amine is important only if the amine is difficult to obtain by other means.

Thus pentachlorophenyl isocyanide dichloride *(70)* can be converted quantitatively into pentachloroaniline (m.p. 232–233 °C) by hydrolysis with sulfuric acid at 100 °C.

Hydrolysis of "tetrameric cyanogen chloride" *(34)* with water yields 2-amino-4,6-dichlorotriazine *(148)*, while hydrolysis in alkaline media proceeds further to 2-amino-4,6-dihydroxytriazine *(149)* [88].



The isocyanide dichlorides react with tertiary amines to form salt-like 1:1 adducts, most of which are very hygroscopic.

We thank Dr. H. Holtschmidt for stimulating suggestions and discussions regarding this work and for the isocyanide dichlorides, which are preparable by high-temperature chlorination.

Received: April 9, 1968 [A 674 IE]
German version: Angew. Chem. *81*, 18 (1969)
Translated by Express Translation Service, London

[86] *H. Meerwein, P. Laasch, R. Mersch,* and *J. Nentwig,* Chem. Ber. *89*, 224 (1956).

[87] Investigated at the suggestion of Dr. *R. Mersch,* Leverkusen.

[88] *Y. Kodama,* J. Soc. org. synth. Chem., Japan *21*, 525 (1963).

Planar Complexes Containing Metal-Metal Bonds

By K. Krogmann[*]

Planar complexes, and particularly those of platinum, can form structures containing linear chains of heavy metal atoms with metal-metal distances as short as 3.1 Å. The bonding in these chains can be strengthened by partial oxidation, and the bond lengths can be reduced to 2.8 Å in this way. Model structures for the novel nonstoichiometric products, such as $K_2[Pt(CN)_4]Cl_{0.32} \cdot 2.6\ H_2O$, are considered. The bonding is also discussed on the basis of a one-dimensional band model.

1. Theoretical Introduction

Square planar complexes are formed mainly by transition metal ions having a d^8 electron configuration. The d^8 system of Pt^{II} forms planar complexes with nearly all ligands, whereas that of Ni^{II} forms such complexes only with ligands situated at the strong field end of the "spectrochemical series" [1], *e.g.* CN^-. This property of d^8 systems is due to the mutual repulsion of the d electrons and the charges, or in general the electrons, of the ligands. The d orbitals of the central atom in a planar complex are shown schematically in Figure 1.

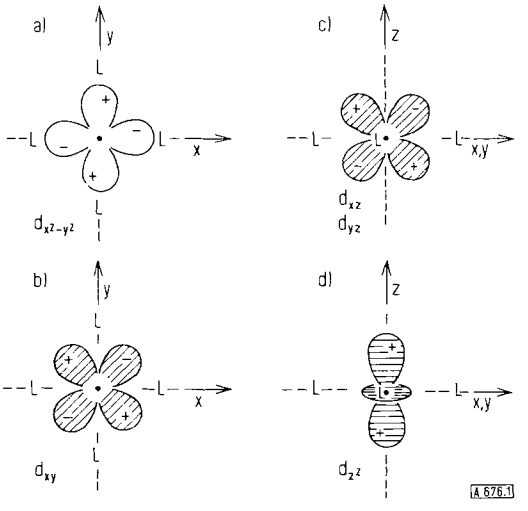


Fig. 1. d orbitals in a planar complex.

Figure 1a shows the $d_{x^2-y^2}$ orbital, which is directed toward the ligands, and Figure 1b shows the d_{xy} orbital, which lies in the plane of the ligands, but is directed between the negative charges or dipole ends. Figures 1c and 1d show "side views" of the complex and the d_{xz}, d_{yz}, and d_{z^2} orbitals, which point out of the plane of the complex. If the bonding of the ligand to the central atom is sufficiently strong and/or the mutual repulsion of the d electrons is sufficiently weak, the most favorable energy relationships are achieved by pairing of the electrons in the shaded orbitals d_{xy}, d_{xz}, d_{yz}, and d_{z^2}. The free $d_{x^2-y^2}$ orbital can then share the electrons of the ligands.

Since 3d electrons repel one another more strongly than 5d electrons, it is understandable why Pt^{II} invariably forms planar complexes whereas Ni^{II} does not always do so.

Figure 2, which shows a "side view" of the complex, is formed by combination of the parts of Figure 1. It can be seen that a considerable part of the "free" d-electron pairs lies above and below the plane of the complex. The simplest reactions that this "*z*-electron

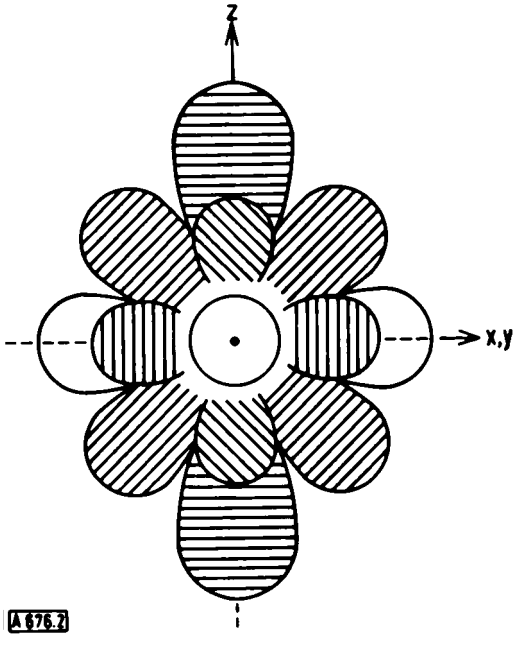


Fig. 2. d^8 system in a planar environment.

cloud" could conceivably undergo, *i.e.* oxidation and addition of Lewis acids, will only be mentioned in passing, and not considered in detail, though the picture they present is often different from that to which we are accustomed in s–p electron systems.

A general characteristic of free d electrons is their tendency to undergo $d_\pi - d'_\pi$ or $d_\pi - \pi^*_\pi$ back bonding (Fig. 3), thus forming donor-acceptor bonds of π symmetry in which the d electrons of the central atom share unoccupied ligand orbitals of suitable symmetry (*e.g.* d orbitals of Cl^- or π^* orbitals of CN^- or CO).

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[1] See, *e.g. H. L. Schläfer* and *G. Gliemann*: Einführung in die Ligandenfeldtheorie. 1st Edit., Akad. Verlagsges., Frankfurt 1967, p. 84.

This often leads to considerable reinforcement of the σ bonds between the ligands and the central atom. Such intramolecular accessory reactions are particularly common in planar complexes.

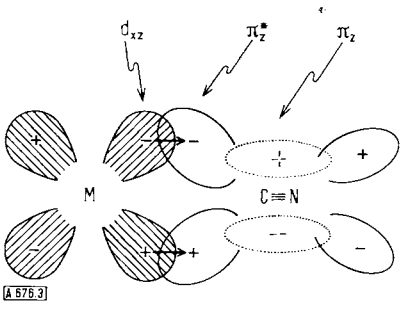


Fig. 3. π back-bonding.

Planar complexes in particular also have the ability to interact with the electron clouds of neighboring complexes; this property is not so easy to understand. Some relevant examples will be discussed below.

2. Planar Complexes in the Crystal Lattice

The $[Pt(CN)_4]^{2-}$ ion is a typical planar complex. Aqueous solutions of the alkali or alkaline earth metal salts are colorless, and absorb far beyond the visible limit in the UV [2]. In the solid state they sometimes form deeply colored crystals. Where there are several phases with different contents of water of crystallization, they can generally be recognized by their different colors. This is particularly well illustrated by the following dehydration reactions at 25 °C.

$$\underset{\text{dark red}}{Mg[Pt(CN)_4] \cdot 7\,H_2O} \xrightarrow[+\,2.5\,H_2O]{-\,2.5\,H_2O} \underset{\text{pale yellow}}{Mg[Pt(CN)_4] \cdot 4.5\,H_2O} \quad (1)$$

and

$$\underset{\text{colorless}}{Sr[Pt(CN)_4] \cdot 5\,H_2O} \xrightarrow[+\,3\,H_2O]{-\,3\,H_2O} \underset{\text{violet}}{Sr[Pt(CN)_4] \cdot 2\,H_2O} \quad (2)$$

These examples also show that the depth of color does not change in the same direction with the water content. Since neither the cations, which are hydrated to a greater or lesser extent, nor the isolated anions can absorb in the long-wave region and so cause the deep color, this property must be associated with the crystal structure.

Following the determination of the unit cell dimensions and the positions of the Pt atoms for some fully hydrated phases, *Yamada* recognized a relationship between the Pt–Pt distance and the color [3]. He showed (Table 1) the presence of an absorption band whose wave number decreases (*i.e.* its wavelength increases) with decreasing distance between the complex nuclei, and also showed that this absorption is polarized parallel to the Pt–Pt axis.

Table 1. Long-wave absorption maxima of some $M^{II}[Pt(CN)_4]$ phases, after *Yamada* [3].

Crystalline phase	Color	Pt–Pt distance (Å)	$\tilde{\nu}_{max}$ (cm^{-1})
$Ca[Pt(CN)_4] \cdot 5\,H_2O$	yellow	3.38	22800
$Ba[Pt(CN)_4] \cdot 4\,H_2O$	yellow-green	3.32	22000
$Mg[Pt(CN)_4] \cdot 7\,H_2O$	red	3.16	18000

These observations are confirmed by further investigations, which were also carried out with dehydrated alkaline earth metal tetracyanoplatinates [4,5]. The basic structure of the colored phases can be illustrated by that of the red magnesium salt, which was studied by *Bozorth* and *Pauling* [6] (Fig. 4).

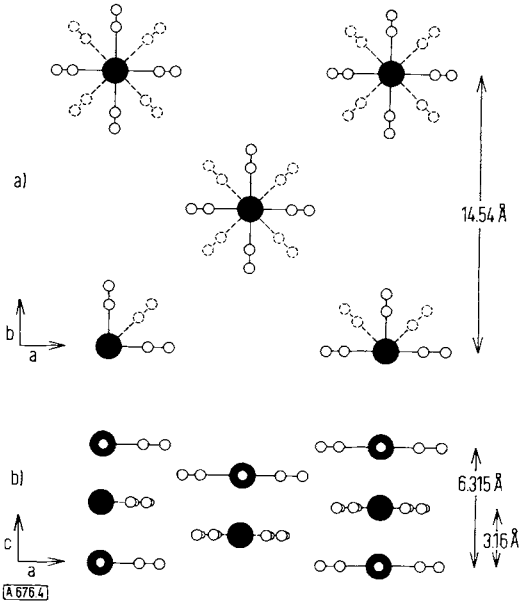


Fig. 4. Crystal structure of $Mg[Pt(CN)_4] \cdot 7\,H_2O$.
(a) Projection parallel to and (b) projection perpendicular to the tetragonal axis
● = Pt, O—O = CN. The sites of the Mg atoms are unknown.

The Pt atoms in $Mg[Pt(CN)_4] \cdot 7\,H_2O$ form a body-centered tetragonal unit cell. Thus Pt chains run through the crystal parallel to the *c* axis. The presence of weak superstructure lines for a cell having double the *c* dimension suggests that the CN groups in successive complex planes are "skew" to one another, as indicated in Figure 4. This arrangement has also been found in other $[Pt(CN)_4]$ structures [7, 8]. However, we are interested only in the chain period of 3.155 Å as given by the dimensions of the Pt cell.

These red crystals lose water even at room temperature to form a yellow phase, in which the Pt atoms form a triclinic cell whose shortest edge measures 3.36 Å. Partial dehydration probably results in a change in the coordination of the Mg^{2+} ions; in any case, the chain period is greater under the new

[2] *C. K. Jørgensen*: Absorption Spectra of Complexes of Heavy Metals. Report of the European Research Office, US Department of the Army, Frankfurt, Contract No. DA 91-508 EUC-247, October 1958.

[3] *S. Yamada*, Bull. chem. Soc. Japan *24*, 125 (1951); distances found in more recent measurements [5] were used in Table 1.

[4] *M. L. Moreau-Colin*, Bull. Soc. roy. Sci. Liège *34*, 778 (1965).

[5] *K. Krogmann* and *D. Stephan*, Z. anorg. allg. Chem., in press.

[6] *R. M. Bozorth* and *L. Pauling*, Physic. Rev. *39*, 537 (1932).

[7] *F. Fontaine*, Bull. Soc. roy. Sci. Liège *33*, 178 (1964).

[8] *K. Krogmann* and *H. D. Hausen*, Z. anorg. allg. Chem. *358*, 67 (1968).

conditions. The bonding interaction in the chain is evidently not very strong, since it can be overcome by other lattice forces. This is also confirmed by the ready solubility of these phases in water.

Nevertheless, it can be seen from Table 2, which shows the Pt–Pt distances of many compounds of this type, that chain formation occurs in several crystal systems.

Table 2. Pt–Pt distances (chain periods) and colors of $M^{II}[Pt(CN)_4]$ phases.

Crystalline phase	Color	Pt–Pt distance (Å)	Crystal system
$Sr[Pt(CN)_4] \cdot 5\,H_2O$	colorless	3.60	monoclinic [5, 10]
$Ca[Pt(CN)_4] \cdot 5\,H_2O$	yellow	3.38	orthorhombic [7]
$Mg[Pt(CN)_4] \cdot 4.5\,H_2O$	yellow	3.36	triclinic [5]
$K_2Sr[Pt(CN)_4]_2 \cdot 6\,H_2O$	green-yellow	3.33	monoclinic [5]
$Ba[Pt(CN)_4] \cdot 4\,H_2O$	yellow-green	3.32	monoclinic [5, 11]
$K_2Sr[Pt(CN)_4]_2 \cdot 2\,H_2O$	violet-red	3.21	monoclinic [5]
$Be[Pt(CN)_4] \cdot 2\,H_2O$	dark red	3.16	orthorhombic [9]
$Mg[Pt(CN)_4] \cdot 7\,H_2O$	dark red	3.16	tetragonal [5, 6]
$Sr[Pt(CN)_4] \cdot 3\,H_2O$	violet	3.09	monoclinic [5]

Special mention should be made of the deeply colored phases formed by the Be, Mg, Sr, and K_2Sr salts, all of which have Pt–Pt distances of less than 3.25 Å. This phenomenon is not confined to tetracyano complexes, but also occurs with other ligands. Thus, in addition to the normal yellow phases containing isolated $[Pt(C_2O_4)_2]^{2-}$ ions with no Pt–Pt interaction [12], the dioxalatoplatinates(II) often form red phases, though these generally rearrange rapidly into the yellow phases.

We determined the constants of the triclinic lattice of a red modification of $Ca[Pt(C_2O_4)_2] \cdot 4\,H_2O$ by single crystal diagrams [13]; the results give a Pt–Pt distance of 3.18 Å. Structures that have been known even longer are those derived from the green Magnus salt

$$\left.\begin{matrix}[(NH_3)_2\ Pt\ (NH_3)_2]^{2+} \\ [Cl_2\ Pt\ Cl_2]^{2-}\end{matrix}\right\} 3.25\ \text{Å}$$

$[Pt(NH_3)_4][PtCl_4]$ [14, 15], containing the complex cations and anions stacked in an alternating sequence, which again gives chains of heavy metal atoms having a period of about 3.25 Å.

The chain formation in this case, unlike that in the earlier examples, is electrostatically favored, since the neighboring complexes are oppositely charged [16]. Closer approach of the metal atoms is presumably prevented by the relatively large ligands. Similar arrangements and distances have also been found for neutral complexes, *e.g.* bis(2,3-butanedionedioximato)-platinum(II) [17, 18], and for corresponding complexes with other central atoms, particularly Pd^{II} and Ni^{II} [19, 20] (Table 3). The term "columnar stacking" has been coined for structures of this type [21]. Similar compounds of Rh^{I} and Ir^{I} have recently also been found; examples of these compounds are dicarbonyl-2,4-pentanedionatorhodium(I) and dicarbonyl-2,4-pentanedionatoiridium(I) [22–25].

The units of these structures are all planar (neutral complexes or planar cations and anions). Even with no bonding metal-metal interaction, parallel stacking of such units would lead to close packing, and would thus be energetically favorable. However, if the central atoms occur as nearest neighbors outside the planes of the complex and form a linear chain, this prevents the closest conceivable packing, and so leads to a loss of van der Waals energy of attraction. On formation of a chain structure, this loss must be compensated for by a corresponding gain in bond energy in the chain.

A clear indication of the existence of a bonding interaction is undoubtedly the occurrence of the deeply colored phases in the complex salts with particularly short Pt–Pt distances (Table 2). Though the planar units in this case are similarly charged, and despite the presence of non-polar cations that are hydrated to a greater or lesser degree a chain structure is formed.

2.1. The Bonding in the Chain

In the series Ni, Pd, Pt, the bonding along the chain is weaker for the first two elements than for Pt. This is shown by the fact that, among the tetracyano complexes, only the Pt derivative forms structures having chain periods of less than 3.25 Å when the other conditions are favorable. In these cases no isomorphism is found with corresponding complexes of the lighter elements, though the distances in the complexes are probably almost the same [7], so that the pure packing effects should be similar. Isomorphism is observed only at chain periods greater than 3.25 Å, and is then the rule, as can be seen from Table 3.

[9] *K. Krogmann* and *D. Stephan*, unpublished.

[10] *H. Lambot*, Bull. Soc. roy. Sci. Liège *12*, 522 (1943).

[11] *H. Brasseur* and *A. de Rassenfosse*, Mém. Soc. roy. Sci. Liège *18*, 1 (1933).

[12] *R. Mattes* and *K. Krogmann*, Z. anorg. allg. Chem. *332*, 247 (1964).

[13] *K. Krogmann*, Z. Naturforsch. *23b*, 1012 (1968).

[14] *E. G. Cox*, *F. W. Pinkard*, *W. Wardlaw*, and *G. H. Preston*, J. chem. Soc. (London) *1932*, 2527.

[15] *M. Atoji*, *J. W. Richardson*, and *R. E. Rundle*, J. Amer. chem. Soc. *79*, 3017 (1957).

[16] *R. R. Miller*, J. chem. Soc. (London) *1961*, 4452.

[17] *C. Panattoni*, *E. Frasson*, and *R. Zannetti*, Gazz. chim. ital. *89*, 2132 (1959).

[18] *C. Panattoni*, *E. Frasson*, and *R. Zannetti*, Acta crystallogr. *12*, 1027 (1959).

[19] *L. E. Godycki* and *R. E. Rundle*, Acta crystallogr. *6*, 487 (1953).

[20] *D. E. Williams*, *G. Wohlauer*, and *R. E. Rundle*, J. Amer. chem. Soc. *81*, 755 (1959).

[21] *J. R. Miller*, Advances inorg. Chem. Radiochem. *4*, 133 (1962).

[22] *F. Bonati* and *G. Wilkinson*, J. chem. Soc. (London) *1964*, 3156.

[23] *F. Bonati* and *R. Ugo*, Chim. e Ind. (Milano) *46*, 1332 (1964).

[24] *N. A. Bailey*, *E. Coates*, *G. B. Robertson*, *F. Bonati*, and *R. Ugo*, Chem. Commun. *1967*, 1041.

[25] *C. G. Pitt*, *L. K. Monteith*, *L. F. Ballard*, *J. P. Collman*, *J. C. Morrow*, *W. R. Roper*, and *D. Ulkü*, J. Amer. chem. Soc. *88*, 4286 (1966).

Table 3. M—M distances (chain periods) and colors of analogous Ni, Pd, and Pt compounds.

Complex	M—M distance (Å)	Color	
Bis(2,3-butanedione-dioximato)Ni(II)	3.25	red [19, 20, 28]	isomorphous orthorhombic
Bis(2,3-butanedione-dioximato)Pd(II)	3.26	yellow [19, 20]	
Bis(2,3-butanedione-dioximato)Pt(II)	3.23	violet [18]	
$Ca[Ni(CN)_4] \cdot 5\ H_2O$	3.38 [27]	orange [26, 28]	isomorphous orthorhombic
$Ca[Pd(CN)_4] \cdot 5\ H_2O$	3.42	colorless [7]	
$Ca[Pt(CN)_4] \cdot 5\ H_2O$	3.36	yellow [7]	
$Sr[Ni(CN)_4] \cdot 5\ H_2O$	3.65	orange [28, 29]	isomorphous monoclinic
$Sr[Pd(CN)_4] \cdot 5\ H_2O$	3.63	colorless [29]	
$Sr[Pt(CN)_4] \cdot 5\ H_2O$	3.58	colorless [29]	
$Mg[Pd(CN)_4] \cdot 4\ H_2O$	?	colorless	no isomorphous phases known
$Mg[Pt(CN)_4] \cdot 7\ H_2O$	3.16	red [6]	

The effect of the 5d electrons of the Pt complex is evidently stronger and extends farther outward than that of the analogous 4d and 3d systems.

To explain the formation of planar complexes, the valence bond (VB) method places eight 5d electrons of Pt^{2+} (Fig. 5a) in four d orbitals in pairs, while the fifth d function combines with a 6s and two 6p functions to form four dsp^2-hybridized functions, whose maxima are directed toward the corners of a square about the central atoms. These are used to bond the lone pairs of electrons in the four ligands, while the third p orbital remains empty (Fig. 5b). If the $5d_{z^2}$ and $6p_z$ functions are used to form two further equivalent hybrid orbitals (Fig. 5c), each of which can be occupied by one electron from the central atom, the Pt^{2+} is then able to form a linear chain with adjacent atoms having the same valence structure. Each of the neighbors contributes one electron per bond in the chain.

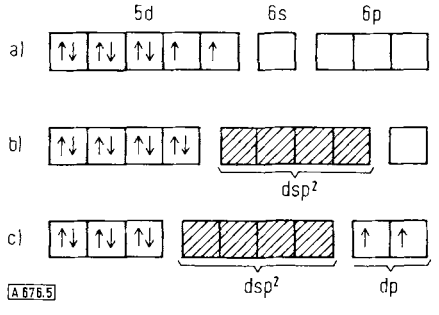


Fig. 5. Electron distribution in the Pt^{2+} ion (a) unperturbed, (b) in the dsp^2 valence state, (c) with additional dp hybridization.

This simple picture has the disadvantage that it does not show the relationship between light absorption and the Pt—Pt distance. A molecular orbital (MO) treatment as suggested first by *Rundle* and later by *Miller* [30, 31] is more suitable for this purpose. The interaction of two adjacent complex nuclei is considered first. The two $5d_{z^2}$ atomic orbitals (AO's), which have symmetry a_{1g}, split to give an antibonding and a bonding MO having symmetries a_{2u} and a_{1g} respectively. The same happens to the $6p_z$ AO's, which have symmetry a_{2u} (Fig. 6a). Since there are four electrons to be accommodated, the two lower levels (one bonding and one antibonding) are occupied. This should give no resultant bonding effect, but since non-degenerate MO's of the same symmetry "repel" each other (configuration interaction), the lower a_{1g} MO is displaced to lower energies and the upper to higher energies (Fig. 6b). The same is true of the a_{2u} MO. The total energy of the system therefore decreases and bonding occurs.

The character of the orbitals is also changed by configuration interaction. The MO's derived from $5d_{z^2}$ orbitals adopt some p character, while those formed from the $6p_z$ orbitals acquire some d character. The result therefore approaches that obtained by the valence bond method.

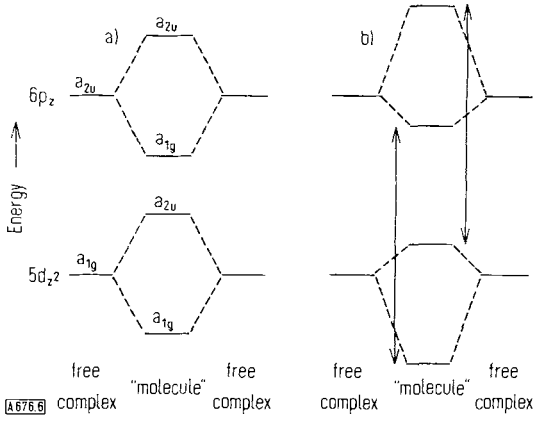


Fig. 6. MO scheme for a "molecule" consisting of two planar complexes (a) without and (b) with configuration interaction.

When this reasoning is extended to a chain of atoms (Fig. 7) the discrete levels are replaced by bands. The shorter the distance between the atoms, the broader the band becomes and the shorter is the distance between the highest occupied level in the d_{z^2} band and the lowest unoccupied level in the p_z band.

As a result of configuration interaction, the average energy of the d_{z^2} electrons decreases with decreasing chain period and so gives a bonding effect.

A clearer description can be arrived at by assuming that incomplete screening of the charge on the Pt nucleus by the 5d electron cloud along the z axis allows this charge to remain partly effective. This could provide some stabilization of the d_{z^2} electrons of the neighboring complex, were it not for the simultaneous development of forces of repulsion between the two pairs of d_{z^2} electrons, the probability densities of which are strongly concentrated around the z axis (Fig. 1d). If the $5d_{z^2}$ electrons could acquire some $6p_z$ character, they would have more lateral freedom of movement around the z axis, and the repulsion between the electrons would decrease.

[26] *H. Brasseur* and *A. De Rassenfosse*, Bull. Soc. roy. Sci. Liège *4*, 68 (1935).

[27] The lattice constant of 3.28 Å given in [26] is inaccurate. The value given here was determined by the present author.

[28] The deeper color of the Ni complexes is due to their ligand field absorption, which, unlike those of the Pd and Pt complexes, lies in the visible range, but occurs even in the absence of metal-metal interaction.

[29] *H. Lambot*, Bull. Soc. roy. Sci. Liège *12*, 522 (1943).

[30] *R. E. Rundle*, J. physic. Chem. *61*, 45 (1957).

[31] *J. R. Miller*, J. chem. Soc. (London) *1965*, 713.

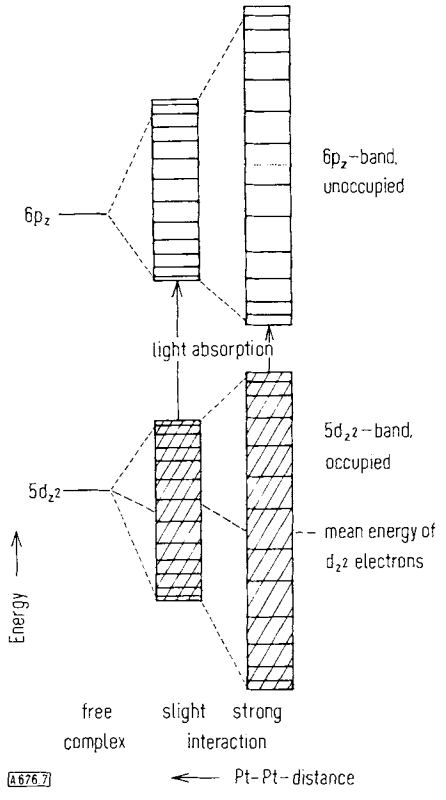


Fig. 7. Bond splitting, light absorption, and Pt—Pt distance in the chain of metal atoms.

The properties of the compounds discussed so far are easy to understand. The long-wave absorption polarized in the chain direction (z axis) corresponds to the transition from the highest occupied orbital of the d_{z^2} band to the p_z band (Fig. 7). The shorter the distance between the Pt atoms, the smaller is the energy required for this transition. When the transition is stimulated by light or heat, conductivity should be observed along the chain of metal atoms. Anisotropic semiconductor effects of this type have in fact been reported [25, 32].

2.2. Partially Oxidized Chain Compounds

The d_{z^2} band is fully occupied in Pt^{II} chains. Despite configuration interaction, the upper orbitals of this band have an antibonding effect on the chain, since they are situated above the d_{z^2} level of the free complex (Fig. 8).

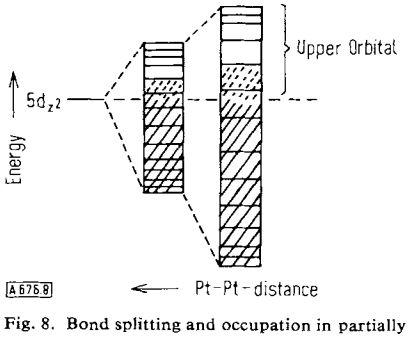


Fig. 8. Bond splitting and occupation in partially oxidized metal chains. The higher orbitals are antibonding.

[32] *H. P. Fritz* and *H. J. Keller*, Z. Naturforsch. *20b*, 1145 (1965).

The bonding in the chain should therefore be strengthened if electrons could be removed from this part of the band. The addition of a corresponding number of negatively charged particles or the removal of positively charged particles would then be necessary to preserve the electrical neutrality of the lattice. We have found examples of both types of compound.

Evaporation of an aqueous solution containing the complex salts $K_2[Pt(CN)_4]$ and $K_2[Pt(CN)_4Cl_2]$ in a molar ratio of 5:1 gives needles with a coppery sheen and having the composition $K_2[Pt(CN)_4]Cl_{0.32} \cdot 2.6\ H_2O$ [8]. On variation of the ratio of the starting compounds, the excess of Pt^{II} or Pt^{IV} complex crystallizes out together with the coppery substance. The latter is therefore a well-defined though non-stoichiometric compound having no recognizable phase range.

The crystals absorb or reflect almost all light polarized parallel to the axis of the needle and traveling perpendicular to this axis; light polarized perpendicular to this direction is absorbed only very slightly in the visible range.

The IR spectrum, unlike that of the $[Pt(CN)_4Cl_2]^{2-}$ complex, has no Pt—Cl vibration at 350 cm^{-1}; this indicates that the compound no longer contains Pt—Cl bonds. The tetragonal structure [8] contains Pt chains (Fig. 9).

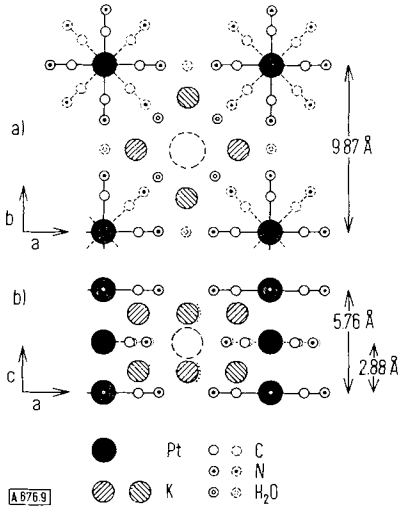


Fig. 9. Crystal structure of $K_2[Pt(CN)_4]Cl_{0.32} \cdot 2.6\ H_2O$
(a) Projection parallel to and (b) projection perpendicular to the tetragonal axis. The large circle in the center indicates the site for the chlorine atom.

In Figure 9a, looking along the c axis, one sees the superimposed planar $[Pt(CN)_4]$ complexes, the central atoms being situated at the corners of the cell and in the center of the c edge, while the CN groups lie parallel to the a and b axes and the diagonals of the faces. The second complex in each cell is thus turned through 45° in relation to the others. Figure 9b is a view perpendicular to the chain, and shows the short Pt—Pt distance of 2.88 Å. Cl^- is situated in the center of the cell, and is surrounded by eight sites for the four K^+ ions, which are arranged tetrahedrally.

The most important features of the structure are as follows: Pt^{II} and Pt^{IV} complexes cannot be distinguished, since all the Pt atoms are crystallographically identical. The period of the Pt chain is 10% shorter than in compounds of Pt^{II}. Each cell contains a site

for one Cl^-, corresponding to 0.5 Cl^- per Pt. However, this space is occupied in only 64 % of the cells, corresponding to 0.32 Cl^- per Pt. Thus the oxidation number of the Pt does not increase above +2.32.

These characteristics are understandable from the above theoretical discussion. The complexes are all of the square planar type. Owing to the partial oxidation, some of the antibonding orbitals (Fig. 8) are empty. This leads to stronger bonding in the chain and hence to a decrease in the Pt–Pt distance.

The structure may be imagined as being built up in steps from a crystallographically analogous (non-existent) phase of Pt^{II} with a Pt–Pt distance of 3.16 Å and an empty Cl^- site. Each defect electron produced in the occupied d_{z^2} band by oxidation strengthens and shortens the bond. At the same time a lattice hole is occupied by Cl^-, which has a further stabilizing effect. The gain in bond energy becomes steadily smaller with increasing oxidation, since the band orbitals being freed now are lower. The forces of repulsion between the free electron pairs and between the ligands of neighboring complexes increase rapidly with decreasing distance. The oxidation number and the distance reach final values that depend mainly on the band structure. These values do not necessarily permit the Cl^- sites to be completely occupied.

The counterpart of this structure with incorporation of extra anions is a partially oxidized chain structure with vacancies in cation sites. Examples have been found in particular among the dioxalatoplatinate complexes. These are formed on addition of a little oxidizing agent such as Cl_2 or $K_2Cr_2O_7$ to a solution of $[Pt(C_2O_4)_2]^{2-}$ salts as a violet precipitate, from which coppery needles can be isolated [33].

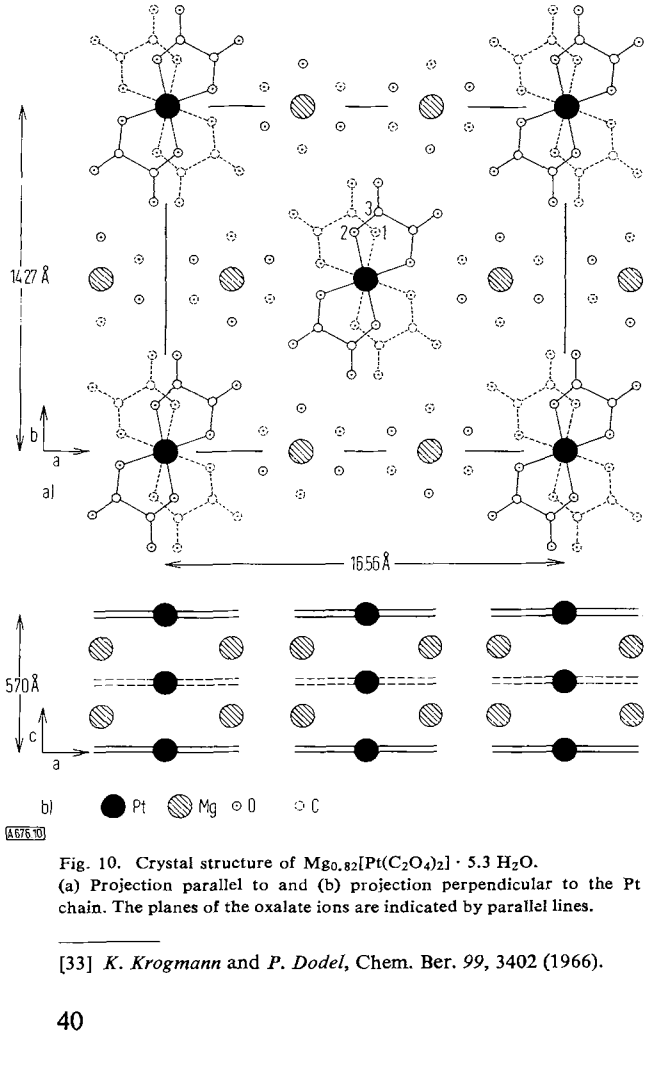


Fig. 10. Crystal structure of $Mg_{0.82}[Pt(C_2O_4)_2] \cdot 5.3\ H_2O$.
(a) Projection parallel to and (b) projection perpendicular to the Pt chain. The planes of the oxalate ions are indicated by parallel lines.

[33] *K. Krogmann* and *P. Dodel*, Chem. Ber. *99*, 3402 (1966).

Single crystals suitable for complete structure investigations were first obtained from $Mg_{0.82}[Pt(C_2O_4)_2] \cdot 5.3\ H_2O$ [34]. In this orthorhombic C-centered structure [*], the $[Pt(C_2O_4)_2]$ complexes are stacked skew one above another (Fig. 10). The Pt chains run parallel to the *c* axis with a period of 2.85 Å (= *c*/2); the Pt has an average oxidation number of +2.36. Eight sites are available for the Mg, each octahedrally surrounded by H_2O, but only 40 % of these sites are occupied. The strength of the bonding in the chains of this structure can be seen from the short distances between some atoms of adjacent complexes. For example, the O atom 1 in Figure 10a is only 2.95 Å from the C atom 3 of the complex above it, and only 2.97 Å from the O atom 2. Such short intermolecular distances are not found in other compounds. In the quinhydrone crystal, in which bonding occurs between the quinone and hydroquinone molecules, the shortest distances between unbonded atoms are greater than 3.1 Å.

Table 4 shows the partially oxidized phases and their principal data. There appears to be no strict relationship between the Pt–Pt distance and the oxidation number. It can be seen that the oxidation numbers are slightly higher and the distances slightly shorter in the dioxalato complexes than in the tetracyanoplatinates. This could mean that the tetracyanoplatinates have a different band structure, and that the orbital density at the upper limit of the band is lower or the configuration interaction fundamentally stronger. However, further examples are required to support this assumption, or measurements to confirm it.

Table 4. Partially oxidized chain compounds of platinum.

Complex	Oxidation number	Crystal system	Pt–Pt distance (Å)
$K_2[Pt(CN)_4]Cl_{0.32} \cdot 2.6\ H_2O$	+2.32	tetragonal	2.880 [8]
$K_2[Pt(CN_4]Br_{0.30} \cdot 2.3\ H_2O$	+2.30	tetragonal	2.887 [8]
$Mg[Pt(CN)_4]Cl_{0.28} \cdot 7\ H_2O$	+2.28	tetragonal	2.985 [35]
$K_{1.74}[Pt(CN)_4] \cdot 1.8\ H_2O$	+2.26	triclinic	2.960 [36]
$Li_{1.64}[Pt(C_2O_4)_2] \cdot 6\ H_2O$	+2.36	orthorhombic	2.81 [37]
$Na_{1.67}[Pt(C_2O_4)_2 \cdot 4\ H_2O$	+2.33	triclinic	2.88 [37]
$K_{1.62}[Pt(C_2O_4)_2] \cdot 2\ H_2O$	+2.38	triclinic	2.85 [37]
$K_{1.62}\ [Pt(C_2O_4)_2] \cdot x\ H_2O$	+2.38	monoclinic	2.81 [37]
$K_{1.64}[Pt(C_2O_4)_2] \cdot y\ H_2O$	+2.36	orthorhombic	2.83 [37]
$K_{1.64}[Pt(C_2O_4)_2] \cdot z\ H_2O$	+2.36	orthorhombic	2.82 [37]
$(NH_4)_{1.64}[Pt(C_2O_4)_2] \cdot 1\ H_2O$	+2.36	orthorhombic	2.82 [37]
$Mg_{0.82}[Pt(C_2O_4)_2] \cdot 5.3\ H_2O$	+2.36	orthorhombic	2.85 [37]
$Mg_{0.82}[Pt(C_2O_4)_2] \cdot x\ H_2O$	+2.36	triclinic	2.84 [37]
$Mg_{0.82}[Pt(C_2O_4)_2] \cdot y\ H_2O$	+2.36	orthorhombic	2.84 [37]
$Ca_{0.84}[Pt(C_2O_4)_2] \cdot 4\ H_2O$	+2.32	orthorhombic	2.83 [37]
$Sr_{0.84}[Pt(C_2O_4)_2] \cdot 4\ H_2O$	+2.32	orthorhombic	2.85 [37]
$Ba_{0.84}[Pt(C_2O_4)_2] \cdot 4\ H_2O$	+2.32	orthorhombic	2.85 [37]
$H_{1.60}[Pt(C_2O_4)_2] \cdot 2\ H_2O$	+2.40	orthorhombic	2.80 [37]
$H_{1.60}[Pt(C_2O_4)_2] \cdot 3\ H_2O$	+2.40	monoclinic	2.82 [37]

[34] *K. Krogmann*, Z. anorg. allg. Chem. *358*, 97 (1968).

[*] A C-centered structure is defined as one in which translation by (*a*/2 + *b*/2) (= one half of the diagonal of the C face) leads to an arrangement of atoms that is identical to the original arrangement.

[35] *K. Krogmann* and *G. Ringwald*, Z. Naturforsch. *23b*, 1112 (1968).

[36] *K. Krogmann* and *H. D. Hausen*, Z. Naturforsch. *23b*, 1111 (1968).

[37] *K. Krogmann* and *P. Dodel*, Z. anorg. allg. Chem., in press.

Mention should be made of the large Pt–Pt distance in the blue-black $Mg[Pt(CN)_4]Cl_{0.28} \cdot 7\ H_2O$ [35], which crystallizes in the same tetragonal structure as the chlorine-free (unoxidized) red salt. The *a* axis is slightly longer (14.66 instead of 14.54 Å) whereas the *c* axis, despite the addition of the chlorine, is considerably shorter (5.97 instead of 6.31 Å). The incorporation of the chlorine prevents contraction of the Pt–Pt distance to the value that would otherwise be reached. Unfortunately, no complete structure investigations have been reported for the two phases [38].

The physical properties of the partially oxidized chain compounds can be explained by the band model. The electrons of the highest occupied orbitals of the d_{z^2} band can be promoted into unoccupied levels of the d_{z^2} or p_z band by polarized absorption of light of all wavelengths. This is the reason for the deep color of the powder, while the coppery sheen of the larger crystals is due to polarized specular reflection. Because of the incompletely occupied band, conductivity and Pauli paramagnetism may be expected, and both are in fact observed [18]. The chains correspond to one-dimensional metals whose electrons exhibit a weak paramagnetism that is practically independent of the temperature. Conductivity values of up to 10^{-2} ohm^{-1} cm^{-1} in the chain direction have been observed; unlike the (appreciably lower) values for the Pt^{II} compounds, these do not increase on exposure to light. The conductivity is very difficult to measure, since lattice imperfections can hinder the one-dimensional movement of the electrons much more than in two-dimensional or three-dimensional conductors.

The phases known at present contain only oxalate and cyanide as ligands of the platinum. This limitation is probably accidental. However, since steric hindrance can be expected to be too strong in the case of larger ligands, the search for further examples should be concentrated mainly on C,N,O, and possibly F complexes. A clue may be provided by *Wöhler*'s observation that the oxidation number of the Pt in freshly precipitated Pt^{II} oxide hydrate gradually increases, but never rises above +2.5 [39]. However, an X-ray study of these phases has not yet been possible. *Waser* and *McClanahan jr.* have reported a compound $NaPt_3O_4$ having a Pt–Pt distance of 2.85 Å [40]. In a compound having this composition, the oxidation number of the Pt is +2.33.

Many of the substances discussed were described a long time ago because of their striking color [41–45]; however, their unusual stoichiometry could not be reconciled with the bonding theories held at the time.

2.3. Behavior of Partially Oxidized Chain Compounds in Solution

Do the solutions of partially oxidized chain compounds contain polymeric anions? The solubility is found to decrease noticeably. If the Pt^{II} complexes such as the alkali metal dioxalatoplatinates(II) are moderately soluble in water, the corresponding partially oxidized phases are sparingly soluble. With few exceptions, the tetracyanoplatinates(II) are very readily soluble, while their oxidized forms exhibit a diminished, though still high solubility. In the case of the tetracyano complexes, the spectra of the solutions can always be regarded as resulting from the superposition of the spectra of corresponding quantities of Pt^{II} and Pt^{IV} compounds, whereas this is true of the dioxalato complexes only at low concentrations. Thus disproportionation invariably occurs in solution. With the dioxalato complexes at sufficiently high concentrations, however, we detected pH-dependent polymerization equilibria [33,46], which undoubtedly also involve chains. Concentrated solutions are blue-black and have high extinctions ($\varepsilon > 10^4$) in contrast with the pale yellow dilute solutions.

A chain compound having an oxidation number of 2.4 contains infinite linear $[Pt(C_2O_4)_2]_n^{1.6n-}$ anions ($n = \infty$). The depolymerization, which really proceeds in many stages, may be idealized by the following equilibrium:

$$[Pt(C_2O_4)_2]_n^{1.6n-} \rightleftarrows 0.8\ n\ [Pt(C_2O_4)_2]^{2-} + 0.2\ n\ [Pt(C_2O_4)_2]^0 \quad (3)$$

The Pt^{IV} complexes complete their coordination by addition of water, from which protons can finally be removed:

$$[Pt(C_2O_4)_2]^0 + 2\ H_2O \rightleftharpoons [Pt(C_2O_4)_2(H_2O)_2]^0 \quad (4)$$

$$[Pt(C_2O_4)_2(H_2O)_2]^0 \rightleftharpoons [Pt(C_2O_4)_2(H_2O)(OH)]^- + H^+ \quad (5)$$

The removal of the proton from the Pt^{IV} complex is suppressed by the addition of acid, which thus favors the removal of H_2O and hence also polymerization. Dilute, pale yellow solutions therefore turn blue on addition of acid. Heating and dilution, on the other hand, cause depolymerization and a color change to yellow.

Corresponding polymerization phenomena in solution have not yet been measured for tetracyano complexes. On dissolution of the crystals, however, blue streaks are observed to start at the surface of the crystals and disappear into the solution.

2.4. Partially Oxidized Chain Compounds with Other Central Atoms

Planar d^8 complexes of Pd^{II}, Ni^{II}, Au^{III}, Ir^{I}, and Rh^{I} are known as well as those of Pt^{II}. It is already known that Pd^{II} and Ni^{II} have less tendency than Pt^{II} to form unoxidized chains. The same is true of Au^{III}, whose d orbitals are not so large because of the higher nuclear charge. No examples of partially oxidized chain compounds of Pd^{II}, Ni^{II}, and Au^{III} have so far been found.

On the other hand, Ir^{I} and possibly Rh^{I} could be suitable central atoms. In planar complexes their d electrons should spread farther outwards; unoxidized

[38] The structure of unoxidized $MgPt(CN)_4 \cdot 7\ H_2O$ is being studied at present in the crystallography laboratory of Liège University (private communication). No single crystals of the oxidized phase have been obtained as yet.

[39] *L. Wöhler*, Z. anorg. allg. Chem. *40*, 457 (1904).

[40] *J. Waser* and *E. D. McClanahan jr.*, J. chem. Physics *19*, 413 (1951).

[41] *W. Knop* and *G. Schneidermann*, J. prakt. Chem. *37*, 462 (1846).

[42] *E. A. Hadow*, Quart. J. chem. Soc. *14*, 104 (1861).

[43] *T. H. Wilm*, Ber. dtsch. chem. Ges. *21*, 1436 (1888).

[44] *L. A. Levy*, J. chem. Soc. (London) *1912*, 1081.

[45] *A. Söderbaum*, Ber. dtsch. chem. Ges. *21*, 567 (1888).

[46] *K. Krogmann* and *P. Dodel*, Chem. Ber. *99*, 3408 (1966).

chain compounds of both are already known [22–25]. However, the d electrons here are so reactive that *e.g.* $[Ir(CN)_4]^{3-}$ ions remove protons even from non-aqueous solvents such as alcohol and form complexes such as $K_3[IrH(CN)_5]$ [47, 48]. Thus the principal problem is still the isolation of suitable complexes.

We have nevertheless come across a known compound that may be regarded as a partially oxidized chain compound. The formula assigned to this compound is $Ir(CO)_3Cl$ [49], but it actually contains slightly more chlorine and should be formulated as $Ir(CO)_{2.9}Cl_{1.1}$. Its structure determination is not yet complete, but the Ir atoms in this compound, which has an orthorhombic crystal structure, are known to form chains having an Ir–Ir distance of 2.85 Å [50]. This is evidently another variant of the chain structures discussed earlier. In the planar complexes, the positive charge resulting from partial oxidation is compensated by statistical replacement of some of the neutral CO groups by Cl^-.

The author thanks Dr. P. Dodel, Dr. R. Mattes, Dr. H. D. Hausen, Dr. D. Stephan, Dr. H. Knittel, Dr. W. Binder, and Fräulein G. Ringwald for their substantial assistance in this work. Thanks are also due to Prof. Dr. J. Goubeau, as well as to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and W. C. Heraeus GmbH, Hanau, for their generous support.

Received: February 29, 1968 [A 676 IE]
German version: Angew. Chem. *81*, 10 (1969)
Translated by Express Translation Service, London

[47] *K. Krogmann* and *W. Binder*, Angew. Chem. *79*, 902 (1967); Angew. Chem. internat. Edit. *6*, 881 (1967).

[48] *K. Krogmann* and *W. Binder*, J. organometallic Chem. *11*, P 27 (1968).

[49] *W. Hieber, H. Lagally*, and *A. Mayr*, Z. anorg. allg. Chem. *246*, 138 (1941).

[50] *K. Krogmann, H. D. Hausen*, and *W. Binder*, Angew. Chem. *80*, 844 (1968); Angew. Chem. internat. Edit. *7*, 812 (1968).

Transport Phenomena in Membranes

By P. Läuger [*]

The realization that many elementary biological processes occur at membrane-like structures has led to renewed interest in the theory of molecular transport through membranes. Coupling phenomena in membranes, some of which are very complex, can now be rationally described with the aid of the thermodynamics of irreversible processes. The investigation of theoretical membrane models has proved a valuable complement to the thermodynamic method.

1. Introduction

The systematic study of mass transport through membranes began about 1830; this early development culminated in *van't Hoff*'s classic investigations on osmotic pressure. To define osmotic pressure, *van't Hoff* used the concept of the "semipermeable membrane", an ideal partition permeable to one component of a mixture and impermeable to all other components. Following the success of *van't Hoff*'s theory, subsequent work was concentrated mainly on the preparation and investigation of semipermeable membranes. When the problems associated with this had been solved in principle, interest in membranes rapidly faded.

Nowadays semipermeable membranes appear as a limiting case of minor importance. Membranes that allow the passage of several components are much more interesting, and frequently exhibit unexpected phenomena. For example, a component may pass from the solution in which its concentration is lower into the more concentrated solution, *i.e.* against its own concentration gradient. Phenomena of this type are always due to coupled movement of molecules in the membrane. It was not until recently that the rational description of these coupling phenomena was made possible by the theory of irreversible processes.

The strongest stimuli for the present development of membrane research have undoubtedly come from biology. Living cells maintain a continuous exchange of matter with their surroundings; at the same time, however, they must also preserve concentration differences between the intracellular and extracellular spaces. The separating membrane generally exercises a complicated regulating function. It allows substances to pass through according to the metabolic requirements, and is able to distinguish sharply between structurally similar compounds such as D- and L-xylose. It is often necessary for the cell membrane to transport substances against their activity gradients by expending chemical energy. Thus according to *Schlögl* [1], biological membranes act as "barriers,

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[1] *R. Schlögl*, Ber. Bunsenges. physik. Chem. *71*, 755 (1967).

gates, and pumps". The elementary processes that take place at the cell membranes are so far known only incompletely.

Industrial interest in membranes has also grown considerably. Work in this field is mainly directed toward the development of selectively permeable membranes suitable for use in the petroleum industry and in metallurgy. The use of membranes for obtaining drinking water from the sea also appears promising.

2. Phenomenological Theory of the Membrane Process. Flow Coupling; Reflection Coefficient and Reverse Osmosis

There are two possibilities for the theoretical description of membrane processes. The first method attributes the macroscopically observed effects to the molecular transport processes in the membrane. This method in principle allows a very detailed description, but frequently fails because the structure of the membrane is not known with sufficient accuracy or is too complicated. The second method is given by the thermodynamics of irreversible processes[2-4]. It is not restricted by any assumptions regarding the molecular nature of the system in question; nevertheless, it leads to a number of far-reaching results.

The second method will be illustrated for the system in Figure 1, which consists of a membrane and two external phases comprising the components A, B, and C. The membrane is assumed to be permeable to A and B, but impermeable to C. We generally allow a difference Δp in the external pressure, but we shall confine ourselves first to the isobaric case ($\Delta p = 0$). If the external phases are sufficiently large and well mixed, after a certain time a stationary state is reached in which the particle flows Φ_A and Φ_B are practically independent of time.

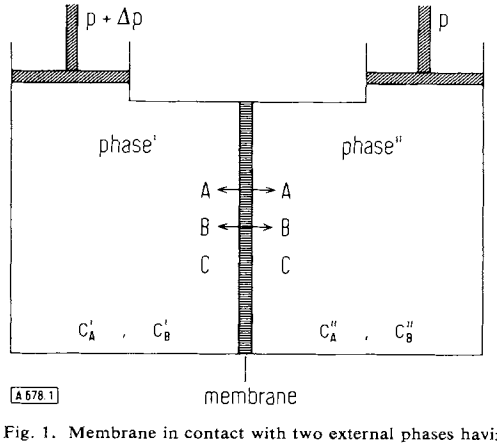


Fig. 1. Membrane in contact with two external phases having different compositions. The membrane is permeable to A and B, but impermeable to C. The volumes are so large that the concentrations c'_A, c''_A, c'_B, and c''_B are practically unchanged during the experiment.

[2] *S. R. De Groot* and *P. Mazur*: Non-Equilibrium Thermodynamics. North-Holland Publ. Comp., Amsterdam 1962.

[3] *R. Haase*: Thermodynamik der irreversiblen Prozesse. Steinkopff-Verlag, Darmstadt 1963.

[4] *D. D. Fitts*: Nonequilibrium Thermodynamics. McGraw-Hill, London 1962.

Let Φ_A and Φ_B be the number of moles of A and B that migrate from left to right through 1 cm² of membrane area per second. The thermodynamics postulates that Φ_A and Φ_B depend on the differences $\Delta\mu_A = \mu_A' - \mu_A''$ and $\Delta\mu_B = \mu_B' - \mu_B''$ of the chemical potentials of A and B[4,5].

$$\Phi_A = L_A\Delta\mu_A + L_{AB}\Delta\mu_B \quad (1a)$$

$$\Phi_B = L_{BA}\Delta\mu_A + L_B\Delta\mu_B \quad (1b)$$

However, these equations are valid only if $\Delta\mu_A$ and $\Delta\mu_B$ are sufficiently small, *i.e.* for external phases that differ only slightly in their composition[*].

The theory gives the following relationships for the coefficients L_A, L_{AB}, L_{BA}, and L_B:

$$L_A \geqslant 0, \quad L_B \geqslant 0 \quad (2)$$

$$L_{AB} = L_{BA} \quad (3)$$

$$L_{AB}^2 \leqslant L_A L_B \quad (4)$$

The modern view of the transport phenomena differs from the old view by the terms $L_{AB}\Delta\mu_B$ and $L_{BA}\Delta\mu_A$ in equations (1a) and (1b). These additional terms, which are demanded by theory as well as by experimental findings, indicate that the flow *e.g.* of component A generally depends not only on its own activity gradient, but also on the activity gradients of all the other components to which the membrane is permeable. Φ_A is therefore generally not zero if the activity (or concentration) of A is the same on both sides of the membrane. With suitable values of L_A and L_{AB}, it is even possible for Φ_A to have the direction opposite to that expected from the sign of $\Delta\mu_A$. Particle flow from low to high activity is known as incongruent transport[7,8]. It is made thermodynamically possible by the fact that a second component (B) is simultaneously migrating congruently, *i.e.* in the direction of its activity gradient.

These phenomena are combined in the concept of flow coupling. For this purpose, equations (1), (3), and (4) are written in the form

$$\Phi_A = L_A\left[(1-q^2)\Delta\mu_A + \frac{q}{\sqrt{L_A L_B}}\Phi_B\right] \quad (5a)$$

$$\Phi_B = L_B\left[(1-q^2)\Delta\mu_B + \frac{q}{\sqrt{L_A L_B}}\Phi_A\right] \quad (5b)$$

$$q \equiv L_{AB}/\sqrt{L_A L_B} \quad (-1 \leqslant q \leqslant 1)$$

[5] *A. J. Staverman*, Recueil. Trav. chim. Pays-Bas *70*, 344 (1951).

[*] In the isobaric case ($\Delta p = 0$), $\Delta\mu_A$ and $\Delta\mu_A$ are given by the differences $\Delta a_A \equiv a'_A - a''_A$ and $\Delta a_B \equiv a'_B - a''_B$ in the activities (R = gas constant, T = absolute temperature):

$$\Delta\mu_A = RT\,\Delta a_A/a_A; \quad \Delta\mu_B = RT\,\Delta a_B/a_B$$

where $a_A \equiv (a'_A + a''_A)/2$, $a_B \equiv (a'_B + a''_B)/2$ are the mean activities. If the external phases are ideal mixtures, the activities may be replaced by the mole fractions.

[6] *A. J. Staverman*, Trans. Faraday Soc. *48*, 176 (1952).

[7] *R. Schlögl*, Naturwissenschaften *50*, 67 (1963).

[8] *R. Schlögl*: Stofftransport durch Membranen. Steinkopff-Verlag, Darmstadt 1964.

The "coupling parameter" q, which was introduced by *Kedem* and *Caplan*[9, 10], is a measure of the extent to which the transport of A influences that of B and *vice versa*. If q is positive the flow of one substance tends to drag the flow of the second substance along in the same direction; if on the other hand q is negative, the first flow is forced back by the second (see Fig. 2).

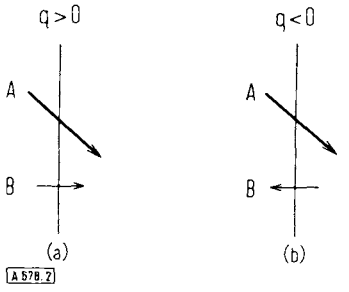


Fig. 2. Flows Φ_A and Φ_B in the special case $\Delta\mu_B = 0$ for positive (a) and negative (b) flow coupling. B migrates in the same direction as A when $q > 0$, and in the opposite direction when $q < 0$. The slope of the arrows corresponds to the gradient of the chemical potential.

When $q = 0$, the two substances migrate through the membrane independently.

A somewhat different situation arises if the pressure difference Δp in Figure 1 is no longer zero. For the sake of simplicity substance C is omitted in this case; moreover, both external phases are assumed to be dilute ideal solutions of A in B. The differences in the chemical potentials now depend not only on the concentration difference $\Delta c_A \equiv c_A' - c_A''$ but also on Δp:

$$\Delta\mu_A = v_A \Delta p + RT \Delta c_A/c_A \tag{6a}$$

$$\Delta\mu_B = v_B \Delta p - v_B RT \Delta c_A \tag{6b}$$

v_A and $v_B \approx 1/c_B$ are the mean partial molar volumes, and c_A and c_B are the mean concentrations. In experiments of this type it is usual to measure not only the flow Φ_A of the solute but also the "volume flow" $Q = v_A \Phi_A + v_B \Phi_B$. A system of equations introduced by *Staverman*[6] and obtained from equations (1), (3), and (6) has proved useful in this connection[11]:

$$Q = L_p[\Delta p - \sigma RT \Delta c_A] \tag{7}$$

$$\Phi_A = \omega_A RT \Delta c_A + c_A(1-\sigma)Q \tag{8}$$

The system is completely described by three phenomenological coefficients L_p, ω_A, and σ[*].

[9] *O. Kedem* and *S. R. Caplan*, Trans. Faraday Soc. *61*, 1897 (1965).

[10] *S. R. Caplan*, J. theoret. Biol. *10*, 209 (1966); *11*, 346 (1966).

[11] *O. Kedem* and *A. Katchalsky*, Biochim. biophysica Acta *27*, 229 (1958).

[*] The following equations are valid for dilute solutions:

$$\sigma = -L_{pD}/L_p\,, \quad \omega = c_A(L_pL_D - L_{pD}^2)/L_p \geq 0$$

$$L_p \equiv v_A^2 L_A + 2v_A v_B L_{AB} + v_B^2 L_B \geq 0$$

$$L_D \equiv \frac{L_A}{c_A^2} - 2\frac{L_{AB}}{c_A c_B} + \frac{L_B}{c_B^2} \geq 0$$

$$L_{pD} \equiv \frac{v_A}{c_A} L_A + \frac{L_{AB}}{c_A c_B} - \frac{v_B}{c_B} L_B$$

The "hydraulic permeability" L_p determines the volume flow due to a difference in external pressures at equal external concentrations ($\Delta c_A = 0$):

$$Q = L_p \Delta p \quad (\Delta c_A = 0) \tag{9}$$

If a concentration difference Δc_A is maintained between the external solutions, the particle flow Φ_A is found to be proportional to Δc_A. In the case $Q = 0$ (volumes of the external phases kept constant), Φ_A is found from equation (8) to be

$$\Phi_A = \omega_A RT \Delta c_A \quad (Q = 0) \tag{10}$$

The quantity ω_A is accordingly known as the "permeability coefficient".

The "reflection coefficient" σ was introduced by *Staverman*[5] for the interpretation of osmotic experiments. It is well known that equilibrium exists at a perfectly semipermeable membrane that is permeable to the solvent B and impermeable to the solute A when an additional pressure

$$\Delta\pi = RT\Delta c_A \tag{11}$$

is exerted on the concentrated solution. In the case of a membrane that is permeable to both components, the volume flow can also be made to disappear by the application of an external pressure Δp, but in this case Δp is no longer equal to the difference $\Delta\pi$ in the osmotic pressures of the external solutions. According to equation (7),

$$\Delta p = \sigma \Delta\pi \quad (Q = 0) \tag{12}$$

$(\Delta p)_{Q=0}$ is occasionally called the "apparent osmotic pressure".

For a semipermeable membrane, σ must have a value of 1[*]. Non-semipermeable membranes generally have σ values between 0 and 1, though σ can also be negative (cf. Section 5.2). Cases in which $\sigma > 1$ do not appear to have been observed so far, but are conceivable in principle[12].

Staverman[6] has shown that the reflection coefficient σ is also important in another experiment. In a system in which the external concentrations were initially equal ($c_A' = c_A'' = c_A$), if liquid is forced through a very wide-pored membrane, the concentration of the emerging solution will still be c_A. With small-pored membranes, in which the permeating molecules interact strongly with the membrane structure, it is generally found that one component is transported preferentially; this phenomenon is known as ultrafiltration or reverse osmosis. The concentration of the transported solution is given by Φ_A/Q; according to equation (8):

$$\Phi_A/Q = c_A(1-\sigma) \quad (\Delta c_A = 0) \tag{13}$$

[*] This condition is not sufficient for semipermeability. Equation (8) shows that since Φ_A for a semipermeable membrane must vanish for all values of Δc_A and Q, the necessary and sufficient conditions for semipermeability are: $\sigma = 1$, $\omega_A = 0$.

[12] Cf. ref. [8], p. 40.

Thus a value of $\sigma = 0$ corresponds to a completely unselective membrane ($\Phi_A/Q = c_A$). For a semipermeable membrane ($\sigma = 1$), on the other hand, $\Phi_A/Q = 0$, *i.e.* the filtrate consists of pure solvent.

3. Experimental Results for Electrically Neutral Membranes

As has already been shown in Section 2 of this article, a system consisting of a membrane and two permeable components is characterized by three mutually independent phenomenological coefficients (L_A, L_B, L_{AB}, or L_p, σ, ω). At a given temperature, these coefficients depend on the mean external concentrations. Measurements covering a wide range of concentrations are still rare. *Krämer* and *Sauer*[13] determined L_A, L_B, and L_{AB} for a cellulose membrane with several methanol/ethylene glycol mixtures (see Fig. 3)[*]. The system examined exhibits positive flow coupling; the values of the coupling parameter $q = L_{AB}/\sqrt{L_A L_B}$ are between 0.8 and 1.

Measurements of the reflection coefficient σ, which can be determined from the value of the apparent osmotic pressure (eq. (12)) and independently by ultrafiltration experiments (eq. (13)), are particularly interesting. The Onsager symmetry relation (eq. (3)) can be checked by comparison of the results obtained by the two methods. *Talen* and *Staverman*[14] obtained a value of $\sigma \simeq 0.20$, which was practically independent of the concentration, in ultrafiltration experiments with aqueous sucrose solutions at a porous quartz membrane (pore diameter about 50 Å). The apparent osmotic pressure of a sucrose solution measured at the same membrane should therefore be $^1/_5$ of the thermodynamic value, as is actually found to be the case.

This result is important for the osmometric determination of molecular weights[14, 15], since it shows that this method can be used even if the membrane is not completely impermeable to the solute. In this case the value of σ is determined by a separate ultrafiltration experiment, and the true osmotic pressure can then be calculated from the apparent value found experimentally.

In some cases the reflection coefficients σ were found to be strongly concentration-dependent, and even assumed negative values, *e.g.* at quartz membranes with solutions of polyethylene glycol in methanol or acetone[16–18]. Very small values of σ are found at quartz membranes with mixtures of low molecular weight organic substances[19].

Table 1. Experimental values of the phenomenological coefficients. The hydraulic permeability L_p and the permeability coefficient ω have been converted into the values for unit membrane thickness:

$$L_p^* = L_p \cdot d, \qquad \omega^* = \omega \cdot d$$

For comparison, the permeability coefficient for the free solution is given by $\omega_0 = D/RT$ (D = diffusion coefficient in the solution). For sucrose in water, $\omega_0 \approx 2.1 \times 10^{-16}$ moles · dyn^{-1} · s^{-1} (25 °C).

Membrane	External phase	σ	ω^* (mole · cm · dyn^{-1} · s^{-1})	L_p^* (cm^4 · dyn^{-1} · s^{-1})	Ref.
Cellulose (Sylvania "Wet Gel")	0.1 M sucrose in water	0.04	6.4×10^{-17}	8.2×10^{-13}	[21]
Cellulose (Visking dialysis tube)	0.1 M sucrose in water	0.11	1.6×10^{-17}	1.4×10^{-13}	[21]
Porous quartz membrane	0.1 M sucrose in water	0.20	—	1.2×10^{-13}	[14, 22]
Cellulose acetate	NaCl in water	≈ 1	1.2×10^{-20}	1.8×10^{-16}	[23]

It is obvious that a porous membrane that can distinguish well between solvent and solute cannot also have a high hydraulic permeability[20]. This is illustrated in Table 1: Large reflection coefficients σ and small permeability coefficients ω are associated with small values of the hydraulic permeability L_p.

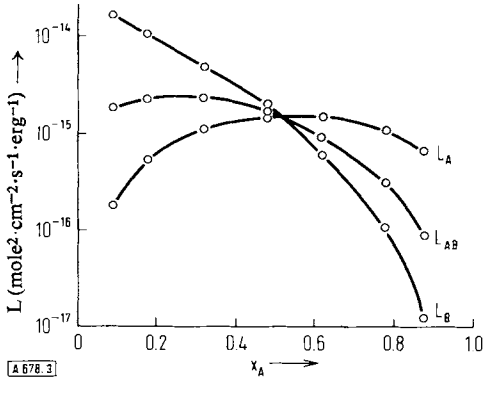


Fig. 3. Coefficients L_A, L_B, and $L_{AB} = L_{BA}$ (eq. (1)) for a cellulose membrane in contact with ethylene glycol (A)/methanol (B) mixtures x_A = mole fraction of ethylene glycol; $T = 20.0$ °C (after *Krämer* and *Sauer* [13]).

4. Transport Mechanisms

In the description of membrane structures it is possible to distinguish two limiting cases, *i.e.* pore membranes and solubility membranes. Pore membranes consist of a more or less rigid skeleton through which

[13] *H. Krämer* and *F. Sauer*, Ber. Bunsenges. physik. Chem. *71*, 855 (1967).

[*] The values of the coefficients at the concentration limits (x_A = mole fraction of component A) are given by the relations [13]:

$$\lim_{x_A \to 0} L_A = \lim_{x_B \to 0} L_B = 0$$

$$\lim_{x_A \to 0} L_{AB} = \lim_{x_A \to 1} L_{AB} = 0$$

[14] *J. L. Talen* and *A. J. Staverman*, Trans. Faraday Soc. *61*, 2794 (1965).

[15] *H.-G. Elias*, Chemie-Ing.-Techn. *33*, 359 (1961).

[16] *H.-G. Elias*, Z. physik. Chem. N.F. *28*, 303, 321 (1961).

[17] *J. L. Talen* and *A. J. Staverman*, Trans. Faraday Soc. *61*, 2800 (1965).

[18] *A. J. Staverman*, *Ch. A. Kruissink*, and *D. T. F. Pals*, Trans. Faraday Soc. *61*, 2805 (1965).

[19] *R. L. Cleland*, Trans. Faraday Soc. *62*, 336 (1966).

[20] *W. Kuhn*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *55*, 207 (1951).

[21] *B. Z. Ginzburg* and *A. Katchalsky*, J. gen. Physiol. *47*, 403 (1963).

[22] *H.-G. Elias*, and *H. Schlumpf*, Helv. chim. Acta *47*, 1503 (1964).

[23] *G. Thau*, *R. Bloch*, and *O. Kedem*, Desalination *1*, 129 (1966).

run liquid-filled cavities. Examples are the above mentioned quartz membranes, which have a sponge-like structure with pore sizes of 20 to 100 Å, or highly swollen plastic films. Solubility membranes, on the other hand, are characterized by the absence of permanent pores. The membrane in this case consists of a continuous phase, which contains the permeating substance in a molecularly dissolved state. The simplest case of a solubility membrane is a thin film of a liquid that is immiscible with the external phases.

Many membranes, *e.g.* many of the interesting biological membranes, cannot be assigned to either of these classes. If the diameter of the "pores" is close to the dimensions of the permeating molecules, the distinction between a pore membrane and a solubility membrane becomes doubtful. In these cases a satisfactory description is possible only with the methods of statistical mechanics.

A number of transport mechanisms that can be described by simple membrane models will be discussed below.

4.1. Transport in Wide-Pored Membranes

Membranes are described as wide-pored if the average pore diameter is very much greater than the diameter of the permeating molecules. In this case the membrane skeleton acts merely as a geometric boundary, while the transport processes take place in the interior of the pores almost as in free solution. For simplicity we shall consider a model membrane with pores perpendicular to its surface, the length of the pores being equal to the thickness d of the membrane. If the membrane is in contact with binary ideal external phases differing in concentrations by Δc_A and Δc_B, and in pressure by Δp, the flows of components A and B for small values of Δc_A, Δc_B, and Δp are given approximately by the following expressions:

$$\Phi_A = c_A Q + w D_{AB} \Delta c_A / d \tag{14a}$$

$$\Phi_B = c_B Q + w D_{AB} \Delta c_B / d \tag{14b}$$

w is the free pore cross section per cm² of membrane surface and D_{AB} is the mutual diffusion coefficient of A and B in free solution.

The volume flow Q is determined by the hydraulic permeability L_p^* for a membrane thickness of 1 cm:

$$Q = L_p^* \Delta p / d \tag{15}$$

Thus the flow of component A consists of two parts, *i.e.* a "convective" contribution $c_A Q$ resulting from the entrainment of the molecules A in the volume flow, and a contribution $w D_{AB} \Delta c_A / d$ corresponding to Fick's first law and due to transport by diffusion. "Pressure diffusion", which makes only a vanishingly small contribution to the total transport in the case of wide-pored membranes, has not been taken into account. In the specific case of circular cylindrical pores of radius r, for which Poiseuille's law is valid, it is found for a membrane having ν pores per cm² that $w = \nu\pi r^2$, $L_p^* = \nu\pi r^4/8\eta$ (η = viscosity of the solution).

Equations (8) and (14a) show that the reflection coefficient σ disappears for a wide-pored membrane. On the other hand, the coupling parameter q (see Section 2) is generally different from zero. As an approximation, it is found [24] that

$$q \approx 1 / \sqrt{(1 + \vartheta\, c_A \nu_A / c_B \nu_B)(1 + \vartheta\, c_B \nu_B / c_A \nu_A)} \tag{16}$$
$$\vartheta \equiv \nu_A \nu_B (c_A + c_B)\, w D_{AB} / RTL_p^*$$

ϑ is of the order of magnitude of (molecular radius/pore radius)², and is therefore very small under these conditions. Thus positive flow coupling occurs in wide-pored membranes.

4.2. Transport in Solubility Membranes

Whereas the transport of the permeating substances in pore membranes is more or less strongly coupled, solubility membranes are characterized by a very low degree of coupling, since the migrating components are generally present in the membrane phase in very dilute solution, and therefore diffuse through the membrane independently of one another. If the external pressures on both sides are equal, the flow of component A is given by

$$\Phi_A = D_A \Delta c_A^m / d \tag{17}$$

D_A is the diffusion coefficient of A relative to the membrane phase and Δc_A^m is the concentration gradient in the membrane. It may be assumed that a partition equilibrium characterized by the partition coefficient $k_A \equiv c_A^m / c_A$ exists at the phase boundaries [*]. Thus

$$\Delta c_A^m = k_A \Delta c_A$$

The flows for components A and B are then given by:

$$\Phi_A = D_A k_A \Delta c_A / d \tag{18a}$$

$$\Phi_B = D_B k_B \Delta c_B / d \tag{18b}$$

The transport through a solubility membrane is thus determined by the product of the partition coefficient and the diffusion coefficient. Since the flows Φ_A and Φ_B are independent of each other, it follows directly that for an idealized solubility membrane the coeffi-

[24] *P. Läuger*, unpublished.

[*] This assumption is generally no longer permissible for very thin membranes. In this case the rate-determining step may be the passage of the particle through the phase boundary, while the diffusion within the membrane is relatively fast [25–27].

[25] *K. J. Laidler* and *K. E. Shuler*, J. chem. Physics *17*, 851 (1949).

[26] *T. L. Hill* and *O. Kedem*, J. theoret. Biol. *10*, 399 (1966).

[27] *A. Essig*, *O. Kedem*, and *T. L. Hill*, J. theoret. Biol. *13*, 72 (1966).

cient L_{AB} of equation (1) and hence also the coupling parameter q disappear.

Solubility membranes are particularly suitable for industrial use in separation processes. The separating efficiency of a membrane is best described by the "separation factor" γ:

$$\gamma \equiv \frac{\Phi_A/\Delta c_A}{\Phi_B/\Delta c_B} = \frac{k_A}{k_B} \cdot \frac{D_A}{D_B}$$

Since γ is independent of the thickness d of the membrane, whereas the flows are proportional to $1/d$, the membrane is made as thin as possible. With a suitable choice of the membrane phase, the partition coefficients k_A and k_B can be very different, so that the separation factor can have values greater than 10^4 [28]. It is possible in practice to use films of amorphous high polymers; useful solubility membranes can also be prepared by impregnation of a porous, inert support with a liquid that is immiscible with the external solutions.

4.3. Experimental Differentiation between Pore Membranes and Solubility Membranes

"Pore membranes" and "solubility membranes" are idealized limiting cases. The extent to which a given membrane approximates to one case or the other can be determined by comparison of the hydraulic permeability L_p with the tracer permeability coefficient ω' [23]. For the measurement of ω', the solvent is isotopically labeled (*e.g.* A = H_2O, B = HTO). A concentration difference Δc_B leads to a flow Φ_B that is proportional to the tracer permeability coefficient ω':

$$\Phi_B = \omega' RT \, \Delta c_B \tag{19}$$

Since A and B have almost identical physical properties, $k_A \approx k_B = k$, $D_A \approx D_B = D$, and $v_A \approx v_B = v$ (= molar volume). It follows from eq. (18b) that

$$\omega' = kD/RTd \tag{20}$$

The hydraulic permeability of a solubility membrane, on the other hand, is given by the equation

$$L_p = vkD/RTd \tag{21}$$

Thus for an ideal solubility membrane,

$$g \equiv L_p/v\omega' = 1 \tag{22}$$

Values of g greater than 1, on the other hand, indicate that the permeating molecules no longer pass through the membrane independently of one another. An extreme case is that of wide-pored membranes, for which $g \gg 1$. Values of g close to 1 were found by *Thau, Bloch,* and *Kedem* for several synthetic membranes [23].

[28] *R. Bloch, A. Finkelstein, O. Kedem,* and *D. Vofsi,* Ind. Engng. Chem., Process Design Development *6,* 231 (1967).

To explain the anomalous isotope flows observed in the squid axon membrane, *Hodgkin* and *Keynes* in 1955 introduced the single-file mechanism [29]. This type of transport occurs if the pores of a membrane become so narrow that adjacent particles can no longer change places (cf. Fig. 4). The movement of each permeating particle is then coupled to the movement of all the other particles in the pore.

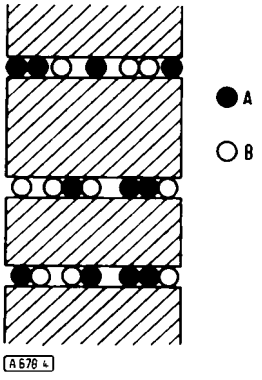


Fig. 4. Single-file transport. Adjacent particles in the pores cannot change places.

In the limiting case of very long pores, the average velocities of the particles A and B (Fig. 4) are the same. The ratio of the particle flows is then equal to the ratio of the concentrations c_A^m and c_B^m in the membrane, irrespective of the differences in the chemical potentials:

$$\Phi_A/\Phi_B = c_A^m/c_B^m \qquad \text{for all values of } \Delta\mu_A, \Delta\mu_B \tag{23}$$

This means that the coupling parameter q in equations (5a) and (5b) is equal to 1. In the limiting case of very long pores, therefore, this mechanism leads to complete positive flow coupling.

The calculation of the particle flows for finite pore lengths has been found to be very difficult. An exact treatment of a very simple model has been described by *Heckmann* [30, 31]. The pore in this case contains only two sites, each of which is either empty or occupied by a particle A or B. It is assumed that A and B can be distinguished analytically, but are physically identical in other respects. The calculations were originally carried out for gaseous external phases, but are also valid for an ideal dilute solution of A and B in a solvent C to which the membrane is impermeable. From *Heckmann*'s results, the coupling parameter is found to be given by the equation

$$q = \lambda \sqrt{\frac{c_A c_B}{(1-\lambda c_A)(1-\lambda c_B)}} \tag{24}$$

[29] *A. L. Hodgkin* and *R. D. Keynes,* J. Physiology *128,* 61 (1955).

[30] *K. Heckmann,* Z. physik. Chem. N.F. *44,* 184 (1965); *46,* 1 (1965).

[31] *K. Heckmann* and *H. Passow,* Ber. Bunsenges. physik. Chem. *71,* 839 (1967).

where λ is a known function of the mean total concentration $c_A + c_B$ and the jump frequencies of the two particles. The phenomenon of flow coupling is thus found even in this simple model.

Other methods have been reported for the calculation of flows in pores having more than two sites [32–36]. Time-dependent effects have also been examined [37]. Attempts to demonstrate this mechanism in synthetic membranes have not led to conclusive results [33, 38].

4.5. Carrier Transport

If the permeation of a substance is facilitated by complex formation with a molecule that is bound to the membrane, the process is referred to as carrier transport. In Fig. 5 it is assumed that the molecule A in

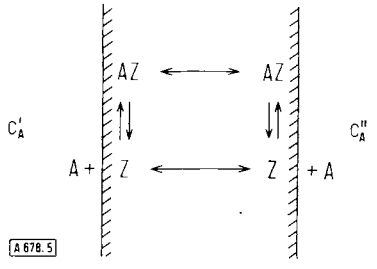


Fig. 5. Carrier transport. The molecule A combines with the carrier Z, which is bound to the membrane, to form a diffusible complex AZ. Vertical arrows: chemical equilibrium. Horizontal arrows: transport.

the free state is completely insoluble in the membrane. By reaction with the carrier molecule Z, which is present only in the membrane, a diffusible complex AZ is formed. If the rate of the reaction $A + Z \rightleftarrows AZ$ is sufficiently fast, the concentrations at the phase boundaries are given by the dissociation constant K_A

$$c'_A c'_Z / c'_{AZ} = c''_A c''_Z / c''_{AZ} = K_A \qquad (25)$$

In this equation, c_Z and c_{AZ} refer to the membrane phase, and c_A to the external phase. If $c'_A > c''_A$, a concentration gradient $(c'_{AZ} - c''_{AZ})/d > 0$ is established in the membrane, with the result that the complex is transported from left to right (see Fig. 5). At the right-hand interface the complex dissociates and A passes into the external phase, while the free carrier Z diffuses back to the left-hand interface.

Carrier transport differs from other types of transport by the phenomenon of saturation [40]. If the concentration c_A'' is kept constant, increasing c_A' brings the system ultimately to a state in which all the carrier molecules on the left-hand side of the membrane are in the form of complexes AZ. No further increase in the concentration gradient of AZ is then possible, and the flow of substance A has reached its maximum $\Phi_{A,max}$. In the special case $c_A'' = 0$:

$$\Phi_A = \Phi_{A,max} \frac{c'_A}{c'_A + 2 K_A D_Z/(D_{AZ} + D_Z)} \qquad (26)$$

$$\Phi_{A,max} = \frac{2 W D_{AZ}}{d^2 (1 + D_{AZ}/D_Z)} \qquad (27)$$

(D_Z, D_{AZ} = diffusion coefficients of the free carrier and of the complex respectively, W = total quantity of carrier in moles/cm² of membrane, d = membrane thickness).

If the external phases contain another substance B that competes with A for the common carrier, flow coupling occurs [39, 40]. Figure 6a shows the concentration profile for the case in which identical solutions of the substance A are present on both sides of the

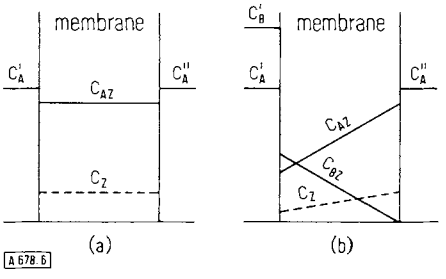


Fig. 6. Concentration profiles in a carrier transport system.
(a) System in equilibrium. The external phases consist of identical solutions of A.
(b) Addition of another substance B to the left-hand external phase. B competes with A for the common carrier Z.

membrane. On addition of the substance B to the left-hand phase (cf. Fig. 6b), the concentration of the complex AZ at the left-hand interface is decreased. A consequently migrates in the membrane from right to left, opposite to the migration of B. Thus negative flow coupling is observed in a carrier system (cf. Fig. 2). The following equation is found for the coupling parameter q:

$$q = -1 \Big/ \sqrt{\left(1 + \frac{D_Z}{D_{AZ}} \frac{K_A}{c_A}\right)\left(1 + \frac{D_Z}{D_{BZ}} \frac{K_B}{c_B}\right)} \qquad (28)$$

where c_A and c_B are the average external concentrations. In the saturation range of the carrier ($c_A \gg K_A$, $c_B \gg K_B$), q becomes equal to -1, *i.e.* complete (negative) flow coupling occurs.

Carrier transport is easily demonstrated experimentally with simple model membranes [41–44]. Carrier mecha-

[32] *W. Kuhn* and *A. Ramel*, Helv. chim. Acta *42*, 293 (1959).
[33] *W. Kuhn* and *P. Läuger*, Helv. chim. Acta *45*, 21 (1962).
[34] *E. J. A. Lea*, J. theoret. Biol. *5*, 102 (1963); *9*, 350 (1965).
[35] *H. Rickert*, Z. physik. Chem. N.F. *43*, 129 (1964).
[36] *S. B. Hladky*, Bull. math. Biophysics *88*, 79 (1965).
[37] *R. J. Macey* and *R. M. Oliver*, Biophysic. J. *17*, 545 (1967).
[38] *W. Kuhn, H.-J. Kuhn, D. H. Walters, H. Mayer*, and *H. Eglin*, Experientia *15*, 275 (1959).
[39] *T. Rosenberg* and *W. Wilbrandt*, Exp. Cell Res. *9*, 49 (1955).
[40] *T. Rosenberg* and *W. Wilbrandt*, J. gen. Physiol. *41*, 289 (1957).
[41] *H. Freundlich* and *I. A. Gann*, Int. Z. Physik. Chem. Biol. *2*, 1 (1915) (cited in [43]).
[42] *W. J. V. Osterhout*, Ergebn. Physiol., biol. Chem. exp. Pharmakol. *35*, 967 (1933); Proc. nat. Acad. Sci. USA *21*, 125 (1935).
[43] *G. M. Shean* and *K. Sollner*, Ann. New York Acad. Sci. *137*, 759 (1966).
[44] *J. B. Wittenberg*, J. biol. Chemistry *241*, 104 (1966).

nisms are very important in biology. For example, the transport of sugar through the erythrocyte membrane exhibits the characteristic phenomena of saturation and negative flow coupling [45]. However, it was necessary to extend the carrier concept considerably for biological membranes. Since the membrane thickness is only about 100 Å in this case, the existence of a freely diffusing carrier molecule is unlikely. It is therefore thought that the carrier molecule P (*e.g.* a protein) is an integral part of the membrane. The transport of a low molecular weight component A may be effected by a rotation or a change in the conformation of the complex A–P. This idea forms the basis of recent theoretical studies on the carrier mechanism [46–51].

4.6. Active Transport

Living cells are able to transport substances through the cell membrane against the activity gradients by consuming metabolic energy. Thus *E. coli* can absorb lactose even when the lactose concentration inside the cell is 2000 times that in the surrounding medium [52]. This formerly mysterious phenomenon has been circumscribed by the term "active transport" [53]. Some authors use this term to denote any particle transport against the gradient of the chemical potential (or the electrochemical potential in the case of ions) [54, 55]. According to this definition, "active transport" for uncharged particles would be identical with incongruent transport (cf. Section 2). A more common definition is as follows [56]. Active transport is a congruent or incongruent particle transport that is coupled with a chemical reaction [*].

This definition is in accordance with the fact that the free energy required for any incongruent transport must ultimately be supplied by metabolic processes. The function of the metabolic process may be simply to maintain activity differences of other substances which, by flow coupling, provoke the incongruent transport of the component in question. There is, however, evidence that a much more direct coupling exists between the chemical reaction and the transport process in biological membranes [39, 61, 62]. It is conceivable that the chemical reaction proceeds *via* an intermediate in which the carrier molecule Z is directly involved. If it is assumed that the bonding of A to the carrier is weakened by the chemical reaction, we obtain the following reaction scheme:

$$AZ + X{\sim}Y \rightarrow A + Z{\sim}X + Y' \quad \text{(a)}$$

$$Z{\sim}X \rightarrow Z + X' \quad \text{(b)}$$

(X′, Y′ = hydrolysis products of the energy-rich compound X∼Y).

If reaction (a) is catalyzed only at the right-hand interface and reaction (b) only at the left-hand interface of the unsymmetrical membrane, the substance A can be transported incongruently from left to right by consumption of the free energy made available by the hydrolysis of X ∼ Y. A reaction of this type appears to be involved in the ATP-dependent transport of Na^+ and K^+ through the cell membrane [39, 63].

5. Ion Exchange Membranes

If the membrane matrix contains electrically charged groups, additional phenomena occur. It is therefore necessary to extend the above equations before applying them to ion exchange membranes. The driving force for the transport of an ion through the membrane is now not only the activity gradient but also the electric field. Accordingly, the current and the electrical potential difference between the external phases occur as additional variables in the flow equations.

A macroscopic ion exchange membrane must satisfy the electroneutrality condition; therefore, in addition to the ions that are bound to the matrix ("fixed ions"), the membrane contains oppositely charged ions ("counter-ions"). Small quantities of "co-ions", which have the same charge as the fixed ions, are also present. In contact with aqueous external phases, ion exchange membranes absorb water; however, the quantity absorbed varies widely between membranes of different types.

Ion exchange membranes of the dissociation type (in *Eisenman*'s terminology [64]) are membranes with a high water content, in whose water-filled pores co-ions and counter-ions can move more or less freely. The ionic groups bound firmly to the matrix may therefore be regarded as completely dissociated, like a strong electrolyte in aqueous solution. This type of membrane is represented by highly swollen synthetic ion exchanger membranes based on synthetic resins.

Ion exchange resins of the association type contain only strongly bound hydration water, and in the extreme case they are practically free from water. The silicate glass membranes used to measure the activities

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[*] There have recently been discussions on whether the introduction of coupling coefficients between chemical reactions and particle flows into the phenomenological equations is contrary to the Curie theorem [57–60]. This theorem imposes restrictions on the combination of scalar with vector quantities.

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of hydrogen and alkali metal ions are of this type. The fixed ions are represented by the SiO^- and $AlOSi^-$ groups. The counter-ions (Na^+, K^+, *etc.*), which are situated in a medium having a low dielectric constant, are more or less associated with the fixed ions. However, they can migrate between adjacent fixed ions (*e.g.* by a defect mechanism), and they can be exchanged to a limited extent for other ions from the aqueous phase.

5.1. Ion Exchange Membranes of the Association Type

These membranes have recently been investigated in particular by *Eisenman et al.* [64–68] in an effort to obtain a better understanding of the operation of the glass electrode, the ion-specificity of which can be greatly varied by variation of the composition of the glass. The electric potential difference across a membrane of pure Na silicate glass is almost exclusively determined by the ratio of the hydrogen ion activities of the external solutions, and is practically unaffected by other cations. Introduction of Al_2O_3 or B_2O_3 into the glass matrix, on the other hand, yields membranes that are selective for alkali metal ions in neutral or alkaline media. If the external solutions contain two types of alkali metal ions i and j, the potential difference measured at vanishing current obeys the relationship:

$$\Delta\varphi = \frac{nRT}{F} \ln \frac{(a_i')^{1/n} + (K_{ij}a_j)^{1/n}}{(a_i'')^{1/n} + (K_{ij}a_j'')^{1/n}} \qquad (29)$$

a' and a'' are the alkali ion activities in the left-hand and right-hand external solutions, respectively, and n and K_{ij} are empirical constants characteristic of the composition of the glass and the ion pair (n is generally close to 1). The selectivity constant K_{ij} can assume values of between 10^5 and 0.03 for the ion pair K^+, Na^+, depending on the glass [65]; Na^+ activities can therefore be measured very accurately even in the presence of K^+. The ion selectivity is due to the following factors:

(a) Owing to the high concentration of fixed ions, co-ions are practically unable to penetrate into the membrane.

(b) The mobilities of different counter-ions differ much more in the membrane than in free solution. Moreover, tracer measurements have shown that the Na^+ and K^+ mobilities are several orders of magnitude lower than in aqueous solution [68].

(c) The exchange equilibrium of two alkali metal ions A^+ and B^+ between the membrane phase and the external solution is strongly dependent on the ionic radii and the glass structure. The equilibrium constant is determined by the free enthalpy change ΔG in the exchange reaction:

$$A^+ (aq.) + B^+ (membrane) \rightarrow A^+ (membrane) + B^+ (aq.)$$

ΔG is made up from the difference in the hydration energies and the ion-matrix interaction energies, which can be approximately calculated from the Coulomb interaction between the counter-ion and the fixed ion, using an effective ionic radius for the fixed ion. The specificity sequences of several types of glasses can be qualitatively interpreted in this way [65, 68].

In addition to their practical importance, ion exchange membranes of the association type are valuable models for biological membranes. According to *Eisenman* [65, 66], association also occurs between inorganic ions and "bonding sites" (*e.g.* $\cdots$—COO^-) in the lipoprotein matrix of biological membranes. This view can form a basis for the interpretation of ion specificities in biology.

5.2. Ion Exchange Membranes of the Dissociation Type

Most synthetic ion exchange membranes have a high water content so that their ionic groups are almost completely dissociated (see [69–77], for reviews see [8, 78–80]).

Ion exchange membranes of the dissociation type have interconnected, water-filled pores, in which co-ions and counter-ions can move rather freely. The pore liquid as a whole is electrically charged; this leads to coupling effects between mechanical and electrical processes in the membrane. For example, as a result of an externally induced volume flow, a potential difference (the streaming potential) builds up across the membrane at vanishing electric current. Conversely, an externally applied potential difference leads at vanishing volume flow to a pressure difference. These phenomena are known as electrokinetic phenomena. Moreover, the flows of all types of ions in the electric field are also coupled with one another.

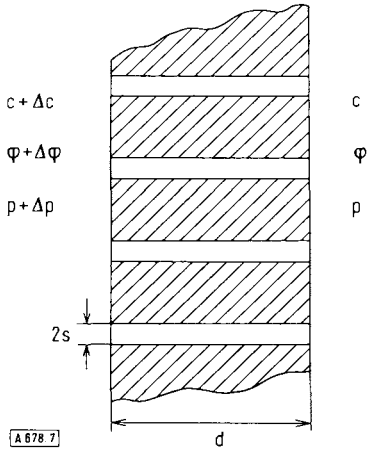


Fig. 7. Ion exchange membrane with parallel slit-shaped pores of width $2s$. The external phases differ in their electrolyte concentrations by Δc, in electric potential by $\Delta\varphi$, and in pressure by Δp.

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The pore structure of true ion exchange membranes is very complicated, and is not yet known in detail. The geometrically simplest model is an arrangement of parallel, slit-shaped pores of width $2s$, which run through the membrane perpendicular to is surface (cf. Fig. 7). If ν pores are present per cm^2, the proportion of the total membrane area occupied by pores is $w = 2\nu s$. The pore walls are assumed to be covered with fixed electric charges having a surface density of γ; the concentration X of fixed ions per unit volume of pore liquid is then $\omega X = \gamma/sF$ (F = Faraday constant, $\omega = \pm 1$ = sign of the charge on the fixed ions).

The membrane is assumed to be in contact on both sides with a $z:z$ electrolyte having an equivalent conductivity $\Lambda = F(\beta_+ + \beta_-)$. Since the pore liquid may be regarded approximately as free solution, the mobilities β_+ and β_- of the cation and the anion and the viscosity η inside the pores are approximately the same as in the external media. In the general case, the external phases differ in their electrolyte concentrations by Δc, in electrical potential by $\Delta\varphi$, and in pressure by Δp. The result is the simultaneous occurrence of a cation flow Φ_+, an anion flow Φ_-, and a water flow Φ_W. It is, however, desirable on practical grounds to consider other flows, *i.e.* the "salt flow" $S \equiv {}^1/_2(\Phi_+ + \Phi_-)$, the volume flow $Q \approx v_W \Phi_W$, and the current density $J = zF(\Phi_+ - \Phi_-)$ (v_W = partial molar volume of water).

S, J, and Q vary linearly with the differences Δc, $\Delta\varphi$, and Δp if these are sufficiently small:

$$S = L_{Sc}\Delta c + L_{S\varphi}\Delta\varphi + L_{Sp}\Delta p \tag{31a}$$

$$J = L_{Jc}\Delta c + L_{J\varphi}\Delta\varphi + L_{Jp}\Delta p \tag{31b}$$

$$Q = L_{Qc}\Delta c + L_{Q\varphi}\Delta\varphi + L_{Qp}\Delta p \tag{31c}$$

The nine coefficients L_{Sc}, $L_{S\varphi}$, *etc.* can, at least in principle, be calculated from the assumptions of the model. The calculation is based on the generalized Nernst-Planck equations [75], which relate the ion flows to the concentration and potential profiles in the pore; the pressure profile in the interior of the pores must also be explicitly taken into account. The transport equations can be integrated in a closed form if the pore width s is much greater or much smaller than the Debye-Hückel distance $1/\varkappa$ [81, 82]. $1/\varkappa$ is approximately the distance over which the diffuse ion atmosphere extends in the vicinity of an electrically charged wall. Membranes for which $\varkappa s \ll 1$ are described as "fine-pored"; this condition is satisfied to a good approximation in many synthetic ion exchange membranes (pore widths between 10 and 100 Å). The calculation [83] for the limiting case $\varkappa s \ll 1$ gives [*]

$$L_{Sc} = \frac{wRT\Lambda}{2zF^2d}\,[y(a+U) + \tau a(ay-1)]$$

$$L_{S\varphi} = -\omega\frac{wX\Lambda}{4zFd}\,[1 + a(\tau+U)]$$

$$L_{Sp} = \frac{ws^2aX}{6z\eta d}$$

$$L_{Jc} = -\omega\frac{wRT\Lambda}{Fd}\,[\tau(ay-1) + y(aU+1)]$$

$$L_{J\varphi} = \frac{wX\Lambda}{2d}\,[\tau + a + U]$$

$$L_{Jp} = -\omega\frac{ws^2FX}{3\eta d} \tag{32}$$

$$L_{Qc} = \frac{2ws^2RT}{3\eta d}\,(ay-1)$$

$$L_{Q\varphi} = -\omega\frac{ws^2FX}{3\eta d}$$

$$L_{Qp} = \frac{ws^2}{3\eta d}$$

$$y \equiv \frac{X}{2zc}, \qquad a \equiv \sqrt{1 + 1/y^2}$$

$$\tau \equiv \frac{2s^2F^2X}{3\eta\Lambda}$$

$$U \equiv -\omega\frac{\beta_+ - \beta_-}{\beta_+ + \beta_-} = \frac{\beta_{\text{counter-ion}} - \beta_{\text{co-ion}}}{\beta_{\text{counter-ion}} + \beta_{\text{co-ion}}}$$

This coefficient scheme allows a rational description of the electrokinetic and osmotic effects occurring in fine-pored ion exchange membranes. For example, insertion of $\Delta c = 0$ and $J = 0$ in equations (31a)–(31c) gives the following equation for the streaming potential:

$$\Delta\varphi = -\frac{L_{Jp}}{L_{J\varphi}}\Delta p = \frac{\omega}{FX}\frac{\tau}{\tau + a + U}\Delta p \quad (\Delta c = 0,\ J = 0)$$

The other electrokinetic phenomena are obtained in a similar manner. The experimental results generally agree satisfactorily with the predicted behavior if an effective value X_{eff} is used for the concentration of fixed ions. X_{eff} can be determined from an electrokinetic experiment and is usually very much smaller than the analytical concentration X. This indicates that a large proportion of the fixed ions are trapped in "blind alleys" or weakly swollen zones of the membrane matrix, and are therefore electrokinetically inactive [84].

Ion exchange membranes also exhibit certain peculiarities in their osmotic behavior toward electrolyte solutions. How can a difference in osmotic pressure occur at a membrane whose pore diameter is much greater than the diameter of the dissolved particles? The reason for this is that the interaction between the ions of the dissolved salt and the membrane matrix is due to long-range Coulomb forces. If the concentration of fixed ions is sufficiently high, the reflection coefficient σ can assume values close to 1. On the other hand, negative σ values can also occur at ion exchange membranes. This means that if the volume transport is suppressed, an excess pressure builds up on the side of the dilute solution, in direct contrast

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[82] *P. Läuger*, Ber. Bunsenges. physik. Chem. *68*, 352 (1964).

[83] *P. Läuger*, unpublished.

[*] Since "flows" and "forces" are not conjugated in equations (31a)–(31c), the Onsager symmetry relations (eq. (3)) take the form $L_{Sp}/c = L_{Qp} + L_{Qc}/2RT$, $L_{S\varphi}/c = L_{Q\varphi} + L_{Jc}/2RT$, $L_{Q\varphi} = L_{Jp}$. These relations are satisfied by equations (32).

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with the behavior at a semipermeable membrane. The theoretical interpretation of these osmotic anomalies was provided by *Schlögl*, who was the first to calculate the potential and pressure profiles inside an ion exchange membrane. For a binary electrolyte solution:

$$\sigma = \Delta p/\Delta\pi = \Delta p/2RT\,\Delta c \quad (J = 0,\ Q = 0) \tag{33}$$

Introducing $J = Q = 0$ into equations (31a)–(31c), we obtain

$$\sigma = \frac{1}{2RT}\,\frac{L_{Q\varphi}L_{Jc} - L_{J\varphi}L_{Qc}}{L_{J\varphi}L_{Qp} - L_{Jp}L_{Q\varphi}} = 1 - \frac{2zc/X}{U + \sqrt{1 + (2zc/X)^2}} \tag{34}$$

Thus the reflection coefficient depends on the concentration ratio c/X and on the difference U in the ion mobilities [equation (32)]. For any $U < 0$ (co-ions more mobile than counter-ions), there is a range of values of c/X in which σ becomes negative. This has been repeatedly confirmed by experiment. Thus *Schönborn* and *Woermann* [85] showed that negative σ values occur at an anion exchange membrane with HCl as the electrolyte ($U < 0$), with a minimum of $\sigma \approx -0.11$ at $c/X \approx 0.16$.

Under isobaric conditions ($\Delta p = 0$), volume transport occurs from the concentrated to the dilute electrolyte solution if the reflection coefficient is negative ("negative osmosis"). Since the activity of water is higher in the dilute than in the concentrated solution, negative osmosis is practically synonymous with incongruent transport of water. The salt transport may also be congruent or incongruent [75]. Figure 8 shows the lines $Q = 0$ and $S = 0$, which separate the domains of congruent and incongruent transport in the $(U, X/zc)$ plane [81].

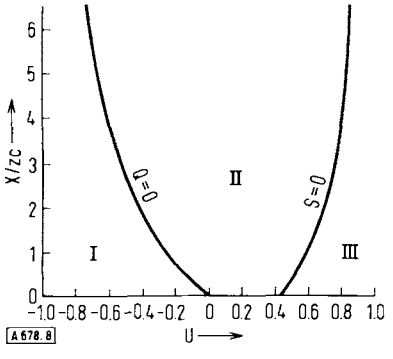


Fig. 8. Osmotic phenomena at an ion exchange membrane ($J = 0$, $\Delta p = 0$).

Region I: Volume transport Q negative, water transport Φ_W incongruent, salt transport S congruent.
Region II: Q positive, Φ_W congruent, S congruent.
Region III: Q positive, Φ_W congruent, S incongruent ($\tau = 2.0$) (see eq. (32)).

5.3. Phenomena in Composite Ion Exchange Membranes

Interesting phenomena are observed at membranes that contain both anion and cation exchange elements. The two simplest combinations are shown in Figure 9.

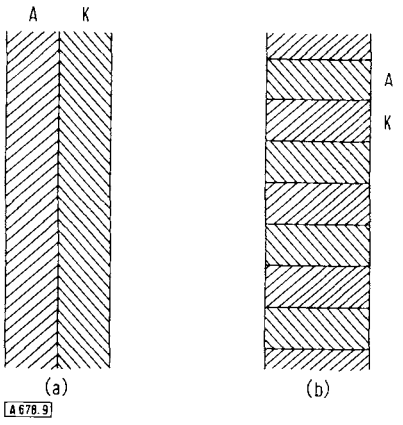


Fig. 9. Formation of composite membranes from anion (A) and cation exchange elements (K).
(a) Sandwich membrane.
(b) Mosaic membrane.

If the individual elements are arranged in series, the result is a "sandwich" membrane, while arrangement in parallel leads to a "mosaic" membrane. These basic structures are also found in biological membranes.

Experiments with synthetic anisotropic membranes were described by *Wilbrandt* [86] as early as 1935. However, a theoretical survey of the possible effects was published much later, by *Kedem* and *Katchalsky* [87]; in particular, these authors formulated the combination rules which allow calculation of the behavior of the composite membrane from the properties of the individual elements.

5.3.1. Sandwich Membranes

Membranes consisting of two parallel anion and cation exchange layers (Fig. 9a) have remarkable electrical properties; for example, they act as rectifiers. This behavior is due to the fact that the charge transport in an ion exchange membrane having a high fixed-ion concentration takes place almost exclusively by migration of counter-ions. Thus an anion-conducting phase and a cation-conducting phase come into direct contact at the interface between the A and K layers of a sandwich membrane.

If there is a potential difference $\Delta\varphi$ between the external solutions (*e.g.* 10^{-2} M NaCl on both sides), so that electric current flows in the membrane from the K layer to the A layer, Na^+ ions migrate to the interface in the K layer and Cl^- ions in the A layer. An appreciable current can be maintained in the membrane in the steady state when the current flows in this direction; NaCl is formed at the interface, and diffuses back into the external phases. If, on the other hand, $\Delta\varphi$ has the opposite sign, the ions in both layers migrate away from the interface. This leads to an increased charge unbalance in the contact zone. At high external voltages, practically the entire voltage appears as a space-charge-induced potential drop across the interface, so that only a small current can flow.

The theoretical description of this rectifier effect is relatively simple if a perfectly symmetrical system is

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[87] *O. Kedem* and *A. Katchalsky*, Trans. Faraday Soc. *59*, 1918, 1931, 1941 (1963).

considered, *i.e.* if it is assumed that the fixed-ion concentrations X in the two layers are equal and that the cation and anion have equal diffusion coefficients ($D_+ = D_- = D$). The current density J is then given approximately by

$$J = J_g \left(e^{\frac{\Delta\varphi}{RT/F}} - 1 \right) \tag{35}$$

$$J_g \equiv \frac{2c^2FD}{bX} \tag{36}$$

(c = concentration of the 1:1 electrolyte in the external phases, b = thickness of the individual layer). The current-voltage curve (eq. (35)) is shown in Figure 10.

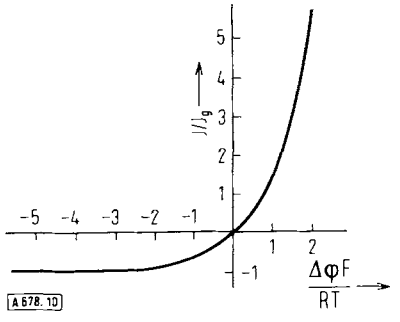


Fig. 10. Current-voltage characteristic of a sandwich membrane consisting of a cation exchange layer and an anion exchange layer (eq. (35)).

For $J > 0$ (forward direction), the current density increases exponentially with the voltage. For $J < 0$ (reverse direction), the current density can never rise above the limiting current density J_g. These predictions are confirmed by experiment [88–100].

Membranes of this type are analogous to pn-type rectifiers [90, 94].

Sandwich membranes are also useful as model systems in which the coupling between chemical reactions and transport processes can be investigated (cf. Section 4.6). *Blumenthal*, *Caplan*, and *Kedem* [101] studied the membrane system

anion exchange membrane (A)	neutral layer containing papain	cation exchange membrane (K)

An amide $R-CONH_2$ is added to the aqueous external phases as an electrically neutral "substrate", which diffuses to the intermediate layer, where it is hydrolyzed by the enzyme papain:

$$R-CONH_2 + H_2O \xrightarrow{\text{papain}} R-COO^- + NH_4^+ \tag{37}$$

Since the electrically charged hydrolysis products tend to leave the membrane by different routes ($R-COO^-$ mainly through the A layer, and NH_4^+ mainly through the K layer), a potential difference is set up between the external phases. Accordingly, an electric current can be drawn from the system, as long as the reaction (37) proceeds from left to right. These experiments show that chemical reactions and transport processes (charge transport in this case) can in fact be coupled in anisotropic membranes.

5.3.2. Mosaic Membranes

In mosaic membranes (Fig. 9b), the total flow of a given particle is made up additively from the flows through the individual elements. The phenomenological coefficients of a mosaic membrane can be obtained from the coefficients of the individual elements [87]. This gives a coefficient scheme similar to (32), which becomes particularly simple for a symmetrical mosaic membrane (A and K elements identical apart from the charge sign) [102].

According to theoretical predictions, the electrochemical properties of mosaic ion exchange membranes are quite different from those of normal ion exchange membranes. For example, the sign of the membrane potential should depend on the ratio of the areas of the A and K elements; this has recently been experimentally confirmed by *Woermann* [103]. Whereas normal ion exchange membranes are practically impermeable to electrolytes at high fixed-ion concentrations, mosaic membranes are characterized by an unusually high salt permeability [104, 105].

This is explained as follows. If all the elements were electrically insulated from one another, potential differences of opposite sign would be set up over the A and K elements when the external solutions have different concentrations. Since adjacent elements are in reality short-circuited *via* the external solutions, the potential differences cancel out and ring currents flow, transporting anions in the A elements and cations in the K elements from the concentrated into the dilute salt solution [104, 106]. In this way the salt permeability of a mosaic membrane can assume values much higher than those of the free solution [87].

The existence of ring currents in the membrane has another important consequence. Owing to the hydro-

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[102] *P. Läuger*, Abh. dtsch. Akad. Wiss. Berlin, Kl. Med. *1966*, 291.
[103] *D. Woermann*, Ber. Bunsenges. physik. Chem. *71*, 87 (1967).
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[105] *F. de Körösy*, Nature (London) *197*, 685 (1963).
[106] *C. W. Carr* and *K. Sollner*, Biophysic. J. *4*, 189 (1964).

dynamic interaction between ions and water molecules, the migrating ions in A and K elements transport water from the dilute to the concentrated salt solution. Negative osmosis is therefore to be expected in mosaic membranes. The reflection coefficient for a symmetrical mosaic membrane is theoretically given by the equation [102]

$$\sigma = 1 - \sqrt{1 - (X/2zc)^2} \qquad (38)$$

As expected, σ is always negative. The approximation $\sigma \approx -X/2zc$ can be used at high fixed-ion concentrations ($X \gg c$). Thus pressure differences many times greater than the equilibrium pressure difference $\Delta\pi$ (eqs. (11) and (12)) should occur in osmotic experiments with mosaic membranes.

According to equation (13), the reflection coefficient σ also determines the filtration behavior of the membrane; for $\sigma < 0$, the solute is enriched in the filtrate. On filtration of a dilute salt solution through a mosaic membrane having a high fixed-ion concentration, the filtrate should be a highly concentrated salt solution. This interesting effect has not yet been verified experimentally.

Received: May 22, 1968 [A 678 IE]
German version: Angew. Chem. *81*, 56 (1969)
Translated by Express Translation Service, London

The Chemistry of Hypervalent Molecules[**]

By J. I. Musher[*]

Molecules formed from atoms of Groups V–VIII of the periodic table in their higher valences are studied and a general theory for their electronic and geometric structure is presented. These molecules, which we call hypervalent molecules, are unique in that a donor atom can possess two identical monovalent ligands which are bonded by different types of chemical bonds. The present study provides a simple theoretical description of such molecules using doubly-occupied lone-pair orbitals to form hypervalent bonds, and these bonds are divided into two classes as to whether they involve p electrons alone or utilize s electrons as well. While the theoretical classification is of some interest in itself, there are even more interesting problems concerning the physico-chemical properties of these molecules and the syntheses of new molecules and polymers. We thus present a brief description of the energetics, possibilities for intermolecular inversion and site-exchange, and synthetic paths for the preparation of hypervalent molecules, as well as indicate a number of new molecules which can probably be synthesized using these ideas.

1. Introduction

The Lewis-Langmuir theory of valence attributed the stability of molecules to their ability to place their valence electrons, appropriately paired off as chemical bonds, into "stable octets" [1, 2]. This theory can be said to have survived the advent of quantum mechanics with the electron-pairs being replaced by doubly-occupied molecular orbitals or approximately-localized bond orbitals, and with the "cubical atom" being replaced by the directed valences of p-bonds, so that undistorted bonds form along perpendicular axes rather than on corners of tetrahedra. Both the classical empirical theory and the modern quantum mechanical theory have been quite successful in treating molecules formed from atoms in their lowest valences such as PH_3, H_2S, and Cl_2, and the molecular orbital theory has had some success in treating coordination complexes of metal ions [3]. However, both types of theories have encountered considerable difficulties in treating the molecules formed by atoms of Groups V–VIII of the periodic table in their higher valences (*e.g.* PCl_5, $(CH_3)_2SO$, and $HClO_4$), with the classical theory referring to "expanded octets" and the quantum mechanical theory invoking d orbital participation in hybridization schemes involving large promotion energies [4]. The fact that these molecules have never received a good theoretical treatment but have some-

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[**] This work was supported in part by the National Science Foundation and the van Leer Fund of the Weizmann Institute of Science.

[1] *G. N. Lewis*, J. Amer. chem. Soc. *38*, 762 (1916).

[2] *I. Langmuir*, J. Amer. chem. Soc. *41*, 868 (1919).

[3] See *C. A. Coulson*: Valence. 2nd Edit., Oxford University Press, Oxford 1961; *C. J. Ballhausen* and *H. B. Gray*: Molecular Orbital Theory. Benjamin, New York 1964; *L. Pauling*: Nature of the Chemical Bond. 3rd Edit., Cornell University Press, New York 1960; *R. J. Gillespie* and *R. S. Nyholm*, Progr. in Stereochem. *2*, 261 (1958).

[4] See, *e.g. P. Palmieri* and *C. Zauli*, J. chem. Soc. (London) C *1967*, 813; *R. J. Gillespie, ibid. 1952*, 1002.

how always been considered as exceptions to the rule, has had the unfortunate consequence that many interesting aspects of their chemistry have been almost completely neglected by the modern chemist.

The present article is devoted to a discussion of molecules formed from higher valence atoms from a new and different point of view, in which the ground atomic configuration, as distinguished from the usual "valence state", is used as the determining factor in the molecular structure. After developing a most natural and straightforward MO theory for these molecules, we go on to discuss their unique physicochemical properties, and predict the stability of a number of new molecules and polymers, a few of which have already been synthesized [5].

We classify as "hypervalent" molecules and ions all those molecules and ions formed by elements in Groups V–VIII of the periodic table in any of their valences other than their lowest stable chemical valence of 3,2,1, and 0 respectively. We refer to these molecules as *hypervalent* (or HV) since they involve atoms, called donor atoms, which exceed the number of valences allowed them by the traditional theory, and thus utilize more electron-pairs of bonding than provide stability in the Lewis-Langmuir theory. As hypervalent molecules have chemical formulas, and often the molecular structure, of the addition product of a stable molecule with two monovalent ligands or a single divalent ligand they could also be called hypermolecules or "molecules made out of molecules" [6].

The hypervalent molecules are by no means obscure despite the fact that they have received highly inadequate consideration in the literature. They include a number of molecules first obtained in the early days of chemistry, such as PCl_5, ICl_3, and $SeCl_4$ which were prepared by *Davy, Gay-Lussac,* and *Berzelius* respectively in the years 1810, 1814, and 1818 [7]. They also include such common molecules as dimethyl sulfoxide, phosphine oxide, and iodosylbenzene, and most acids such as chloric, phosphorous, and sulfuric acids. In discussing some of these, *Moffitt* felt obliged to say "the structure of the sulphoxides and sulphones has been a point of dissension since the earliest days of valency theory [8]."

In recent years interest in some of the HV molecules has been reawakened by the spectacular discovery of the xenon fluorides in 1962. This discovery led to the publication of a number of theoretical papers on the inert gas halides with a few of these recognizing the similarity of such molecules to the classic halides PF_5, SF_4, and ClF_3 [6, 10–12]. None, however, recognized the relationship to the hypervalent oxides and sulfides, the significant difference between the p-bonded molecules SF_4, ClF_3, and XeF_2, and the molecules PF_5, SF_6, and IF_7 which also utilize the s-electrons of the donor atom. Furthermore, the application of such ideas to synthetic and physical chemistry has not previously been considered. The generality of the description of the xenon fluorides was observed by *Waters* and *Gray* who said that "the inert gas halides fit naturally into the sequence of halides of the non-metallic elements in their higher valence states" [11] and by *Rundle* in the converse sense, "From this discussion [on the polyhalide ions] it should be clear that a simple extrapolation was all that was needed to predict the rare gas fluorides" [12] although he went on to note that such an application of the theory is "not impressive after-the-fact" which was especially pertinent as he had previously gone on record against the whole idea of applying the polyiodide ion theory to molecules, as well as to other interhalogen ions [13].

On the experimental side there has been some interest shown in the properties of hypervalent molecules within the past few years particularly by *Muetterties* [14], *Cady* [15], *Holmes* [16], and their co-workers who performed NMR studies on a number of new (and old) HV compounds of sulfur and phosphorus. Other studies have used electron diffraction [17], IR [18], Raman [18], and Mössbauer spectroscopy [19] on a number of HV halides and the now classic studies of *Cornwell* and *Yamasaki* [20] examined the iodine chloride ions with EQR. The recent literature has also showed a number of differing opinions as to the interpretation of some of the experiments on hypervalent molecules [21].

In the present article a classification of the hypervalent molecules is developed by observing the several significant features which distinguish them from "octet" molecules. We first note that only in HV molecules can there exist two different types of single bonds on a given atom so that this atom is able to undergo isomerization, and that only in HV molecules can two single bonds be actually colinear. We then recognize that in a number of HV molecules, such as SF_4 and ICl_3, the pairs of colinear bonds to monovalent ligands can be described in terms of MO's – using a doubly-occupied p orbital on the donor atom in the ground atomic configuration – in the manner now accepted for the xenon fluorides follow-

[5] a) *W. C. Agosta*, Tetrahedron Letters *31*, 2681 (1965) – For a similar As-containing compound see *J. T. Braunholtz* and *F. G. Mann*, J. chem. Soc. (London) *1957*, 3285; b) *H. K. Livingston, J. W. Sullivan*, and *J. I. Musher*, J. Polymer Sci., Part C, *1968*, 195; *J. I. Musher*, Bull. Amer. physic. Soc. *9*, 286 (1964).

[6] *J. I. Musher*, Science (Washington) *141*, 736 (1963).

[7] a) *H. Davy*, Phil. Trans. *100*, 231 (1810); *101*, 1 (1811); b) *J. L. Gay-Lussac*, Ann. chim. Physique (1) *91*, 5 (1814); c) *J. J. Berzelius*, Acad. Handl. Stockholm *39*, 13 (1818).

[8] *W. Moffitt*, Proc. Roy. Soc. (London) Ser. A *200*, 409 (1950).

[9] *C. A. Coulson*, J. chem. Soc. (London) *1964*, 1442; *H. H. Hyman*: Noble Gas Compounds. University of Chicago Press, Chicago 1963.

[10] *K. S. Pitzer*, Science (Washington) *139*, 414 (1963).

[11] *J. H. Waters* and *H. B. Gray*, J. Amer. chem. Soc. *85*, 825 (1963).

[12] *R. E. Rundle*, J. Amer. chem. Soc. *85*, 112 (1963).

[13] *R. J. Hach* and *R. E. Rundle*, J. Amer. chem. Soc. *73*, 4321 (1951); see also [12] and *R. E. Rundle*, Survey Progr. Chemistry *1*, 81 (1963).

[14] a) *E. L. Muetterties* and *W. D. Phillips*, J. Amer. chem. Soc. *79*, 322, 2975 (1957); b) *81*, 1084 (1959); c) *W. Mahler* and *E. L. Muetterties*, J. chem. Physics *33*, 636 (1960); d) *E. L. Muetterties*, J. Amer. chem. Soc. *82*, 1082 (1960); e) *R. M. Rosenberg* and *E. L. Muetterties*, Inorg. Chem. *1*, 756 (1962); f) *E. L. Muetterties, W. Mahler*, and *R. S. Schmutzler, ibid. 2*, 613 (1963).

[15] a) *H. E. Kluksdahl* and *G. H. Cady*, J. Amer. chem. Soc. *81*, 5285 (1959); b) *J. M. Shreeve* and *G. H. Cady, ibid. 83*, 4521 (1961); c) *C. I. Merrill, S. M. Williamson, G. H. Cady*, and *D. F. Eggers jr.*, Inorg. Chem. *1*, 215 (1962); d) *G. H. Cady* and *C. I. Merrill*, J. Amer. chem. Soc. *84*, 2260 (1962).

[16] a) *R. R. Holmes* and *W. P. Gallagher*, Inorg. Chem. *2*, 433 (1963); b) *R. R. Holmes* and *R. N. Storey, ibid. 5*, 2146 (1966).

[17] *K. W. Hansen* and *L. S. Bartell*, Inorg. Chem. *4*, 1775 (1965); *L. S. Bartell* and *K. W. Hansen, ibid. 4*, 1777 (1965).

[18] *G. C. Hayward* and *P. J. Hendra*, J. chem. Soc. (London) *A 1967*, 643.

[19] *C. L. Chernick et al.*, Physics Letters *5*, 103 (1963).

[20] a) *C. D. Cornwell* and *R. S. Yamasaki*, J. chem. Physics *27*, 1060 (1957); *30*, 1265 (1959); b) *J. C. Evans* and *G. Y.-S. Lo*, Inorg. Chem. *6*, 836 (1967); J. physic. Chem. *71*, 2730 (1967).

[21] a) *R. J. Gillespie*, Inorg. Chem. *5*, 1634 (1966); b) *L. S. Bartell, ibid. 5*, 1635 (1966); c) *E. L. Muetterties* and *W. D. Philips*, J. chem. Physics *46*, 2861 (1967); d) *R. L. Redington* and *C. V. Barney, ibid. 46*, 2862 (1967).

ing the ideas of *Pimentel*[22] and *Rundle*[13]. This leads to the observation that when divalent ligands bond to these same donor atoms, they lie almost along the same axis as the pair of monovalent ligands, and we realize that the same type of theory can be applied to these molecules as well. The next and last step is to note that the bonds in molecules like PF_5, SF_6, IF_7, and $(CH_3)_2SO$ cannot be described in terms of doubly-occupied p orbitals since the donor atoms have reached their maximum possible valence and consequently all valence electrons including the s electrons must be used; the molecular geometry therefore takes on the highest possible symmetry, as is the case with methane.

While this classification scheme includes a large number of molecules either left out of, or inadequately represented by, the octet scheme, and variously rationalized but not in any uniform manner over the years by the quantum theory[3], it does not pretend to include all or even most molecules. The various electron-deficient molecules, and radical species, *etc.*, which are being discovered almost daily must probably remain outside any such general scheme. We have thus the benefit of considerable chemical experience, unavailable to *Lewis* and *Langmuir*, which enables us to recognize that no single empirical or theoretical picture of valence can be applied or should be distorted to fit all known molecules.

We are, however, more interested in the new aspects of physicochemical studies and the syntheses of new varieties of "non-metallo-organic" molecules that this study might encourage, than in the classification scheme itself. How deleterious an effect an oversimplified theory can have is exemplified by the fact that the chemistry of hypervalent molecules was an active area of investigation until publication of the Lewis-Langmuir theory which showed such molecules to be exceptional and ionic. From that time on their chemistry has been almost meticulously avoided by mainstream chemists until perhaps the past few years.

2. Definition and Classification

Consider the formation of chemical bonds to the representative atoms in Groups V-VIII of the periodic table, P, S, Br, and Xe. The simple quantum mechanical description of an ordinary chemical bond[3] combines one atomic orbital, singly-occupied in the ground configuration, from the donor atom with one from the ligand, to form a bond orbital or localized approximate molecular orbital,

$$\psi = \psi_d + \lambda\psi_l$$

into which the two electrons are to be placed, or the valence-bond analog thereof. Stability of molecules is inferred, for the most part, when all singly-occupied atomic orbitals are involved in chemical bonds, which, as there are 8 electrons in each atomic shell, explains why *Lewis* and *Langmuir* deduced stability empirically for electronic octets. Thus, the ground atomic configurations $P(s^2p_xp_yp_z)$, $S(s^2p_x^2p_yp_z)$, $Br(s^2p_x^2p_y^2p_z)$, and $Xe(s^2p_x^2p_y^2p_z^2)$, have, according to Hund's rule, lowest stable valences of 3, 2, 1, and 0, respectively, and form molecules such as PF_3, SCl_2, BrF, and Xe. We henceforth refer to the chemical bond so formed as covalent or CV to distinguish it from the types of bonds formed in hypervalent molecules. The simple theory argues that CV bonds should be essentially oriented along perpendicular axes, in accord with the experimental bond angles of 100° found for both PF_3 and SCl_2, and with the angles of 93.5° and 92.1° found for the corresponding hydrides PH_3 and SH_2[23].

Notice that the concept of stability we use refers to thermodynamic stability in the restricted sense in which the atoms are in local minima of potential energy even though these systems can dissociate such as by tunneling to form ion pairs; on the other hand, molecules containing an unpaired electron can be excluded – not a fully consistent procedure but relatively free of ambiguity. Thus, we are not interested in the kinetic stability which governs the lifetime of molecules in certain chemical and physical environments except insofar as to recognize that, for example, it might be their kinetic instability which makes molecules of divalent carbon atoms so rare. Also, for this argument, we explicitly refer to the ground atomic configuration since the (unobserved) diatomic molecule PF could also be considered stable when the fluorine is bonded by a CV bond to the excited atom $P(s^2p_x^2p_y)$ which now has all of its electrons paired. In this sense the octet theory was based on the fact that Hund's rule does not permit such an electron configuration as the ground state of an atom. It should be observed that the phrase "lowest stable" valence does not imply "most probable" valence, since for example, by analogy, carbon $(s^2p_xp_y)$ has the "lowest stable" valence of 2, even though the only atoms of the same configuration which have a significant number of known divalent molecules are tin and lead.

On examination of the remaining non-bonding atomic electrons ("lone pair" electrons) of the CV bonded atoms $P'(s^2)$, $S'(s^2p_z^2)$, $Br'(s^2p_x^2p_y^2)$, and $Xe(s^2p_x^2p_y^2p_z^2)$ we find that the non-bonding parts are different from those of the phosphorus (and from all elements in Groups I–V of the periodic table) in that they have respectively one, two, and three pairs of doubly-occupied p orbitals. When these atoms "expand" their valence by adding ligands, *e.g.* as in forming SCl_4, BrF_3, and XeF_2 they add them colinearly and along the axis of one of these pairs of p electrons, with little distortion to the remainder of the previously existing molecule. It thus seems reasonable to infer that these two p electrons provide the binding to the two ligands in bond wave functions of the form

[22] *G. C. Pimentel*, J. chem. Physics *19*, 446 (1951).

[23] Thoughout this paper, bond lengths and angles are taken from Tables of Interatomic Distances and Configurations in Molecules and Ions and Supplement, Special Publications 11 and 18 of The Chemical Society (London) (1958, 1965); and *A. F. Wells*, Structural Inorganic Chemistry, 3rd Edit., Oxford (1962) unless otherwise indicated.

$$\psi_1 = \psi_d + \lambda\psi_a$$
$$\psi_2 = \psi_d + \lambda\psi_b$$

where a and b refer to the singly-occupied orbitals on each of the ligands and d refers to the donor atom p orbital, the signs being appropriately chosen. We call this type of bond, and its analog for divalent ligands, *hypervalent*, or HV, and it is distinguished from covalent (CV) bonds by using only one donor orbital to form two HV bonds, as in the theory of the polyhalide ions first proposed by *Pimentel* [22], and *Hach* and *Rundle* [13]. The same argument can be seen to explain the formation of the square pyramidal BrF_5, the square planar XeF_4, and the approximately octahedral [24] XeF_6, as well as the molecules obtained by replacing each pair of monovalent ligands by a divalent ligand, such as Cl_2SO where the ClSO angle is 106°, $HOIO_2$ where all the OIO angles are 98°, and XeO_3 where the angles are ~103° [25]. Thus we can explain all molecules containing atoms of Groups VI, VII, and VIII in their valences 4, 3, and 5, and 2, 4, and 6 respectively in a unified manner in terms of hypervalent bonds, the more detailed theory of which will be discussed in Section 3. Such molecules are referred to as "hypervalent molecules of the first class" (or HV_I) since they represent most but not all of the hypervalent molecules.

It is easy to observe that atoms cannot attain their highest valences – 5, 6, 7, and 8 for atoms in Groups V–VIII – by bonding to pairs of p electrons since in the lower valence states, *i.e.* 3, 4, 5, and 6, all the p electrons are already used for either CV or HV bonding, or equivalently, there are already bonds along each of the three perpendicular axes through the donor atom. This necessitates the use of the remaining pair of non-directional, *i.e.* spherically symmetric, s electrons in forming the last pair of single bonds or the last double bond – as, for example, in PF_5, SF_6, IF_7, and XeO_4. (The donor atoms are actually of the highest possible valence for the neutral atoms in each group only because experience shows that inner shell electrons apparently do not form chemical bonds in the non-metals. Such molecules can nevertheless be considered to be particularly stable because of the inability of the donor atoms to increase their valence still further.) Based on the highly symmetrical geometry of all the molecules in this classification – which we call "hypervalent molecules of the second kind" (or HV_{II}) – it seems reasonable to suppose that the last two bonds are not formed with the two s electrons as such, but that the molecular structure of minimum energy requires complete electronic and geometric reorganization. Thus, for example, PF_5 in which the donor atom s^2p^3 electrons are used for the bonding is a trigonal bipyramid, SO_3 and SF_6 which use s^2p^4 electrons are planar and octahedral respectively, IF_7 which uses s^2p^5 electrons has the highest possible symmetry of a pentagonal bipyramid that a 7-membered system, with of necessity three-dimensional structure, can have, and XeO_4 using s^2p^6 electrons is tetrahedral (further examples are given in Section 4). Notice that in this sense methane is like an HV molecule in that it requires use of its atomic s electrons and electronic reorganization, or hybridization, it possesses a structure of the highest possible symmetry, and does not easily undergo chemical reaction [26]; furthermore it has little in common with the accepted bonding scheme for the CV molecules of atoms in Groups V–VII discussed above. In the same sense SiF_6^{2-} is an HV_{II} type ion with an electronic structure similar to that of the molecule SF_6.

Hypervalent molecules and ions are thus of two kinds and consist of the class of molecules and ions formed from elements in Groups V–VIII in valences other than their lowest stable valence.

Hypervalent molecules of the first kind can be characterized as being formed from existing molecules by the addition of two colinear monovalent ligands or a single divalent ligand such that the structure of the original molecule is essentially preserved. The hypervalent bonds utilize for the most part the doubly-occupied p orbitals on the donor atom.

Hypervalent molecules of the second kind can be characterized as being formed from existing molecules by the addition of two monovalent ligands or a single divalent ligand to bring the donor atom to its highest possible valence, such that the resultant geometry is governed principally by steric factors, the electronic structure bearing no obvious relation to that of its predecessor.

It is important to recognize the fact that in hypervalent molecules there are two different types of bonds: HV bonds using doubly-occupied p orbitals and CV bonds using singly-occupied p orbitals, and also the pseudo-HV (colinear pair) and pseudo-CV analogs in HV_{II} molecules. This occurrence of two non-equivalent ligands has no parallel in all of classical octet-theory chemistry, since the usual tri-coordinated molecules are always trigonal or pyramidal and the usual tetra-coordinated molecules are always tetrahedral (although as noted above there is a question as to these molecules possessing strictly CV bonds).

Because of the different types of bonds it is useful to have a notation which distinguishes between the possible isomers: A prime is used to signify that a monovalent (or when necessary a divalent) ligand is HV, so that, for example, the four isomers of SF_2Cl_2 would be written as SF_2Cl_2', SCl_2F_2', $SFClF'Cl'$ (d and l). The appelations "equatorial" and "axial" for CV and HV bonds respectively that have been used previously, particularly for molecules with Group V donors, have explicitly not been used for two simple reasons: First, their use is based on the idea that all of these molecules are trigonal bipyramids [27], which although true for PF_5,

[24] It does not seem productive to place great emphasis on the apparent deviation from octahedral symmetry of this molecule at the present time. The simple description presented here is intended only to provide the zeroth-order description, there surely being mixing in of other orbitals, as discussed by *Gillespie*, steric effects, and the like. Thus, we have also not been concerned with the fact that bond angles almost always deviate from the idealized 90° and 180°, ICl_4^-, XeF_2, and XeF_4 being exceptional in that they do not so deviate.

[25] *P. H. Templeton, A. Zalkin, J. D. Forrester*, and *S. M. Williamson*, J. Amer. chem. Soc. *85*, 817 (1963).

[26] Cf. *J. I. Musher* in *L. van Gerven*: Magnetic Resonance and Relaxation in Solids. North-Holland, Amsterdam 1965, p. 360ff.

[27] *E. L. Muetterties* and *R. A. Schunn*, Quart. Rev. (chem. Soc., London) *20*, 245 (1966).

etc., is difficult to accept for the others, and as no one has as yet observed "lone pairs" experimentally it does not seem reasonable to consider them in a steric sense as ligands[28]. Second, the geometrical non-equivalence of HV and CV bonds should not be confused with that of the equatorial and axial CH bonds in cyclohexane. The latter are non-equivalent only due to the geometry of their second neighbors while the former are non-equivalent due to essentially different electronic bonding.

The fact that hypervalent molecules have two different types of chemical bonds has two most interesting and important consequences for their chemistry (in addition to the trivial observation that they possess different quantities for physico-chemical measurement such as bond lengths, bond energies, acidities, reactivities, and chemical shifts, spin-spin splittings, and quadrupole coupling constants if the nuclei are magnetic): (1) there is the unique possibility of their undergoing (unimolecular) geometrical isomerism upon a single atom, with one type of bond converting to another, either by vibrations or rotations, as well as the less unusual intermolecular processes for exchanging of sites; and (2) as distinguished from traditional chemistry in which almost any combination of monovalent ligands can form the appropriate number of CV bonds to almost any donor atom, the limited experience with HV molecules shows that not all atoms can serve as donor atoms, nor can all monovalent functional groups serve as HV ligands in each given case. This allows for a larger number of interesting physico-chemical and synthetic studies than has hitherto been recognized.

Tables 1 to 4 contain examples of the numerous types of HV_I molecules, both with monovalent and divalent ligands, and of a small number of HV_{II} molecules. From these examples, and particularly from Table 1, which leaves blanks where no appropriate molecule has yet been found, it can be seen that HV molecules are more likely to exist the larger the donor atom and the lower the group in the periodic table, and the higher the electronegativity of the ligand. This statement is, of course, an oversimplification, but as has previously been observed it does provide a relatively reliable first approximation[6,9,10].

Included among the HV molecules in the Tables are all the "onium" salts even though it is well known that the solid-state structures of some of them, particularly the ammonium salts, are strictly ionic with tetrahedral coordination about the N atom. This has been done, however, for a number of reasons: (1) X-ray studies on the highest member of the series, $C_6H_5IC_6H_5'Cl'$ have shown it to have the same dimeric T-shaped geometry as ICl_3[29]; (2) the diphenylbromonium and chloronium iodides undergo some reactions which *Nesmeyanov*[30] has been able to explain only through "covalent" structures; (3) the molecule $(C_6H_5)_3P(OH)_2$ has been described by *Sidgwick*[31a] as being wholly covalent; (4) molecules such as $C_6H_5ICl_2$ and $C_6H_5I(CH_3COO)_2$ which are also

Table 3. Hypervalent molecules of the second (HV_{II}) kind with monovalent ligands [a].

Group VIII	–
Group VII	IF_7
Group VI	SF_6, SF_5OF, SF_5NSF_2 [b], SeF_6, $Te(OH)_6$, $Te(OCH_3)_6$
Group V	PF_5, $P(OCH_3)_5$, $P(C_6H_5)_5$, PF_4CF_3', $As(C_6H_5)_5$, $Sb(CH_3)_5$, $Sb(CF_3)_3Cl_2$, $[(CH_3)_3N(OH)_2]$, $[(CH_3)_3N(OH)I]$, $[(CH_3)_4AsCl]$

[a] Molecules indicated in brackets are of unknown non-ionic structure.
[b] *B. Cohen, T. R. Hopper,* and *R. D. Peacock,* Chem. Commun. *1966,* 32.

Table 4. Hypervalent molecules of the second kind (HV_{II}) with divalent ligands.

Group VIII	XeO_4
Group VII	OIF_5, $HOIO_3$, $FClO_3$, $HOClO_3$, $O_3ClOClO_3$
Group VI	SO_3, $(HO)_2SO_2$, Cl_2SO_2, $(CH_3)_2S(O)CH_2$, $(C_6H_5)_2SeO_2$
Group V	$(CH_3)_3NO$, Cl_3PO, Cl_3PS, $(HO)_3PO$, $(HO)_2HPO$, $(C_6H_5)_3PCHSO_2CH_3$

Table 1. Hypervalent molecules of the first kind with monovalent ligands [a].

Donor-atom	Ligand							
	F	other halogens	OR	C_6H_5	Fluoroalkyl	NR_2	SR	Alkyl
Xe	XeF_2, XeF_6	$XeCl_2$	$Xe(OAc)_2$ [b]	–	–	–	–	–
Kr	KrF_2	$KrCl_2$	–	–	–		–	–
I	IF_5	ICl_3, $C_6H_5ICl_2$	$C_6H_5I(OAc)_2$	$(C_6H_5)_3I$, $C_6H_5ICl'C_6H_5'$	–	benziodazoles [c]	–	–
Br	BrF_3	$[(C_6H_5)_2BrI]$	$Br(ONO_2)_3$	$[(C_6H_5)_2BrI]$	–	–	–	–
Cl	ClF_3	$[(C_6H_5)_2ClI]$	–	$[(C_6H_5)_2ClI]$	–	–	–	–
Te	TeF_4	$(CH_3)_2TeCl_2'$	$(C_6H_5)_2Te(ONO_2)_2$	$(C_6H_5)_4Te$	–	–	–	$[(CH_3)_3TeCl]$
Se	SeF_4	$(C_6H_5)_2SeBr_2'$	$C_6H_5Se(OH)_2ONO_2$	$(C_6H_5)_4Se$	–	–	–	$[(CH_3)_3SeCl]$
S	SF_4	SCl_4	$(CH_3)_2S(OH)ONO_2$	–	$SF_3[(CF_3)_2CF]'$	–	–	–
O	–	$[(C_6H_5)_3OBr]$	–	$[(C_6H_5)_3OBr]$	–	–	–	–

[a] Molecules indicated in brackets are of unknown non-ionic structure.
[b] *J. I. Musher,* unpublished. [c] *W. Wolf* and *L. Steinberg,* Chem. Commun. *1965,* 449.

Table 2. Hypervalent molecules of the first kind (HV_I) with divalent ligands.

Group VIII	XeO_3, $OXeF_4$.
Group VII	C_6H_5IO, $C_6H_5IO_2$, $HOIO_2$, $HOClO$, $HOClO_2$
Group VI	O_3 [a], SO_2 [a], $(CH_3)_2SO$, $C_6H_5Se(OH)O$, Cl_2TeO, F_2SNSF_5 [b]

[a] See Section 4. [b] *B. Cohen, T. R. Hopper,* and *R. D. Peacock,* Chem. Commun. *1966,* 32.

[28] Cf. also [17].

[29] *T. L. Khotsyanova,* Doklady Akad. Nauk SSSR *110,* 71 (1956).

[30] *A. N. Nesmeyanov, L. G. Makarova,* and *T. P. Tolstaya,* Tetrahedron *1,* 145 (1957).

[31] a) *N. V. Sidgwick:* The Chemical Elements and their Compounds. Oxford University Press, Oxford 1950, p. 733; b) see *R. Manne,* Theoret. chim. Acta *6,* 312 (1966) for an approximate calculation.

usually described as ionic have been shown to have bonds of the HV type; and (5) the structures of many of these compounds in the gas phase, or non-aqueous solution, is unknown. The solid state structure of $NH_4^+Cl^-$ should not be generalized since crystal forces can significantly change the structure, *e.g.* PCl_5 crystallizes as $PCl_4^+PCl_6^-$; PCl_5 and $(C_6H_5)_5P$ are now accepted as being non-ionic pentacoordinated molecules, why then should $(C_6H_5)_4PCl$ be singled out as a "phosphonium salt"? In fact, most of the HV molecules have been explained theoretically since the days of *Lewis* and *Langmuir* only on the basis of their being salts and it might be in part due to the theory and the "onium" nomenclature that the covalent or hypervalent nature of these molecules has not been previously given serious consideration. Thus, it seems likely that compounds with five-coordinated nitrogen can be prepared – *e.g.* a molecule analogous to compound *(9)* (cf. Section 7 and Ref. [5a]; the I atom is replaced by an N atom whose two "free" valences are occupied by phenyl groups).

3. Theory

From the types of existing HV molecules we can deduce empirically the qualitative condition governing the formation of hypervalent bonds to be simply that: there must be a particularly strong electronic affinity between the donor atom whose valence is to be increased and the monovalent or divalent ligand to be added. An electronic affinity, of course, must exist for the formation of ordinary covalent bonds, but must be significantly greater here in order to be able to decouple and delocalize the paired electrons in the donor atom of the already stable covalent molecule. The somewhat more quantitative statement of this is that (a) the first ionization potential of the donor atom must be relatively small (which is why Sb is most likely and He least likely to serve as donor atoms); and (b) the ligand must have a relatively high electronegativity (which is why F forms HV bonds to almost all atoms and CH_3 forms them only to Sb if the "onium salts" are excluded).

It is these qualitative ideas which are included in, and serve as, the justification for the simple theory developed in this section. There will, of course, be numerous additional factors, both steric and electronic in origin, which cannot be generalized and also cannot be rationalized by even the best of the theoretical schemes presently available. It would be these factors which might exclude the existence of HV molecules such as $AsCl_5$ and CH_3ICl_2, despite their "theoretical" likelihood, if such molecules truly cannot be prepared. Furthermore, since the formation of HV_{II} molecules involves the reorganization of the pseudo-CV bonds themselves, their nature will also have a significant effect on the stability of the resultant molecules and bond energies cannot be considered as additive.

It would be highly desirable if current methods of theoretical chemistry were able to provide us with accurate wave functions for molecules as complex as even the simplest HV molecules PF_5, SF_4, and ClF_3 [31b], and if they were able to provide us with interpretations of these wave functions in terms of the limited sets of valence functions on which we "base" our "understanding" of the structure of molecules. It is doubtful that theory will ever answer the second of these wishes to the precision which the semi-empiricist expects of it. Nevertheless, it remains useful to consider, in the simplest possible way, reasonable, although crude, electronic structures for HV molecules, so that one can feel somewhat confident about their existence and their mutual relationships; furthermore, in contrast to the complicated theories invoked to explain the structures of all the new electron-deficient boron compounds and other exotic molecules of modern chemistry, the simple theory of HV-bonding is in fact simple. Many researchers have attempted to make other such simple theories quantitative in order to approximate the results that would be obtained by the exact solutions; we are rather of the opinion – on the basis of experience with small molecules, for which we have much better wave functions, but still no "understanding" of *e.g.* the dipole moment of NH_3 or the bond angle in H_2O – that such approximations can at best be deceptive.

The simple theoretical description of bonding in hypervalent molecules and ions presented here is based on the procedure used by *Pimentel* [22] and *Rundle* [13], and extended by *Havinga* and *Wiebenga* [32], for bonding in the polyhalide ions, and later applied by *Pitzer* [10], *Rundle* [12], and *Jortner et al.* [33] to the xenon fluorides. As shown in the Tables 1 to 4, there are essentially four types of hypervalent compounds, and we indicate here the theory for only one molecule of each type, taking as examples the sulfur compounds, SF_4, F_2SO, SF_6, and SO_4^{2-}, the theory for almost any other HV molecule being described in an exactly analogous manner. Only the form of the wave function is indicated in each instance, since as observed above we feel that calculations "can only lead to a symbolic and not always convenient restatement of these [physical and electronic] properties when they are already known", to quote *Moffitt*'s remarks on valence-bond theory calculations out of their original context [34].

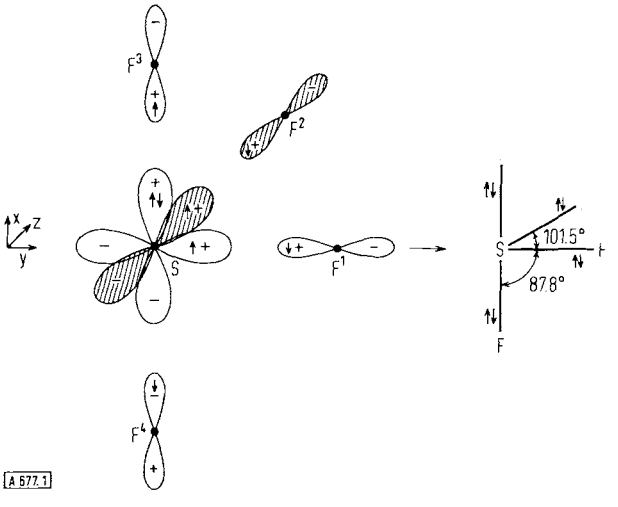


Fig. 1. The electronic and geometrical structure of SF_4.

[32] *E. E. Havinga* and *E. H. Wiebenga*, Recueil Trav. chim. Pays-Bas *78*, 724 (1959); *E. H. Wiebenga*, *E. E. Havinga*, and *K. H. Boswijk*, Advances inorg. Radiochemistry *3*, 133 (1961).

[33] *J. Jortner*, *S. A. Rice*, and *E. G. Wilson*, J. chem. Physics *38*, 2302 (1963).

[34] See [8], p. 410.

SF_4 is formed from the donor atom $S(s^2p_x^2p_yp_z)$ and four fluorine atoms oriented with their holes, or singly-occupied p orbitals, located two along the x-axis and one each along the y- and z-axis (Fig. 1). In the simple description of the CV molecule SF_2 the p_y and p_z orbitals, from both the fluorine atoms and the sulfur atom, are paired to form bond orbitals (or bonding "MO's"),

$$\psi_1 = \psi_{S(y)} + \mu\psi_{F^1}$$

and

$$\psi_2 = \psi_{S(z)} + \mu\psi_{F^2}$$

each of which is doubly-occupied, and where the parameter μ which determines the polarity of the bond can be obtained variationally, the functions being orthogonalized to each other and to the core orbitals if so desired. There remain in the molecule SF_2 non-bonding electrons which are essentially those electrons that were already paired off in the atomic configurations, including the core electrons. Thus the $3p_x^2$ electrons on the sulfur atom are available for HV bonding to the fluorine atoms F^3 and F^4. These bonds are formed by taking linear combinations of the single p_x sulfur orbital and each of the two p_x fluorine orbitals to form what look like ordinary polar bonds (or bonding MO's)

$$\psi_3 = \psi_{S(x)} + \lambda\psi_{F^3}$$

and

$$\psi_4 = \psi_{S(x)} + \lambda\psi_{F^4}$$

each of which is doubly occupied and where the polarity parameter λ is to be determined variationally.

The reason that stable HV bonds occur only in pairs is trivially seen to be due to the fact that both the decoupled p_x electrons from the sulfur have to be used in some form of bonding. These orbitals, so formed, differ from the usual bonding orbitals only in that the same sulfur orbital, $\psi_{S(x)}$, is used in two different bonds, and consequently the two functions, ψ_3 and ψ_4, have larger overlaps than the CV bond functions ψ_1 and ψ_2. Thus when the bond orbitals are orthogonalized, there will be more ψ_{F^4} in the orthogonalized ψ'_3 than there will be ψ_{F^2} in ψ'_1.

When the simple orbitals ψ_3 and ψ_4 are combined with the third linearly independent orbital

$$\psi_0 = \psi_{F^3} + \psi_{F^4}$$

provided by the limited basis set of $\psi_{S(x)}$, ψ_{F^3}, and ψ_{F^4}, and the matrix of coefficients diagonalized, the so-called delocalized three-center bonding orbital and non-bonding orbital, analogous to the functions given in the previously mentioned works of *Rundle* [12], *Pimentel* [22], and *Jortner et al.* [33], which are to be doubly-occupied in the MO scheme, are obtained. These can then be made again into localized or equivalent orbitals which are of the form

$$\psi'_3 = \psi_{S(x)} + \alpha\psi_{F^3} - \beta\psi_{F^4}$$
$$\psi'_4 = \psi_{S(x)} + \alpha\psi_{F^4} - \beta\psi_{F^3}$$

where α and β are constants, and these functions are the "best" functions that a minimal basis set MO calculation can provide. *Coulson* [9] has given an explicit illustration of such equivalent orbitals for the p bonding in XeF_2 as

$$\psi'_1 = \psi_{Xe} + 1.71\ \psi_{F^1} - 0.29\ \psi_{F^2}$$
$$\psi'_2 = \psi_{Xe} + 1.71\ \psi_{F^2} - 0.29\ \psi_{F^1}$$

so that the degree of "delocalization" is not very high, but the bonds are quite polar.

Notice the similarity of these functions to the equivalent orbitals *Coulson* obtained from an analogous calculation for methane many years ago [35], where the tetrahedral CH bond orbital was given by

$$\psi_1 = 2.56\ \psi_s + 2.94\ \psi_p + 3.31\ \psi_{H^1} - 0.69\ (\psi_{H^2} + \psi_{H^3} + \psi_{H^4})$$

in terms of 2s- and tetrahedrally directed 2p-orbitals of the carbon, the hydrogen 1s-orbital along the tetrahedral axis, and those along the three other tetrahedral axes. This illustrates the fact that just as for HV bonds, where the atomic orbitals involved in two bonds need not be orthogonal (they are one and the same) so, too, when there is any mixing of atomic orbitals or hybridization, the resultant atomic orbitals need not even be approximately orthogonal. The hybridization ratio of s to p functions in CH_4, for example, is seen to be 1:1.3 instead of 1:3 as is required by orthogonality. The same type of function will occur below when we treat HV_{II} molecules which is why we argue the similarity of CH_4 to SF_6, and have previously suggested the discarding of the accepted usage of orthogonalized hybrids as zeroth-order approximate wave functions [26].

Whether a stable SF_4 molecule can be formed according to this conception depends on the values of the parameters α and β – for example if α becomes very large ψ'_3 and ψ'_4 become essentially $2p_x$-orbitals on the fluorine atoms F^3 and F^4 – and these in turn depend on the molecular integrals. The molecular integrals themselves depend on the choice of exponents in the atomic orbitals, the estimate of the core potential, *etc.*, in the more exact method, or on the Hückel-type parameters in the SCF-Hückel procedures, all of which are related, but only qualitatively, to the electron affinity of F and the ionization potential of S. Thus the quantitative results that can be obtained by going through the calculation using different values of these parameters can give no information other than the qualitative requirements on the electron affinity and ionization potential that we had deduced empirically from the start.

There is probably very little qualitative difference between the simple bond orbital theory presented here and the Hartree-Fock theory (the "best" orbital theory) or the minimal basis set LCAO–MO theory (the most commonly used theory which includes all the electrons). These more accurate theories will differ from the simple theory as regards HV bonds mostly in that they will mix the $2p_x$ doubly-occupied orbitals of the CV bonded F atoms with the $3p_x$ doubly-occupied orbital of the S atom. There will thus be three doubly-

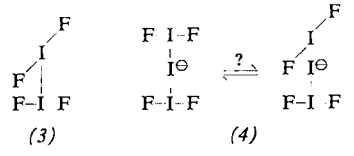
[35] *C. A. Coulson*, Trans. Faraday Soc. *38*, 433 (1942).

occupied x orbitals which could give HV bonding. However, these orbitals can be transformed so that they are essentially located one on each of the atoms S, F^1, and F^2, and since we know that the F atom does not have a low enough ionization potential to donate electrons to form HV bonds this clearly does not change our qualitative result at all. Had we instead started with the CV molecule SCl_2 and considered the addition of two fluorine atoms, we would have found, both by the bond orbital description and by the complete minimal basis set MO theory, that the two molecules *(1)* and *(2)* are likely to be formed, as well



(1) *(2)*

as SCl_2F_2', the analog of SF_4. It should be emphasized that on the basis of our present experience, such wild looking molecules as these, and the propellor shaped molecule *(3)* suggested previously [6] as well as its ionic analog *(4)*



(3) *(4)*

should be stable at least in the thermodynamic sense. Judging from the ease of making the usual interhalogen molecules and their kinetic stability, it should be quite possible to prepare such molecules in gas phase reactions (cf. Section 6). A particularly likely reaction to try would be

$$ICl + 2F_2 \rightarrow a\ I(F_2)Cl(F_2) + b\ I(F_4)Cl + c\ ICl(F_4).$$

The molecule F_2SO can be considered as related to SF_4 by having the two HV F atoms replaced by the single divalent oxygen atom which is bonded to the S atom using the orbitals sketched in Fig. 2. Thus, after

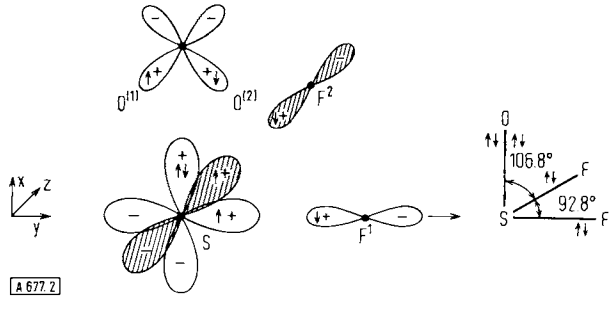


Fig. 2. The electronic and geometric structure of OSF_2.

the formation of SF_2, the two S–O bonds, *i.e.* the HV "double" bond, otherwise known as "dative", "co-ordinate-link", "dπ-dπ", *etc.*, can be described as

$$\psi'_3 = \psi_{S(x)} + \alpha\psi_O^{(1)} - \beta\psi_O^{(2)}$$
$$\psi'_4 = \psi_{S(x)} + \alpha\psi_O^{(2)} - \beta\psi_O^{(1)}$$

where

$$\psi_O^{(1)} = -2^{-1/2}(\psi_{O(x)} + \psi_{O(y)})$$
$$\psi_O^{(2)} = -2^{-1/2}(\psi_{O(x)} - \psi_{O(y)})$$

and the constants α and β as before are calculated variationally and depend on the assumptions made for the molecular integrals. The analog of "delocalized" MO theory wave functions, as in the literature for the xenon fluorides [12, 33], although not given explicitly above, has simply

$$\chi_1 = \psi_{S(x)} + \lambda\psi_{O(x)} \quad \text{(bonding, occupied)}$$
$$\chi_2 = \psi_{O(y)} \quad \text{(non-bonding, occupied)}$$
$$\chi_3 = \lambda\psi_{S(x)} - \psi_{O(x)} \quad \text{(anti-bonding, unoccupied)}$$

From this description, albeit oversimplified, the polar nature of the bond, and the necessity for the high electron affinity of the ligand are readily appreciated. In this sense, one can argue for the validity of the ionic structure $F_2S^+O^-$ which preserves the "octet" picture as emphasized by *Rundle* for the analogous case of XeF_2 [12]. We prefer not to give too much weight to this argument, since in addition to its being excessively model-dependent, it assumes arbitrarily that the bonding orbital χ_1 is non-polar, which it clearly is not.

The organic chemist may, however, continue to write the ylides as $R_2S^+C^-RR'$ with perfect equanimity. It is more cumbersome, however, to write SF_4 as $S^+F_2(F^{-1/2})_2$ and, not only more cumbersome, but more ambiguous to write SF_6 or PF_5 (or for that matter, CH_4) in the appropriate analogous manner. Incidentally, the similarity, among the various oxides of S, Se, I, *etc.*, which justifies empirically their receiving similar theoretical treatment, has been noted by a number of authors, among them *Sidgwick* [36], who has observed that "there is a marked resemblance between diphenyl selenoxide, $(C_6H_5)_2SeO$, and iodosobenzene, C_6H_5IO ... and a similar parallel may be instituted between diphenyl selenone, $(C_6H_5)_2SeO_2$, and iodoxybenzene, $C_6H_5IO_2$". Thus, it is of interest, for example, to search for ylides of I and Xe by analogy with S and Se.

While the HV_I molecules are simply described in terms of "molecules made out of molecules" without rearrangement or hybridization of electronic or geometric structure, such is clearly not the case for HV_{II} molecules. The hypervalent molecules of the second kind must involve a somewhat different description since, for example, there are not three doubly-occupied p orbitals in the ground configuration of $S(s^2p^4)$ to use in making the three pairs of colinear bonds in SF_6. Notice, however, that in the theory of HV_I molecules we dropped from the very beginning the traditional restriction that the atomic orbitals involved in bonding to different atoms be orthogonal, since actually we used a single orbital to form two bonds, and it was this restriction which had necessitated the introduction of d orbitals with their high "energy of promotion" in the traditional hybridization scheme [3]. With

[36] Cf. [31], p. 964.

the relaxation of this unnecessary and undesirable restriction, we can immediately describe the bond orbitals for SF_6. The ground hybridized "configuration", involving no energy of promotion, is $S(s^2p_x^{4/3}p_y^{4/3}p_z^{4/3})$ from which can be constructed six non-orthogonal sp^2 hybrids pointing towards the faces of an octahedron

$$\psi_{S(a)} = 3^{-1/2}(\psi_S + \sqrt{2}\,\psi_x)$$
$$\psi_{S(b)} = 3^{-1/2}(\psi_S - \sqrt{2}\,\psi_x), \textit{ etc.}$$

From these hybrid orbitals we construct the bond orbitals

$$\psi_a = \psi_{S(a)} + \lambda\psi_{F^1}$$
$$\psi_b = \psi_{S(b)} + \lambda\psi_{F^2}, \textit{ etc.}$$

where ψ_{F^1} and ψ_{F^2} are the p_x orbitals of the two fluorine atoms along the x axis. When the minimal basis-set six-electron problem is solved in the usual simple way and the solution is transformed into equivalent orbitals, the bonds will be described by wave functions of the form

$$\psi'_a = \psi_a + \alpha\psi_b + \ldots$$

or equivalently

$$\psi'_a = \psi_{S(a)} + \lambda'\psi_{F^1} + \alpha'\psi_{S(b)} + \alpha''\psi_{F^2} + \ldots$$

where the α's are relatively small. However, since there is no clear dividing line between pure CV bonds and pure HV bonds once some hybridization is introduced, we refer to these bonds in SF_6 as pseudo-HV just because they are colinear; for the same reason we refer to PF_5 as containing two pseudo-HV bonds and three pseudo-CV bonds.

There are, of course, other ways to describe the bonds in SF_6, just as there are other ways to describe the bonds in HV_I molecules, one such way being to use atomic geminals

$$\varphi_a(1,2) = 3^{-1/2}[\psi_S(1)\psi_S(2) + \sqrt{2}\,\psi_x(1)\psi_x(2)]$$

but there is no particular advantage to indicate these further at this time. It should be remembered that the exact wave function for SF_6 will be far different from any wave function we might describe here no matter how "rigorously" it has been obtained.

The HV description of a molecule such as SF_6, all of whose bonds are identical, is relatively unambiguous, whereas the HV description of, say PF_5, can utilize different amounts of s hybridization in the pseudo-CV and the pseudo-HV bonds, since these bonds can never be considered equivalent. Thus, for example, for PF_5, we can use the "configuration" $P(s^2p_x^2p_y^{1/2}p_z^{1/2})$ to form two pure HV bonds with the doubly-occupied p_x orbital, and three pseudo-CV bonds with the non-orthogonal s^2p hybrid orbitals

$$\psi_a = 3^{-1/2}(\sqrt{2}\,\psi_s + \psi_z)$$
$$\psi_{b,c} = 3^{-1/2}(\sqrt{2}\,\psi_s - \tfrac{1}{2}\psi_z \pm \frac{\sqrt{3}}{2}\psi_y)$$

or we can use the configuration $P(s^2p_xp_yp_z)$ to form pseudo-HV bonds with the usual and orthogonal sp hybrids

$$\psi_{d,e} = 2^{-1/2}(\psi_s \pm \psi_x)$$

and pseudo-CV bonds with the usual sp^2 hybrids

$$\psi'_a = 3^{-1/2}(\psi_s + \sqrt{2}\,\psi_z)$$
$$\psi'_{b,c} = 3^{-1/2}(\psi_s - \frac{\sqrt{2}}{2}\psi_z \pm \frac{\sqrt{6}}{2}\psi_y)$$

which are orthogonal among themselves but are not orthogonal to the sp hybrids, or we can use any intermediate configuration. Clearly the physical properties of molecules like PF_5 will differ from the properties of HV_I and other HV_{II} molecules as the details of the actual bonding schemes differ or are similar. The best that could be hoped for would be that the "axial" bonds of PF_5 are pure HV so that they could be compared with those of HV_I molecules, but there seems no way to evaluate the likelihood of this occurring at the present time. Incidentally, the fact that the PF bond length in PF_3 (1.53_5 Å) is exactly the same as the pseudo-CV bond length in PF_5 (1.534 Å)[17] argues for some but not too much electronic reorganization, as the CV bonds in CV and HV molecules, *e.g.* BrF(1.756 Å) and BrF_3(1.721 Å), generally differ by $\gtrsim 0.02$ Å. (In BrF_5 the CV bond length is 1.68 Å.)

The last example we describe here is the negative ion SO_4^{2-} made from the fully occupied M shell of $S^{2-}(s^2p_x^2p_y^2p_z^2)$ where the relative ionization potential which governs the formation of HV bonds is an average of the values for the electrons of S^{2-} in place of an average over the values for neutral S. The doubly-occupied orbitals can now be rewritten as orthogonal sp^3 hybrid orbitals (which we do not feel to be justifiable for the case of neutral carbon) and the simple bond orbital scheme will be exactly the same as that for F_2SO except that the orbital $\psi_{S(x)}$ will be replaced by the sp^3 hybrid orbitals, a, b, c, and d, and the $\psi_{O(x)}$ and $\psi_{O(y)}$ orbitals will be replaced by the four pairs of orbitals, $\psi_{O(a)}$, $\psi_{O(a\perp)}$, *etc.* Thus we can write, in terms of the "delocalized MO" or "ionic" description, as distinguished from the bond-orbital or equivalent orbital description,

$$\chi_1 = \psi_{S(a)} + \lambda\psi_{O(a)}$$
$$\chi_2 = \psi_{O(a\perp)}$$
$$\chi_3 = \psi_{S(b)} + \lambda\psi_{O(b)}, \textit{ etc.}$$

In this example, however, the orthogonalized equivalent orbitals will mix the "non-bonding" (χ_2, χ_4, *etc.*) into the bonding functions (χ_1, χ_3, *etc.*) so that they will not be of the simple form as for F_2SO. Furthermore, one has to choose a different axis at each oxygen atom so that the results are not affected by the arbitrary choice of the perpendicular singly-occupied orbitals. However, there is nothing new in principle and the procedure for obtaining these wave functions is straightforward.

It would be interesting to speculate as to why so many molecules and ions made from atoms in their highest valence states have such unusual kinetic stability. The present theory does not afford any significant clue as to why this should be so, other than the relatively obvious one that these molecules are unable to form even quasistable intermediates through an additive step, all the possibilities for bonding already being utilized.

4. Geometry of Some Ions

The ideas discussed in Section 3 can be applied directly to numerous specific problems in structural inorganic chemistry and we only present here the description of a few inorganic ions in order to illustrate how the theory applies in specific examples. It is assumed that these are actually ionic, being in either the solid state or in an ionizing solvent, so that they are truly represented as possessing unit quantities of electronic charge. Furthermore, the extra charge is assumed to be localized on the donor atoms for the purpose of determining the atomic configuration – an assumption which is then immediately removed by the allowance for arbitrary polarity of the bonds through the parameter λ in the bond orbitals.

Consider first the two octahedral ions PCl_6^- and $SeBr_6^{2-}$. The atomic configuration of the phosphorus atom is s^2p^4 so that all the bonding is with rearranged s-p orbitals and the ion is of the HV_{II} type, analogous to SCl_6 with which it is isoelectronic. The atomic configuration of the selenium atom is, however, s^2p^6 so that all the bonding is with p orbitals, and the ion is of the HV_I type with the s electrons inert, being isoelectronic to $KrBr_6$.

Now consider the very stable tetrahedral ions SO_4^{2-} and IO_4^- in both of which the donor atomic configurations are s^2p^6. These ions are both of HV_{II} type and possess four sp^3 HV double bonds. The donor atoms, being bound with an octet of bonds using 16 electrons, have reached the maximum valence possible under usual chemical conditions; the ions are isoelectronic respectively with ArO_4 (and ClO_4^-) and XeO_4 (and TeO_4^{2-}). The differences therefore between PCl_6^-, $SeBr_6^{2-}$ and, say IO_4^-, are that PCl_6^- and IO_4^- are both HV_{II} while $SeBr_6^{2-}$ is HV_I, but the phosphorus of PCl_6^- could in principle increase its valence to form PCl_6^{3-} as in the known PO_4^{3-}, whereas IO_4^- is of maximum possible valence. This explains in a different way from the octet theory, but in agreement with its results, why ions such as IO_5^{3-} are not formed; the atomic configuration $5s^25p^66s^2$ involves too great a difference in energies among the atomic orbitals for them to be utilized together. From the stability of these s^2p^6 ions it would seem that octacoordinated molecules with monovalent ligands are not formed more often due to the steric difficulties involved in getting eight atoms to approach sufficiently closely to provide stable bonds.

Since we have considered the tetrahedral ions SO_4^{2-}, IO_4^-, and PO_4^{3-} it is of interest to point out that the remaining oxy-ions and simple oxides also have similar geometries due to the same considerations. Thus SeO_3^{2-}, XO_3^- (with X = Cl, Br, and I), and presumably SO_3^{2-} are all distorted right pyramids, with bond angles of $\sim 100°$ since they utilize only the p electrons in s^2p^6 configurations; NO_3^- and the molecule SO_3 are both planar as they involve reorganization of the atomic configuration s^2p^4 to use all the electrons, and thus have a symmetrical structure; ClO_2^- is approximately L shaped (bond angle of 110 °), four chlorine p electrons taking part in the bonding. The less-approximately L shaped molecules SO_2 and O_3, with bond angles of 120 °, would presumably have non-equivalent oxygens if the bonding followed the typical HV pattern using the p_x and p_y electrons to form a double CV bond, and the p^2 electrons to form the HV double bond. However, as opposed to other HV molecules, the "ionic" orbital on the HV-bonded oxygen could mix with the ordinary π bond on the other two atoms, and this must lead to rearrangement of the electron configuration to agree with the symmetrical molecular structure observed experimentally. Notice, incidentally, that despite the trivial planarity of these molecules the use of the s^2 for bonding instead of the p^2 electrons is ruled out by analogy with SF_4 and F_2SO, both of which would be planar if the bonding did not use the $p_x^2p_yp_z$ electrons. This is an explicit demonstration of what has been presupposed throughout the paper: that p bonds are more easily formed than s bonds, as is expected from the relative energies of the various atomic configurations. Notice that CO_2 is linear since it involves the s electrons in s^2p^2, and so is analogous to SO_3; notice also that the geometry of the sulfuryl halides *e.g.* F_2SO_2 is such that by replacing the two halogens with an oxygen along the bisector of the XOX angle it gives exactly the planar molecule SO_3.

The "unusual" ions SbF_5^{2-} [23] and the recently discovered XeF_5^+ [37a] are isoelectronic with IF_5 and therefore it is no great surprise that they have approximately square pyramidal structures, as does IF_5; such a structure is accounted for by considering each of the species to be built from the atomic configuration s^2p^5 with the s electrons not greatly involved in the bonding. As with all HV_I molecules the ligands are somewhat bent towards each other, even in the gas phase in which there are no crystal interactions to add to the distortions. We feel that the significance attributed to these relatively small distortions and the common reference to these molecules as "distorted octahedra", with the "lone pair" electrons assigned a physical site as if they were actually observed, to be quite unwarranted. Due to the crude nature of even the best theoretical calculations presently available on these molecules no argument can be given with sufficient accuracy to show

[37] a) *N. Bartlett, F. Einstein, D. F. Stewart,* and *J. Trotter,* J. chem. Soc. (London) *A 1967,* 1190; b) *J. L. Huston,* J. physic. Chem. *71,* 3339 (1967); *H. H. Claasen, E. L. Gasner, H. Kim,* and *J. L. Huston,* J. chem. Physics *49,* 253 (1968).

that the s electrons are anything other than "essentially" inert [24,28,31b].

Let us now examine an instance of positive and negative ions of the same chemical composition, ICl_2^- and ICl_2^+. The first of these is linear, like I^-, and has the configuration s^2p^6; it is therefore an HV_I linear ion, which is most likely formed from ICl_3 by breaking the CV bound chlorine atom off as Cl^+. Notice that since this happens quite easily the HV bonds are less ionizable, *i.e.* less reactive, under certain conditions, than is the CV bond. In the cation on the other hand the iodine has the configuration s^2p^4, as in Te, so that ICl_2^+ is expected to be an L shaped CV ion – as is actually observed. For ICl_2^+ to have been linear would have required the HV bonds to exist on an atom where covalent valences were not already "saturated", which is contrary to all previous experiences. As a final example we consider $F_2IO_2^-$ which has FIF and OIO bond angles of 180° and 100° respectively just as would be expected for an HV_I ion with an atomic configuration s^2p^6, and is isoelectronic with the as yet unknown F_2XeO_2 [37b]. When the two fluorines in this ion are replaced by single divalent oxygen, the position of the latter deviates only 9° from the axis along which the two fluorines lay, with the angle between the remaining oxygens being distorted only 1° (within experimental error); the new ion IO_3^- is a symmetrical approximate right pyramid with bond angles of 99°, and of the same geometry as the molecule XeO_3 (OXeO angle of 100°) [25]. When a proton is added to make the molecule $HOIO_2$ the angles remain roughly the same and approximately equal (98 ± 3°), again as we would expect.

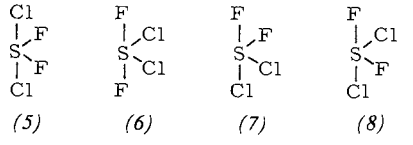
In concluding this section we would like to emphasize that it is not at all the iso-electronic nature of some of these ions with each other and with stable molecules that makes them take on analogous geometries and be stable. It is rather the fact that when the extra electron or hole can be considered as located on the donor atom, the addition of an electron during anion formation leads to the breaking of one CV bond (or to the formation of an HV double bond from a single CV bond) and at the same time to the stabilization of the HV bonds because the new ionization potential is lower; the removal of an electron to form the cations allows one CV bond to form where there had previously been two HV bonds, and this compensates sufficiently to let the rare example of Xe^+ in XeF_5^+ be able to donate electrons to the HV bonds. Thus, we do not subscribe to the analogy between HF_2^- and HeF_2, since the exceptionally low ionization potential of H^- (≈0.7 eV), which (crudely speaking) permits the formation of HF_2^-, becomes replaced by the drastically higher I.P. of He (24 eV). If helium could actually donate its electrons to form the proposed HeF_2 [38], which one cannot rule out despite all theoretical attempts to do so, then probably almost all combinations of atoms such as HeH_2 will also make HV molecules.

[38] *G. C. Pimentel* and *R. D. Spratley*, J. Amer. chem. Soc. *85*, 826 (1963).

5. Geometrical Isomers

Among the most interesting consequences of the occurrence of two types of bonds in hypervalent molecules should be the existence of geometrical isomers which may possess different energies and be able to convert one to the other. However, until the present time, there has not been detected more than one isomer for any hypervalent molecule, although intramolecular inversion has been observed by NMR in the phosphorus pentahalides. The explanation for this is simple. Since the geometrical isomers involve different types of chemical bonds, as distinguished from isomers created in usual organic preparations which differ only in neighbor interactions, they will certainly differ in energy by several kcal/mole. Under equilibrium conditions only the energetically most favored isomer will be obtained.

The argument is best appreciated by considering a specific example, such as the (hypothetical) group of molecules of chemical structure SF_2Cl_2 of which there are four isomers, two of which being mirror images of each other.



(5) *(6)* *(7)* *(8)*

If we could assume that the bond energies of these molecules were additive, and if we had an estimate either from theory or experiment of these bond energies, we should be able to predict the ordering of the energy levels, and thus the most energetically favorable isomer without having to perform a complete calculation for all four. Unfortunately the crude theory described above or any tractable modification of it are not sufficiently accurate to give theoretical bond energies, and the appropriate experiments have never been performed, so that all we can do here is indicate the type of argument involved and under what conditions each of the isomers is likely to be favored.

The only information we have available is that HV bonds between two atoms are likely to be of lower energy than the corresponding CV bonds, as can be deduced either from the theory described above, or from the limited experimental data. Thus, the XeF bonds being 30 kcal/mole, have an energy less than all other halogen–F bonds, and the energy involved in bonding the two pseudo-HV chlorines in PCl_5 is ≈40 kcal/mole (if electronic rearrangements are neglected) while the CV bond energies of PCl_3 are 79 kcal/mole. However, this information alone can make no prediction as to the more energetically favorable isomer, but can only show that as long as the energies are strictly additive the d,l pairs of isomers can never be of lower energy than the two symmetrical isomers. Thus unless all the isomers have just about the same energy, isomers *(7)* and *(8)* will never be observed in equilibrium mixtures.

The energies of isomers *(5)* and *(6)* can be given in terms of the bond energies as

$$\varepsilon_{(5)} = 2\,\varepsilon_{CV}(S-F) + 2\,\varepsilon_{HV}(S-Cl)$$

and

$$\varepsilon_{(6)} = 2\,\varepsilon_{HV}(S-F) + 2\,\varepsilon_{CV}(S-Cl)$$

If we take $\varepsilon_{CV}(S-F)$ and $\varepsilon_{CV}(S-Cl)$ to be -110 kcal/mole and -80 kcal/mole respectively, *i.e.* close to the values determined for PF and PCl bonds in CV molecules, then the relative energies depend only on the way the ε_{HV}'s are related to the ε_{CV}'s. It is here that theory could really help if it were in the position to do so. If the values are related by a constant fraction, say $^1/_2$, then $\varepsilon_1 < \varepsilon_2$ and the $\Delta\varepsilon$ which determines the thermodynamic populations is 30 kcal/mole, *i.e.* the ratio of *(5)* to *(6)* is e^{50} at room temperature. If their difference is constant, *i.e.* if, say $\varepsilon_{CV} - \varepsilon_{HV} = 40$ kcal/mole, which is not so unreasonable as it sounds since this would exclude HV bonds between atoms whose CV bond strength is < 40 kcal/mole (*e.g.* F_2), then $\varepsilon_{(5)} = \varepsilon_{(6)}$ and the populations of the four isomers would be equal. The third possibility, of $\varepsilon_{(5)} < \varepsilon_{(6)}$, is obtained if say $\varepsilon_{HV}(S-Cl) = 0.5\ \varepsilon_{CV}(S-Cl)$ while $\varepsilon_{HV}(S-F) > 0.64\ \varepsilon_{CV}(S-F)$, and if the latter ratio is 0.77 then $\varepsilon_{HV}(S-F) = -85$ kcal/mole and the ratio of *(5)* to *(6)* at room temperature is e^{-50}. Thus, small changes in the relative energies of the different bonds cause large changes in the populations as argued above.

It is a very interesting and, for the most part, uninvestigated question, as to which of these population ratios will occur in a given case. Since in most of the HV molecules the more electronegative substituent will have a larger ε_{CV}, the question can be formulated as whether the more or the less electronegative substituent will be in an HV bond in the energetically favored isomer. The experimental observation, based on the data given in Tables 1–4, that only electronegative substituents form HV bonds is not pertinent to this question since it implies that non-electronegative substituents have positive ε_{HV}'s and consequently that no such isomer would even form.

The majority of the experimental evidence we have that does bear on this problem is from HV_{II} mixed pentavalent phosphorus molecules, which shows that an isomer with a pseudo-HV fluorine and a pseudo-CV chlorine is energetically favorable, but that an isomer with a pseudo-HV CF_3 group and a pseudo-CV fluorine is energetically favorable [14–17]. The latter is argued to be due to steric interactions since CF_3 is less electronegative than F; on the other hand the CH_3 group is not "sterically hindered" when it is pseudo-CV in CH_3PF_4 and $(CH_3)_2PF_3$. The other experimental data on molecules is from the halides $(C_6H_5)_2SeX'_2$ and $(C_6H_5)_2TeX'_2$ which are observed to have HV halogens and not be of the structure $X_2Se(C_6H_5)'_2$ [18,31]. It might, however, be possible that these molecules have not been able to equilibrate – NMR studies have not, as yet, been performed on them – and the synthetic procedure might have permitted the formation of only the observed isomers.

Although this discussion has not given any detailed understanding of the energetics of HV molecules – it has not even distinguished between HV_I and HV_{II} molecules – it does nevertheless show that if equilibration among isomers is permitted, information on the stability of an isomer cannot be inferred from its absence among the reaction products. The only chance for obtaining this information is to find synthetic procedures by which to prepare the energetically unfavorable isomers directly and then observe them spectroscopically or otherwise before equilibration has time to take place. We now discuss some of the possible intramolecular and intermolecular mechanisms for such equilibration and in Section 6 we consider some possible synthetic pathways that might enable the preparation of these energetically unfavorable isomers.

The possibility of conformational inversion or intramolecular isomerization such as the exchange of one CV ligand for an HV ligand, *e.g.* in the conversion of the SF_2Cl_2 molecule *(5)* into isomers *(7)* or *(8)*, is a phenomenon unique to hypervalent molecules. It is unique since it involves a considerable change in the electronic distribution of two of the ligands, electrons which were involved in an ordinary CV bond having to distort in such a way as to partially couple with the electrons in the HV bond to which it is to become colinear, and *vice versa*, not to speak of the large amounts of energy which must be involved in such a process. The conformational inversions one is accustomed to in ethane and cyclohexane derivatives, and the racemization of optically active hydrocarbons involve no such drastic changes in electron structure and the relevant energy differences and barriers are only in the vicinity of 1 kcal/mole and 3–12 kcal/mole respectively, since it is just the next neighbor interactions that are changing, the bonds themselves retaining their usual character.

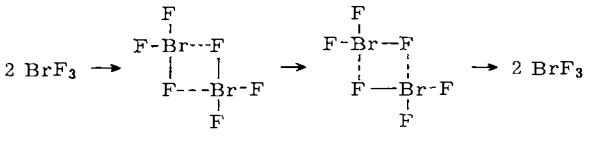
As to whether hypervalent molecules such as BrF_3, SF_4, and PF_5, can unimolecularly isomerize has not been considered theoretically outside of a classic paper by *Berry* [39], which, however, took no cognizance of the different types of bonds, so that at present we have no precise idea of what must be involved in this type of process. Our intuitive feeling is that the "barrier", if it really can be called that, would be inordinately high, so that if such molecules were infinitely dilute in inert gases at room temperature they would retain their configuration indefinitely. We should observe, however, as mentioned above, that the pseudo-CV bonds in PF_5 are quite different from the CV bonds in other molecules, and the "bond energies" might not be very different from the HV bond energies. In this case the intramolecular inversion would be less unfavorable than for other HV molecules ... to which can be added *Berry*'s arguments on the easier approach of pentavalent molecules to an inverted configuration *via* vibrations and rotations. The analysis of the

[39] *R. S. Berry*, J. chem. Physics *32*, 933 (1960).

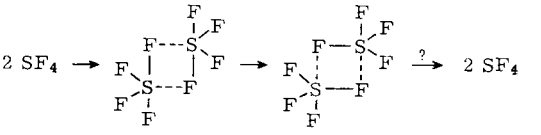
various "mechanisms" by which pairs of HV bonds can be uncoupled electronically to become CV bonds still remains the critical problem that has yet to be investigated.

The experimental side of this problem has also not received much attention and the experiments that have been performed using NMR spectroscopy to study the lifetimes of ligands in HV and CV sites have not been designed to distinguish between unimolecular inversion and site-exchange; these experiments can certainly be extended to give more significant results. (It should be recalled that in ethane and cyclohexane derivatives the unimolecular inversion is measured NMR spectroscopically since the rate for site-exchange from carbon bonds is relatively negligible.) Measurements on PF_5 and its derivatives have shown unimolecular inversion to take place since only then is the P–F spin-spin splitting retained when the F(HV)–F(CV) splitting disappears; the occurrence of a dimeric intermediate cannot be fully ruled out [40]. Recent studies on PF_3H_2 and PF_4H [16b], however, have shown site-exchange to take place, whilst in the case of PF_5 itself "unimolecular inversion" has never been slowed sufficiently to enable the NMR observation of the different ligands. The few experiments which have been carried out on BrF_3 and SF_4 have shown a dramatic concentration dependence, which has never been extrapolated to infinite dilution, but clearly indicates the presence of a dimeric process in the inversion [14b]. Site-exchange in SF_4 has also been inferred from the absence of ^{33}S spin-spin satellites [21c]; however, only high temperature experiments on highly dilute solutes, for which site-exchange can be ruled out, will give information on the minimum energy „barrier" for unimolecular inversion. It appears that appropriate studies are currently being undertaken in the laboratories of *Muetterties* and *Holmes* and perhaps within the next few years we will have a better understanding of some of these problems.

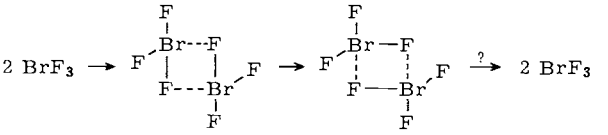
Since we have argued that true unimolecular inversion is not likely, it must, if NMR equivalence is established experimentally, be due to a chemical reaction which alone is sufficient to change electronic structures of chemical bonds. The most probable reaction – as postulated by *Muetterties et al.* [14] for BrF_3 and SF_4 – is one which involves the formation of dimeric intermediates. This is easily envisaged for the interhalogens as



since such dimeric structures have been observed in ICl_3 and $(C_6H_5)I(C_6H_5)'Cl'$ in the solid state [29] and there is also evidence for the dimeric behavior of these compounds in non-aqueous solution [41]. A similar mechanism has been proposed for the reaction in which two iodosobenzene molecules react to give iodoxybenzene and iodobenzene [42]. The same mechanism could also provide for the exchange of sites in SF_4, but would require the readjustment of not only bond lengths from the intermediate state, but bond angles as well, *i.e.*



since the intermediate state leaves the molecules as trigonal pyramids. This mechanism is analogous to the following scheme for site exchange in BrF_3



which differs from the previously suggested scheme by a 90° rotation of the BrF_3 molecules about the axis of the HV bonds. Such mechanisms are, of course, oversimplifications, but we agree with *Muetterties* [21c] that they are more likely explanations than the others which have been proposed. As to PF_5, any dimeric postulates (on the basis of site-exchanges or of intramolecular inversion) must at present be considered mere speculation, although one can make some arguments for site-exchange in the hydrofluorophosphoranes.

One further possibility for intramolecular inversion and site-exchange is afforded by ionization – a mechanism which usually takes place mostly in aqueous solution. Thus a study of the behavior of ligands in substituted diphenyliodonium chlorides cannot be performed in aqueous solution because the carbon-iodine bonds in the $(C_6H_5)_2I^+$ ion are equivalent and have CV character (see Section 4).

6. Synthetic Procedures

Since equilibration among the isomers of hypervalent molecules will result in only a single isomer being observable, it becomes important to look for stereospecific syntheses for each of the possible isomers so that they can at least be observed spectroscopically before they equilibrate, or even be prevented from equilibrating by freezing them onto rare gas matrices. The fact that there are two different types of bonds in an HV_I molecule only one of which occurs in the corresponding CV sub-molecule leads us to suspect the possibility that the reaction can be made to go with the retention of the original bonding structure. This

[40] A most recent and preliminary experiment reported by *S. Brownstein* [Canad. J. Chem. *45*, 1711 (1967)] argues for the likelihood of an intermolecular mechanism for the observed intramolecular site-exchange of fluorines in PF_5, and justifies this statement.

[41] *F. M. Beringer* and *M. Mausner*, J. Amer. chem. Soc. *80*, 4534, (1958).

[42] *I. Masson, E. Race*, and *F. E. Pounder*, J. chem. Soc. (London) *1935*, 1669.

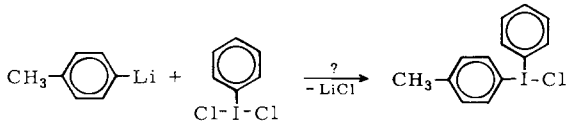
would be ideal since then we could prepare, for example, the four isomers of SF_2Cl_2 by the following procedures, assuming the existence of the (hypothetical) reactants:

$SF_2 + Cl_2 \rightarrow SF_2Cl'_2$

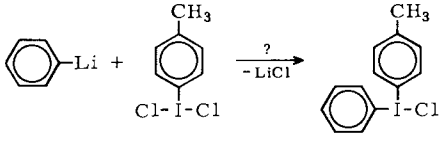
$SCl_2 + F_2 \rightarrow SCl_2F'_2$

$SFCl + ClF \rightarrow SFClF'Cl'$ (d and l)

The idea of preservation of bond-type is perhaps difficult to accept for the experimentalist who is accustomed to the configurational inversions that ordinarily occur in organic chemistry, and in any case, it is only presented here as a working hypothesis for further study. However, the reasonableness of such a postulate can be better appreciated by considering the following possible synthesis of two isomeric iodonium salts. In the reaction of *p*-tolyllithium with iodobenzene dichloride as



and of phenyllithium with *p*-iodotoluene dichloride as



it seems most likely that under certain conditions the reaction products will be the two different isomers as shown, since the phenyl groups will attack at the site of the chlorine. This type of retention of configuration will, of course, be possible only if the reaction is weak enough so as not to cause intramolecular inversion, and if the solution is dilute enough so that intermolecular inversion *via* dimerization or other mechanisms can be excluded.

The problem of obtaining different synthetic mechanisms for the preparation of HV_{II} molecules, such as PCl_xF_{5-x} is more difficult since the obvious guess of retention of configuration here involves a CV bond being retained as a pseudo-CV bond in a flattened pyramid. Nevertheless, there should be some distribution of the initial CV bonds among the final pseudo-CV bonds, through which it should be possible to make preferentially the various products using the appropriate PCl_xF_{3-x} molecules along with ClF, F_2, or Cl_2 as starting materials.

There have been as yet few experiments which can shed light on these reactions. Among these are kinetic studies on the two gas phase reactions [15a]

$BrF_3 + F_2 \rightarrow BrF_5$

and [43]

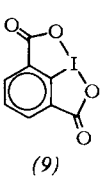
$IF_5 + F_2 \rightarrow IF_7$

[43] *J. Fischer* and *R. K. Steunenberg*, J. Amer. chem. Soc. *79*, 1876 (1957).

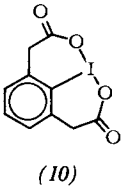
which show the formation of the HV molecules BrF_5 and IF_7 to involve a single bimolecular collision which is a prerequisite for the types of syntheses suggested here. We have, however, no idea of the amount of retention of configuration, and also how general this kinetic mechanism actually is. There was also an earlier study on the addition of Cl_2 to PCl_3 as well as on the exchange of Cl_2 with PCl_5 and on the reduction of PCl_5 with Hg [44]. While the results of the experiments on the addition of Cl_2 were "not clear-cut" they definitely favored some form of addition at the pseudo-CV site. It would be interesting to perform a similar study on a molecule such as $P(CH_3)_3Cl_2$ for which intramolecular inversion could more definitely be excluded.

7. New Molecules

One of the interesting implications of the present study is the likely existence of large classes of HV molecules of the mixed "non-metallo-organic" kind, rarely if ever considered previously in the literature. While it is generally not considered proper to propose the existence of unusual molecules in advance of their preparation, we chose to do so here in order to illustrate the unusual possibilities for hypervalent molecules. This can be perhaps justified to a certain extent by the fact that some molecules and polymers of trivalent iodine discussed in an earlier version of the present article have since been synthesized and fully characterized [5]. We restrict our discussion to the analogs of molecules *(9)* and *(10)*

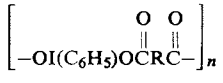


(9)



(10)

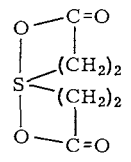
synthesized by *Agosta* [5a]; there are, however, clearly many other possible classes of HV molecules using different polyvalent HV ligands. A number of polymers analogous to the recently synthesized iodine-containing polymers of the form [5b]



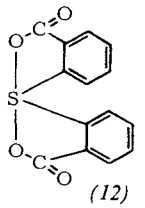
have been described elsewhere.

[44] *J. J. Downs* and *R. E. Johnson*, J. chem. Physics *22*, 143 (1954); J. Amer. chem. Soc. *77*, 2098 (1955). In discussing their results, these authors noted that "Consequently theoretical considerations of bond hybridization are conjectural and unsatisfactory". For other discussions on this point see pp. 1065-6 of Ref. [20a] and also *R. D. Burbank* and *F. N. Bensey*, J. chem. Physics *21*, 602 (1953), especially p. 608. Also, in view of the tendency of many workers to use NMR parameters to distinguish between "ionic" and "covalent" bonding in hypervalent molecules the author's comments on the difficulties inherent in such interpretations should be noted [*J. I. Musher*, Adv. in Magnetic Resonance *2*, 177 (1966)].

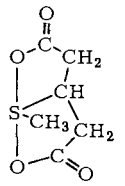
Without overqualifying our predictions, other than to observe that they are not so fanciful as they might seem, we suggest that it might be possible to synthesize molecules *(11)–(16)*.



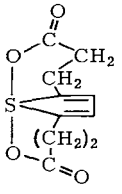
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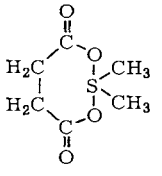
(12)



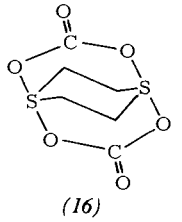
(13)



(14)



(15)



(16)

These molecules are all related to the as yet unknown 2-thia(IV)-isopropylidene diacetate, $(CH_3)_2S(OAc)_2$, just as *(9)* and *(10)* are related to the known phenyliodonium diacetate $C_6H_5I(OAc)_2$. The fact that *(9)* and *(10)* are so unusually stable to decomposition by boiling water, as compared with the relative instability of $C_6H_5I(OAc)_2$, would argue for the likelihood of stable molecules *(11)–(16)* even though the corresponding diacetate might be sufficiently reactive as to be not isolable. From Tables 1 and 2 it seems likely that sulfur will form HV bonds to OC(O) groups, and if for some reason this does not actually occur, it will surely occur for S replaced by Se or Te. It should be noted that *(11)–(14)* will be optically active and there seems to be little likelihood of unimolecular racemization (cf. Section 5); molecule *(14)* is fixed with a bridge so as to prevent racemization[45].

[45] *K. Mislow*, private communication.

8. Conclusion

An attempt has been made to place the molecules and ions formed from atoms using their higher valences in a unified scheme through a detailed but simple theoretical description of hypervalent bonds. From the discussion it is evident that such a description is eminently reasonable and that there are numerous implications for the chemistry of these hypervalent molecules but that the experimental information necessary for a proper understanding of their physicochemical behavior is lacking. It is hoped that the present study[46], which does not intend to provide the final answers to such questions as mechanisms of inversion, synthetic paths, and the existence of unusual new molecules, will at least stimulate further consideration of this very interesting, but until now highly neglected, field of chemistry.

I am deeply indebted to numerous colleagues for their patience in discussing these ideas over the past several years. I am particularly indebted to E. J. Corey, P. Laszlo, R. Mechoulam, and my father, S. Musher, without whom these ideas might never have crystallized. I would also like to thank W. C. Agosta and H. K. Livingston who successfully synthesized the first HV molecules to be inspired by the present study in the course of their varied research programs. The manuscript was drafted while I was a guest at the Weizmann Institute of Science, Rehovot, Israel, in the summer of 1964, and the final version was completed at the same Institute this past summer. I am grateful for the kind hospitality shown me there by S. Lifson, D. Samuel, and their colleagues.

Received: June 20, 1968 [A 677 IE]
German version: Angew. Chem. *81*, 68 (1969)

[46] *R. J. Gillespie*, Angew. Chem. *79*, 885 (1967); Angew. Chem. internat. Edit. *6*, 819 (1967); *R. F. Hudson*, Angew. Chem. *79*, 756 (1967); Angew. Chem. internat. Edit. *6*, 749 (1967). The reader's attention should also be directed to the numerous studies on hypervalent molecules by *Hellwinkel et al., e.g. D. Hellwinkel* and *G. Fahrbach*, Chem. Ber. *101*, 574 (1968).

COMMUNICATIONS

An Optically Active Tribenzoxepin[**]

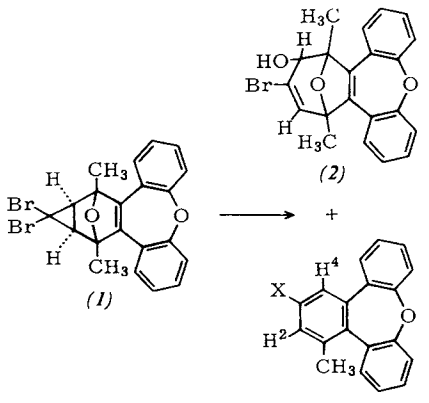
By *W. Tochtermann* and *C. Franke*[*]

Optically active 1-methyltribenzoxepin-3-carboxylic acid *(3b)* has been prepared as a model substance for a study of the intramolecular mobility of boat-shaped seven-membered rings[1] since the energy barriers for conformational inversion are often relatively low in oxygen heterocycles[2].

The dibromocyclopropane derivative *(1)* was obtained from 1,4-epoxy-1,4-dihydro-1,4-dimethyltribenzoxepin[3], bromoform, and potassium *tert*-butoxide in benzene at 25 °C, the yield being 31% after chromatographic separation from unchanged starting material on Al_2O_3 with CCl_4 and $CHCl_3$; it had m.p. 184–186 °C (from cyclohexane) and a ^{1}H-NMR spectrum (in $CDCl_3$)[4] τ = 2.5–2.9 (8H, M), τ = 7.53 (2H, S), τ = 8.05 (6H, S). When heated for 48 h at 100 °C with silver sulfate (molar ratio 1:1.4) in 2 N H_2SO_4/dioxane (1:2 v/v) it afforded directly[5] 3-bromo-1-methyltribenzoxepin *(3a)* [33% yield; m.p. 114–116 °C (from cyclohexane); ^{1}H-NMR spectrum (in $CDCl_3$), τ = 2.3–3.0 (10H, M), τ = 7.57 (3H, S)] as well as the cyclopropyl-allyl rearrangement product *(2)* (44% yield; m.p. 211–212 °C). The product *(2)* was isolated by recrystallization of the crude product from CCl_4; chromatography of the mother liquors therefrom on Al_2O_3 with CCl_4 gave pure *(3a)*. Polyphosphoric acid converts the alcohol *(2)* into *(3a)* in 30% yield in 2.5 h at 130 °C.

The same process can be used for preparation of 3-bromo-1-methyl-9*H*-tribenzo[*a,c,e*]cyclohepten-9-one [*(3a)*, C=O in place of O], which can be reduced to the known 1-methyl-9*H*-tribenzo[*a,c,e*]cyclohepten-9-ol by $LiAlH_4$[6].

The action of *n*-butyllithium in light petroleum on *(3a)* at −50 °C in tetrahydrofuran and subsequent carboxylation affords the carboxylic acid *(3b)* [80% yield; m.p. 220–222 °C (from benzene)], whose structure is proved by elemental analysis and IR and ^{1}H-NMR spectra [$CDCl_3$: carboxyl proton at τ = 0.2; AB system at τ = 1.80 and 1.92 with J_{AB} = 1.8 Hz (H^4, H^2), τ = 2.2–3.0 (8H, M), τ = 7.48 (3H, S)].



(1) *(2)* *(3a)*, X = Br *(3b)*, X = COOH

Keeping equimolar amounts of *(3b)* and brucine in ethanol/methanol (1 : 1–1 : 2 v/v) for some time gives a 60% yield[7] of a crystalline brucine salt that shows rapid mutarotation in acetone at 20.5 °C ($t_{1/2}$ = 200 sec; extrapolation of the specific rotation to t_0 gives $[\alpha]_{436}^{20.5} = +87°$, changing to −43 °, c = 0.013 g/ml). The dextrorotatory acid can be obtained by dissolving this salt as fast as possible in acetone at −20 °C and precipitating it rapidly with 2N HCl. Solutions of (+)–*(3b)* in acetone racemize at +20.5 °C with a half-life period of 195 sec; $[\alpha]_{436}^{20.5}$ was +135 ° after 105 sec (extrapolated to t_0: $[\alpha]_{436}^{20.5} = +190°$, c = 0.02 g/ml). Thence the free enthalpy of activation for ring inversion of *(3b)* is calculated to be $\Delta G_{20.5}^{\neq}$ = 20.8 kcal/mole, *i.e.*, *(3b)* is much more mobile than comparable systems[1].

Received: October 23, 1968 [Z 893 IE]
German version: Angew. Chem. *81*, 32 (1969)

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

[1] *W. Tochtermann, C. Franke*, and *D. Schäfer*, Chem. Ber. *101*, 3122 (1968).

[2] *K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon*, and *G. H. Wahl jr.*, J. Amer. chem. Soc. *86*, 1710 (1964); *R. K. Harris* and *R. A. Spragg*, J. chem. Soc. (London) *B 1968*, 684; further references are given there; for the mobility of oxepins see *E. Vogel* and *H. Günther*, Angew. Chem. *79*, 429 (1967); Angew. Chem. internat. Edit. *6*, 385 (1967); *H. Günther, R. Schubart*, and *E. Vogel*, Z. Naturforsch. *22b*, 25 (1967).

[3] *W. Tochtermann, K. Oppenländer*, and *M. Nguyen-Duong Hoang*, Liebigs Ann. Chem. *701*, 117 (1967).

[4] All spectra were determined with TMS as internal standard on a Varian A-60 instrument.

[5] For a discussion of this reaction sequence see ref. [1].

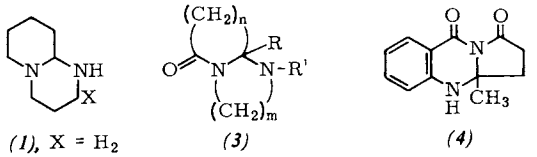
[6] *W. Tochtermann* and *D. Schäfer*, unpublished work; *W. Tochtermann* and *K. Stecher*, Tetrahedron Letters *1967*, 3847.

[7] A second order asymmetric transformation is indicated in this case; weakly dextrorotatory *(3b)* was obtained from the mother liquors of the brucine salt.

Synthesis of *ortho*-Condensed α,γ-Diazabicyclanes Containing a Bridgehead Nitrogen Atom

By *H. Wollweber*[*]

ortho-Condensed α,γ-diazabicyclanes such as *(1)*, being formaldehyde aminals, are unstable to acids. Only introduction of at least one oxo group next to one of the nitrogen atoms is expected to stabilize derivatives to acid. The compounds *(2)*[1] and *(4)*[2] have been obtained previously. The expected stability to acids has now been observed also for compounds of type *(3)*, which moreover are now readily accessible.



(1), X = H_2
(2), X = O

(3) *(4)*

n	*m*	R′	R	B.p. (°C/torr) M.p. (°C)
2	3	H	CH_3	128/0.3 [d]
2	3	CH_3	CH_3	64–65
2	3	CH_2–CH_2OH	CH_3	82–83
2	3	H	C_6H_5	133
2	2	H	CH_3	108–109/0.4
2	2	H	CH_3 [a]	90–92/0.3
2	2	H	CH_3 [b]	90–92/0.3
2	2	C_6H_5	CH_3	64–64.5
2	2	C_6H_5–CH_2–CH_2	CH_3	165–170/0.3
2	2	*n*-$C_{10}H_{21}$	CH_3	178–180/0.3
2	4	H	CH_3 [c]	118–119
3	2	H	CH_3	79–80

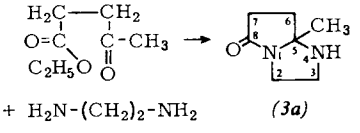
[a] Also CH_3 on C-2.

[b] Also CH_3 on C-3.

[c] NMR spectrum in $CDCl_3$ (TMS as internal standard): τ = 6.03 (H_{eq} on C-2), 7.36 (H_{ax} on C-2), 8.1–8.8 (4H on C-3 and C-4), 7.45 (H_{eq} on C-5), 7.07 (H_{ax} on C-5), 8.05 (2H on C-8), 7.61 (2H on C-9), 8.7 (CH_3); Varian AH 100 and 220 instruments. IR spectrum in KBr: broad band at 1630 cm^{-1} (lactam).

[d] M.p. of the hydrochloride 178–179 °C.

For the synthesis of *(3)* a γ- or δ-keto acid or an ester thereof is treated in an inert solvent with a 1,2-, 1,3-, or 1,4-alkanediamine at 100–150 °C.



+ H_2N-$(CH_2)_2$-NH_2 *(3a)*

5-Methyl-1,4-diazabicyclo[3.3.0]octan-8-one (3a):

Ethyl levulate (100 g) is heated with ethylenediamine (150 g) and ethanol (200 ml) for 8 h at 130–140 °C. On evaporation and distillation in a vacuum the product *(3a)* (83.5 g), b.p. 108–109 °C/0.4 torr, can be isolated. Its structure is proved by the following spectroscopic findings[3]: NMR spectrum in $CDCl_3$ (TMS as internal standard): τ = 6.43 (H on C-2), 7.07 (H′ on C-2), 6.81 (H on C-3), 6.77 (H′ on C-3), 7.83 (H on C-6), 7.97 (H′ on C-6), 7.24 (H on C-7), 7.63 (H′ on C-7), 8.7 (CH_3); IR spectrum in CCl_4: 1700 cm^{-1} (lactam).

Received: October 23, 1968 [Z 892 IE]
German version: Angew. Chem. *81*, 34 (1969)

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[1] *R. Adams* and *I. J. Pachter*, J. Amer. chem. Soc. *74*, 4907 (1952); *C. A. Grob, H. P. Fischer, H. Link*, and *E. Renk*, Helv. chim. Acta *46*, 1194 (1963).

[2] *G. Westphal* and *H. H. Stork*, Z. Chem. *7*, 456 (1967).

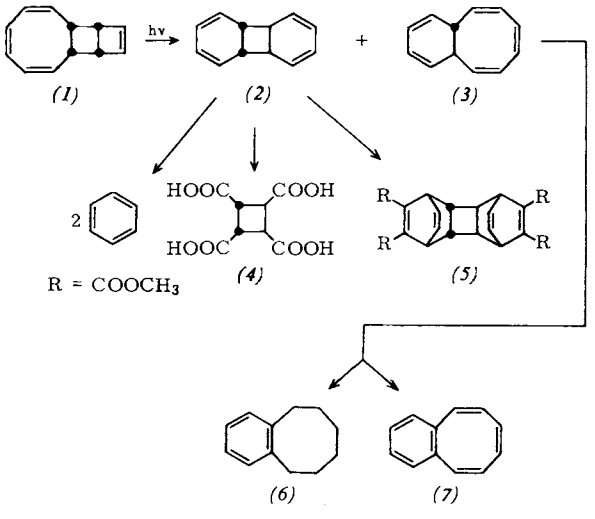
[3] I wish to thank Dr. *W. Naegele*, Dr. *J. Kurz*, and Dr. *W. Geiger* for recording and discussing the spectra.

Two New Valence Isomers of [12]Annulene

By *G. Schröder, W. Martin*, and *H. Röttele*[*]

We report here two new valence isomers of [12]annulene, a compound that has not yet been detected[1,2], namely, *cis, anti,cis*-tricyclo[6.4.0.$0^{2,7}$]dodeca-3,5,9,11-tetraene (dimeric benzene) *(2)* and *trans*-bicyclo[6.4.0]dodeca-2,4,6,9,11-pentaene (*trans*-4a,10a-dihydrobenzocyclooctene) *(3)*.

If the readily accessible *cis,syn,cis*-tricyclo[8.2.0.0^{2,9}]dodeca-3,5,7,11-tetraene *(1)* [3] (2.8 g) is irradiated in ether (240 ml) for 10 h at *ca.* −30 °C with a low-pressure UV lamp, a mixture containing at least four substances is obtained. Most of the unchanged *(1)* (≈ 70%) is removed therefrom as a crystalline complex by adding solid $AgBF_4$ to a tetrahydrofuran solution. Then the products *(2)* (lower retention time) and *(3)* can be obtained 90–95% pure by column chromatography, first on silica gel impregnated with 0.7% of $AgBF_4$ and then on neutral Al_2O_3, in both cases with pentane as eluant. Under the stated conditions the yields of *(2)* and *(3)* are respectively 9 and 11 %, calculated on the amount of *(1)* used [4].



The dimeric benzene *(2)* is crystalline up to *ca.* 15 °C, colorless, and thermolabile; its half-life in CCl_4 solution at 40 °C, determined by NMR spectroscopy, is 3½ h; its decomposition gives only benzene [5]. (NMR spectrum [6] of *(2)*: two singlets at τ = 4.4 (8H) and 6.78 (4H); UV spectrum [6]: λ_{max} = 266 nm, ε = 4100.) Ozonolysis in 90% acetic acid, followed by oxidation with hydrogen peroxide, leads to the known tetracarboxylic acid *(4)* [7]. With dimethyl acetylenedicarboxylate, *(2)* affords the known diadduct *(5)* [3].

The constitution of *(3)* is proved by basic isomerization (potassium *tert*-butoxide in DMSO) and subsequent hydrogenation to *(6)* [8], also by dehydrogenation by chloranil in benzene at 20 °C to *(7)* [8]. Compound *(3)* does not react with maleic anhydride at 20 °C, which clearly indicates a distorted 1,3-cyclohexadiene system that can be contained only in the *trans*-compound. (NMR spectrum [6] of *(3)*: narrow multiplet at τ = 4.28 (10H) and a pseudosinglet at τ = 6.55 (2H); UV maximum [6] at 252 nm, ε = 6000.).

Formation of *(2)* and *(3)* in a single step during photolysis of *(1)* can be excluded. These compounds are very probably the end products of a series of electrocyclic reactions that are photochemically or thermally induced, follow the Woodward-Hoffmann rule [9], and can include [12]annulene as an intermediate.

Received: October 28, 1968 [Z 894 IE]
German version: Angew. Chem. *81*, 33 (1969)

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[1] *R. Wolovsky* and *F. Sondheimer*, J. Amer. chem. Soc. *87*, 5720 (1965).

[2] *G. Wilke*, Angew. Chem. *69*, 397 (1957).

[3] *G. Schröder* and *W. Martin*, Angew. Chem. *78*, 117 (1966); Angew. Chem. internat. Edit. *5*, 130 (1966)

[4] The fourth substance, which has not yet been identified and always contained *(3)* as impurity, shows, *inter alia*, aromatic absorption in the NMR spectrum.

[5] The decomposition does not follow the Woodward-Hoffmann rule for cycloadditions [5a] and is thus to be formulated as a diradical process. It is remarkable that the *syn*-2:2-dimer of cyclooctatetraene decomposes only at *ca.* 100 °C, then slowly giving, *inter alia*, 2 molecules of cyclotetraene [5b].

[5a] *R. Hoffmann* and *R. B. Woodward*, J. Amer. chem. Soc. *87*, 2046 (1965).

[5b] *G. Schröder* and *J. F. M. Oth*, Angew. Chem. *79*, 458 (1967); Angew. Chem. internat. Edit. *6*, 414 (1967).

[6] The UV spectra were measured for cyclohexane solutions with a Beckman DK-2 instrument, and the NMR spectra for CCl_4 solutions with a Varian A 56/60a instrument with tetramethylsilane as internal standard.

[7] *R. Criegee* and *H. Höver*, Chem. Ber. *93*, 2521 (1960); *G. W. Griffin, A. F. Vellturo*, and *K. Furukawa*, J. Amer. chem. Soc. *83*, 2725 (1961). *(4)* was identified by comparision with an authentic sample.

[8] NMR, IR, and UV spectra, as well as C,H analyses are in accord with formulas *(6)* and *(7)*. The refractive index of *(6)*, and the m.p. and IR spectrum of *(7)*, accord with data in ref. [8a].

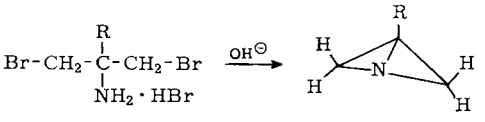
[8a] *R. Huisgen* and *W. Rapp*, Chem. Ber. *85*, 826 (1952); *G. Wittig, H. Eggers*, and *P. Duffner*, Liebigs Ann. Chem. *619*, 10 (1958).

[9] *R. B. Woodward* and *R. Hoffmann*, J. Amer. chem. Soc. *87*, 395 (1965).

Synthesis and Properties of 1-Azabicyclo[1.1.0]butanes

By *W. Funke* [*]

3-Phenyl-1-azabicyclo[1.1.0]butane, recently described, was the first example of this highly strained bicyclic ring system [1]. We have now prepared the parent compound *(2a)* and the alkyl-substituted 1-azabicyclo[1.1.0]butanes *(2b)* and *(2c)* by a simple procedure based on the Gabriel aziridine synthesis [2].



(1) *(2)*

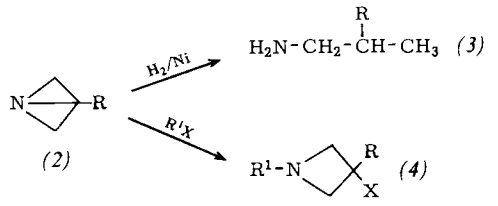
(a), R = H; *(b)*, R = CH_3; *(c)*, R = C_2H_5

(2)	B.p. (°C)	n_D^{20}	Yield (%)	Method	^{1}H-NMR [a]	Mol. ion (*m/e*)
(a)	51	1.4198	7	A	9.07 (2H), M; 7.87 (2H), M; 7.67 (1H), M;	55
(b)	65	1.4150	42	B	9.04 (2H), M; 8.41 (3H), S; 7.97 (2H), M;	69
(c)	87	1.4229	75	B	9.07 (2H), M; 9.03 (3H), T, J = 7 Hz; 8.08 (2H), Q, J = 7 Hz; 7.92 (2H), M	83

[a] In CCl_4 solution; τ values are given; TMS as internal standard.

The salts *(1a)–(1c)*, which are obtained from the amino diols by means of concentrated aqueous hydrogen bromide at 170 °C [3], afford the 1-azabicyclo[1.1.0]butanes *(2a)–(2c)* when heated at 70–95 °C in 17% sodium hydroxide solution (method A) or in potassium hydroxide/triethylene glycol (method B). The products *(2)* are stable in absence of air and can be distilled, but they polymerize in the presence of catalytic amounts of acid or alkylating agent.

NMR and IR spectra, elemental analysis, and molecular weights determined by mass spectroscopy confirm the structures assigned. The chemical shifts are different for the *exo*- and the *endo*-methylene protons, the multiplets at higher field being assigned to the *endo*-protons [1]. Catalytic hydrogenation



of *(2)* with Raney nickel and alcohol leads to primary amines *(3)* with absorption of 2 moles of hydrogen[4]. Acid chlorides, acid anhydrides, and thiophenol are added with formation of azetidines *(4)*.

1-Azabicyclo[1.1.0]butane (2a):

A solution of *(1a)* (40.0 g, *ca.* 0.13 mole) in water (80 ml) is added dropwise to a solution of sodium hydroxide (80.0 g, 2.0 moles) in water (400 ml) at 80 °C within 45 min. An aqueous solution of *(2a)* distils over continuously at 270 to 300 torr and is collected in a receiver cooled to −78 °C. When all the *(1a)* has been added, distillation is continued under the same conditions for a further 20 min, the distillate, which solidifies, is treated with solid potassium hydroxide, and the *(2a)* that is liberated on thawing of the mixture is evaporated at water-pump vacuum through a tube of sodium hydroxide into a cold trap. The yield is 0.5 g (7%) of gas-chromatographically pure (Apiezon) material, b.p. 51 °C.

3-Ethyl-1-azabicyclo[1.1.0]butane (2c):

(1c) (65.0 g, 0.2 mole) is added to a solution of potassium hydroxide (84.0 g, 1.5 mole) in triethylene glycol (360 ml). The mixture is warmed with stirring, at 85 °C/300 torr, and the product *(2c)* is distilled into a receiver cooled to −78 °C. After 30 min the reaction mixture is warmed rapidly to 150 °C and the distillation then interrupted. Addition of solid potassium hydroxide to the distillate led to separation of gas-chromatographically (Apiezon) pure *(2c)* (12.4 g, 75 %), b.p. 87 °C.

Received: October 29, 1968 [Z 897 IE]
German version: Angew. Chem. *81*, 35 (1969)

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[1] *A. G. Hortmann* and *D. A. Robertson*, J. Amer. chem. Soc. *89*, 5974 (1967).

[2] *S. Gabriel*, Chem. Ber. *21*, 1049, 2665 (1888).

[3] *W. J. Gensler*, J. Amer. chem. Soc. *70*, 1843 (1948).

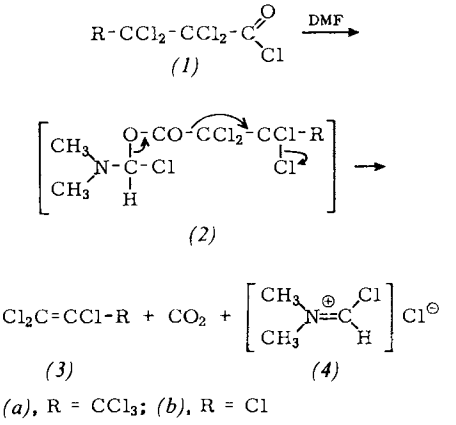
[4] *(2a)* polymerizes partly during the hydrogenation, so that only 1.2 moles of H_2 are taken up.

Vilsmeier Reaction of Acid Chlorides Capable of Fragmentation

By *A. Roedig* and *W. Wenzel*[*]

Perchlorobutyryl chloride *(1a)*[1] in dimethylformamide fragments even at room temperature extremely rapidly and completely to hexachloropropene *(3a)*. Since this reaction occurs in absence of a base, preliminary formation of an anion as reactive substrate does not come into consideration. Moreover, it is to be assumed that *(1a)* and DMF form a sort of Vilsmeier complex *(2a)* as intermediate.

In that case, a compound *(4)* must also be formed which is the actual active species in formation of acid chlorides from carboxylic acids and sulfonic acids by means of phosphoryl chlorides, thionyl chloride, or phosgene in DMF[2]. To find out whether fragmentation of *(1a)* is connected with formation of *(4)* we carried out the reaction in the presence of *p*-nitrobenzoic acid, which resulted in the formation of *p*-nitrobenzoyl chloride as well as *(3a)*.



(a), R = CCl_3; *(b)*, R = Cl

Since *(4)* can also be considered as a Vilsmeier reagent for aldehyde synthesis[3], fragmentation of *(1a)* in the presence of *N,N*-dimethylaniline should afford *p*-dimethylaminobenzylidene chloride, and this too we observed.

Perchloropropionyl chloride *(1b)* can be used in place of *(1a)* in the above-mentioned reactions, but less effectively, and trichloroacetyl chloride cannot used at all. The utility of *(1a)* and *(1b)* and the failure with trichloroacetyl chloride show that the organic acid chlorides and DMF must combine to a complex *(2)* capable of fragmentation and able to yield the chloride ion necessary for formation of *(4)*. The non-fragmenting DMF complex of trichloroacetyl chloride[4] is very unstable and is decomposed by water to chloral, trichloro-*N,N*-dimethylacetamide, CO_2, and CCl_4.

p-Nitrobenzoyl chloride:

p-Nitrobenzoic acid (6.4 g, 38 mmoles) is treated with *(1a)* (14 g) or *(1b)* (10.6 g) (in both cases 40 mmoles) with exclusion of moisture. Dry DMF (60 ml) is then added dropwise at room temperature and, as soon as gas evolution ceases, the mixture is heated for a further hour at 100–105 °C. The product *(3)* and DMF are distilled off at 0.01 torr, and the residual pale yellow, liquid acid chloride solidifies on cooling. M.p. and mixed m.p. 70–71 °C. Yield 7.0 g (99%) from *(1a)*, 2.3 g (32%) from *(1b)*.

p-Dimethylaminobenzylidene chloride and p-dimethylaminobenzaldehyde[5]*:*

Dimethylaniline (6.7 g, 55 mmoles) is added to *(1a)* (19.1 g, 55 mmoles) in dry DMF (40 ml) with ice cooling. When the mixture has been warmed for 2 h at 40 °C and then cooled, *p*-dimethylaminobenzylidene chloride separates as long, pale yellow needles, m.p. 64–68 °C (yield 10.0 g, 89%). [When *(1b)* is used in place of *(1a)* the yield falls to 47%.]

When this product is gently warmed with water and sufficient dilute sodium hydroxide solution is added to cause a permanent alkaline reaction, the aldehyde can be filtered off and dried; it has m.p. 73–74 °C, and the yield is 83% calculated on the benzylidene chloride used (6.0 g).

Received: October 30, 1968 [Z 898 IE]
German version: Angew. Chem. *81*, 36 (1969)

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[1] *A. Roedig* and *W. Wenzel*, Chem. Ber., in press.

[2] *H. H. Bosshard, R. Mory, M. Schmid*, and *H. Zollinger*, Helv. chim. Acta *42*, 1653 (1959).

[3] *H. H. Bosshard* and *H. Zollinger*, Helv. chim. Acta *42*, 1659 (1959).

[4] *I. L. Knunyants, Ju. A. Cheburkov*, and *Ju. E. Aronov*, Izvest. Akad. Nauk SSSR, Ser. Chim. *1966* (6), 1038; Chem. Abstr. *65*, 10491 (1966).

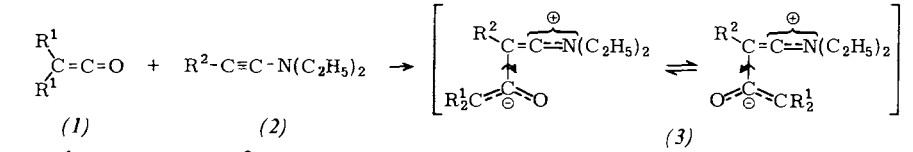
[5] According to reference [3] stoichiometric amounts of DMF are used and the aldehyde is isolated by working up with water or acid.

Cycloadditions of Ketenes to Ynamines

By *M. Delaunois* and *L. Ghosez*[*]

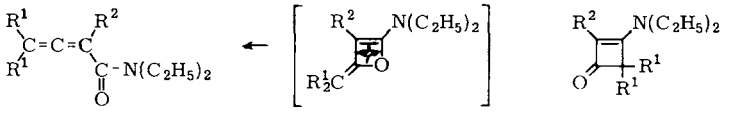
The *cis*-stereospecific formation of cyclobutanones[1] from ketenes and olefins, dienes, and vinyl ethers proceeds *via* a one-step multicenter cycloaddition. The reaction of ketenes with enamines, however, follows a different path involving a dipolar intermediate[2].

We have found that ketenes react readily with ynamines even at very low temperatures. Here also the cycloaddition apparently proceeds through the formation of a zwitterionic intermediate[3].



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

(a), $R^1 = C_6H_5$ *(a)*, $R^2 = C_6H_5$
(b), $R^1 = H$ *(b)*, $R^2 = N(C_2H_5)_2$
(c), $R^2 = CH_3$



(9), $R^1 = C_6H_5$, $R^2 = CH_3$
(10), $R^1 = H$, $R^2 = CH_3$
(11), $R^1 = H$, $R^2 = C_6H_5$

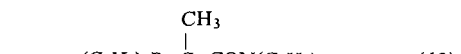
(4)

(5), $R^1 = R^2 = C_6H_5$
(6), $R^1 = C_6H_5$, $R^2 = N(C_2H_5)_2$
(7), $R^1 = H$, $R^2 = C_6H_5$
(8), $R^1 = H$, $R^2 = CH_3$

Reaction	Yield (%)	M.p. (°C) B.p. (°C/torr)	IR [a] (cm^{-1})	NMR [b]
(1a) + *(2a)* → *(5)*	95	188.5	1735 1609 1580	2.62 (15H) M 6.63 (4H) M 8.95 (3H) T 9.51 (3H) T
(1a) + *(2b)* → *(6)*	94	147	1738 1578	2.72 (10H) S 6.55 (4H) Q 7.1 (4H) Q 8.92, 9.15 (12H) (T in both cases)
(1b) + *(2a)* → *(7)* (main product)	78	72.2	1728 1578	2.8 (5H) M 6.62 (4H) Q 6.89 (2H) S 8.85 (6H) T
(1b) + *(2c)* → *(8)* (by product)	7 [c]	132°C/0.7	1740 1580	—
(1a) + *(2c)* → *(9)*	96	78	1940 1610	2.72 (10H) S 6.78 (4H) Q 7.93 (3H) S 9.09 (6H) T
(1b) + *(2c)* → *(10)* (main product)	83	45–55/0.7	1955 1625	5.18 (2H) Q 6.6 (4H) Q 8.15 (3H) T
(1b) + *(2a)* → *(11)* (by product)	9 [c]	140/0.5	1942	8.87 (6H) T —

[a] In chloroform.
[b] τ values; Varian A-60, CCl_4 solution (except for *(5)* which was dissolved in $CDCl_3$), TMS as internal standard.
[c] Determined by gas chromatography.

The addition of diphenylketene *(1a)* to an ethereal solution of *N,N*-diethylphenylethynylamine *(2a)* or bis(*N,N*-diethylamino)acetylene *(2b)* at −50 °C leads to almost quantitative formation of cyclobutenones *(5)* and *(6)* respectively. The structure determination was based on IR and NMR findings. The reaction product from diphenylketene *(1)* and *N,N*-diethylpropynylamine *(2c)*, however, was shown to be the allenic amide *(9)* whose constitution was proved by an independent synthesis[4] from diphenylketene and the phosphonium ylid *(12)*.



(12)

When the ketene *(1b)* was treated with *(2a)* under the same experimental conditions, the crystalline cyclobutenone *(7)* was isolated in 78 % yield. Examination of the mother liquor showed a small amount of allenic amide *(11)* which was isolated by preparative gas chromatography (carbowax 20 M). With *(2c)*, however, the liquid allenic amide *(10)* was the major product. Its constitution was proved by independent synthesis from the ylid *(12)* and acetyl chloride[4]. The minor constituent was purified by gas chromatography and characterized as the cyclobutenone *(8)*.

We think these results are best explained by a multistage process involving the formation of the resonance-stabilized zwitterion *(3)* as first step. This intermediate could then cyclize in two ways leading either to a cyclobutenone *(5)* to *(8)* or to an oxete *(4)*[5] which would rapidly rearrange to the corresponding allene.

Preparation of 3-dimethylamino-2,4,4-triphenylcyclobut-2-en-1-one (5)

Diphenylketene *(1a)* (2.7 g, 0.014 mole) is added dropwise at −50 °C to a solution of *(2a)* (2.5 g, 0.014 mole) in dry ether (25 ml). After 2 h at −50 °C the reaction is slowly warmed to room temperature (1 h). The precipitate is filtered off and recrystallized from pentane. Yield 4.8 g (95 %) of *(5)*.

Preparation of N,N-diethyl-1-methyl-1-allenecarboxamide (10)

An ethereal solution of *(1b)* (0.75 g, 0.018 mole) is added dropwise at −60 °C to a solution of *(2c)* (2 g, 0.018 mole) in dry ether (25 ml). After 80 min at −60 °C, the mixture is slowly warmed to room temperature. Evaporation of the solvent and distillation gave 2.19 g (83 %) of *(10)* as a yellow liquid, b.p. 45–55 °C/0.7 torr as well as 0.19 g (7 %) of *(8)*, b.p. 132 °C/0.7 torr, purified by preparative gas chromatography (Carbowax 20 M).

Received: November 4, 1968 [Z 899 IE]
German Version: Angew. Chem. *81*, 33 (1969)

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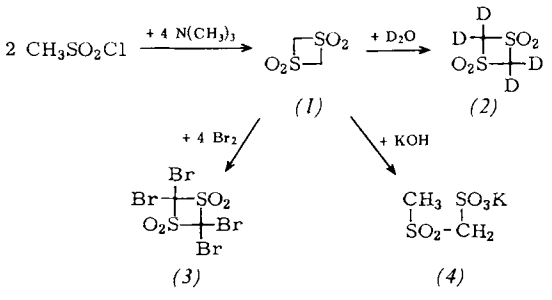
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Disulfene

By *G. Opitz* and *H. R. Mohl*[*]

The sulfene dimer *(1)*, which has been looked for in vain in previous formations of sulfene ($H_2C{=}SO_2$) from methanesulfonyl chloride and triethylamine and from diazomethane and SO_2, has now been obtained as follows: Methanesulfonyl chloride and an excess of trimethylamine in tetrahydrofuran at −20 °C give a powdery addition product of unknown structure[1]. When this suspension is slowly warmed to room temperature, HCl is eliminated and an ocher-brown color develops (75% of the sulfene thus formed can be detected by cycloaddition to 1-(2-methyl-1-propenyl)pyrrolidine[1]). If, after 90 h, the tetrahydrofuran is distilled off and the residue is stirred with dilute hydrochloric acid, disulfene (1,3-dithietane 1,1,3,3-tetraoxide) *(1)* remains undissolved (yield 18%).



Disulfene *(1)* is slightly soluble in most solvents but can be recrystallized from dimethylformamide (DMF) or aqueous dimethyl sulfoxide (DMSO). It decomposes with formation of a brown color above 280 °C. The calculated molecular weight is obtained by mass spectrometry and osmometry.

The NMR spectra (60 MHz) show four protons as a singlet at $\tau = 3.62$ (in DMF), 3.58 (in DMSO), 3.43 (in hexamethylphosphorotriamide), 3.13 (in pyridine)[**]. Shaking the solution with D_2O causes this signal to disappear. Addition of triethylamine to solutions of *(1)* leads to strong signal broadening, which can be reversed by an excess of trifluoroacetic acid. When triethylamine and water are both added, the H_2O and CH_2 signals of *(1)* coalesce to a common signal which is shifted to higher field on increase in the water content. Similar exchange phenomena have been observed for the somewhat less CH-acidic compound $(C_6H_5SO_2)_2CH_2$ and are ascribed to CH-acidity.

The IR spectrum of *(1)* in KBr has bands at 2830–2990 (CH), 1340 (SO_2 asym.), 1200 and 1090 (coupled vibrations), 860 (CS), and 680 cm^{-1}, indicating a symmetrical compound. The disturbance in the region of SO_2 stretching vibrations is removed on replacement of the H atoms.

The IR spectrum of the tetradeuterio derivative *(2)*, obtained by heating *(1)* with D_2O in [D_6]-DMSO, in KBr contains bands at 2150–2270 (CD), 1350 (SO_2 asym.), 1150 (SO_2 sym.), 1020, and 825 cm^{-1}. If the solution of *(1)* in DMF and a little pyridine is treated at room temperature with bromine until a permanent yellow color results, storage of the resulting mixture for 30 min and then pouring it into water affords the crystalline tetrabromo compound *(3)*, which can be recrystallized from methanol. *(3)* decomposes at 210 °C with discoloration. Its IR spectrum contains only four bands, at 1375 (SO_2 asym.), 1155 (SO_2 sym.), 825, and 695 cm^{-1}.

The most striking property of the disulfene *(1)* is its sensitivity to bases but complete stability towards acids, even towards hot concentrated sulfuric acid. Trimethylamine, triethylamine, and pyrrolidine have no effect, even when hot, if water is excluded, but ring opening occurs slowly in the presence of aqueous amines and instantaneously in the presence of dilute alkali hydroxide solutions. Reaction with potassium hydroxide solution yields potassium mesylmethanesulfonate *(4)*, identical with authentic material prepared from trimethylammonium mesylmethanesulfonate[2] and potassium hydroxide solution.

Received: November 6, 1968 [Z 901 IE]
German version: Angew. Chem. *81*, 36 (1969)

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[**] TMS as internal standard.

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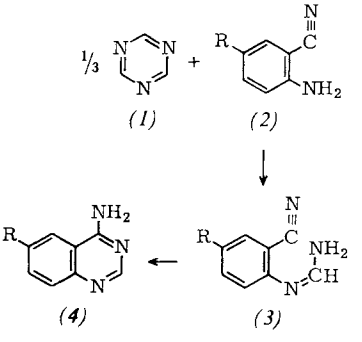
A New Synthesis of Aminoquinazolines

By *M. F. G. Stevens* and *A. Kreutzberger*[*]

The class of aminoquinazolines contains members with antimalarial[1], antiviral[2], and analgesic activity[3]. We have now prepared aminoquinazolines by a general method in which the quinazoline ring is closed before the amino group is introduced, and which proceeds by a one-stage additive cyclization.

It was known that (*o*-cyanophenyl)triazenes[4] cyclize readily and that various ring closures can be effected generally by *s*-triazines *(1)*[5]. It was thus to be expected that nitriles *(2)* of anthranilic acids would, in reaction with *(1)*, initially afford N^2-(*o*-cyanophenyl)formamidines *(3)*[6] which are the CH analogs of (*o*-cyanophenyl)triazenes. The products *(3)* are then stabilized by conversion into 4-aminoquinazolines *(4)*.

This ring closure on reaction with *(1)* is the more remarkable because *(2a)* is not cyclized by the triethyl orthoformate method (although boiling it with formic acid yields 4-hydroxyquinazoline).



	R	Yield (%)	Purification	M.p. (°C)
(4a)	H	64	Sublimation	266–268
(4b)	CH_3	63	Recrystn. from H_2O	275–277
(4c)	Br	7	Recrystn. from C_2H_5OH	338–340

4-Amino-6-methylquinazoline (4b):

2-Amino-5-methylbenzonitrile *(2b)* (2.6 g, 0.02 mole) and *s*-triazine *(1)* (0.8 g, 0.01 mole) in anhydrous ethanol (10 ml) are boiled together for 8 h. The solid material is filtered off

and the mother liquor is worked up by fractional crystallization for product *(4b)* (2 g, 63 %); this has m.p. and mixed m.p. 275–277 °C (cf. [7]).

Received: November 14, 1968 [Z 904 IE]
German version: Angew. Chem. *81*, 84 (1969)

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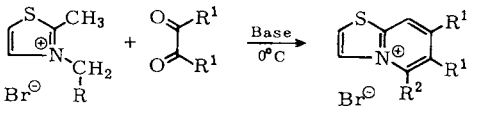
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Synthesis of New Thiazolo-[3,2-*a*]pyridinium Salts[**]

By *O. Westphal* and *A. Joos*[*]

Quinolizinium salts can be synthesized by cyclocondensation of *N*-substituted 2-picolinium salts with 1,2-diketones[1]. We have similarly prepared thiazolo[3,2-*a*]pyridinium salts *(2)* from *N*-substituted 2-methylthiazolium salts *(1)* and 1,2-diketones[2] (cf. also[3]).



(1) *(2)*

(1a), R = COC_6H_5
(1b), R = CN
(1c), R = $COOC_2H_5$

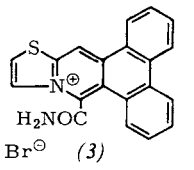
(1)	*(2)*			
	R^1	R^2	M.p. (°C)	Yield (%)
(1a)	C_6H_5	H	296	76
(1b)	2-Pyridyl	H	295 [a]	81
(1a)	2-Furyl	H	312 [a]	91
(1b)	CH_3	$CONH_2$	320	45
(1b)	C_6H_5	$CONH_2$	308–310	21
(1b)	2-Furyl	$CONH_2$	above 280 [a]	26
(1b)	2-Pyridyl	$CONH_2$	320	63

[a] With decomposition.

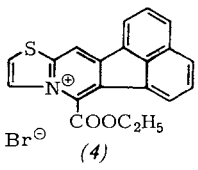
Condensation of *(1b)* with 9,10-phenanthraquinone leads to the pentacyclic compound *(3)*. The salt *(1c)* condenses with acenaphthaquinone to form *(4)*, whose ester group can be eliminated by heating the compound with CaO at *ca.* 220 °C.

Diacetyl and *(1a)* give the compound *(5)* which is converted into *(2)*, $R^1 = CH_3$, $R^2 = COC_6H_5$, on heating with acetic anhydride. When treated with aqueous bases, both *(5)* and *(2)*, $R^1 = CH_3$, $R^2 = COC_6H_5$, give *(2)*, $R^1 = CH_3$, $R^2 = H$.

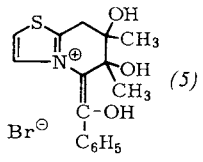
The constitution of the salts prepared is confirmed by elemental analyses, IR and NMR measurements, and chemical degradation to 3,4-disubstituted pyridines[2,4].



(3)



(4)



(5)

6,7-Di-(2-furyl)thiazolo[3,2-a]pyridinium bromide

2-Furil (10 g) and *(1a)* (15 g) (readily accessible from phenacyl bromide and 2-methylthiazole in a little acetone at room temperature) are suspended in acetone (500 ml). A solution of di-*n*-butylamine (7 g) in acetone (50 ml) and ethanol (20 ml) is added dropwise at 0 °C with stirring over a period of 30 min. The starting material dissolves and separation of the product soon begins. Stirring is continued for a further 2 h at 0 °C, then the crystals are filtered off and washed with acetone. Ocher crystals (16 g, 91 %) are obtained which decompose above 312 °C after recrystallization from ethanol.

Received: November 14, 1968 [Z 905a IE]
German version: Angew. Chem. *81*, 84 (1968)

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

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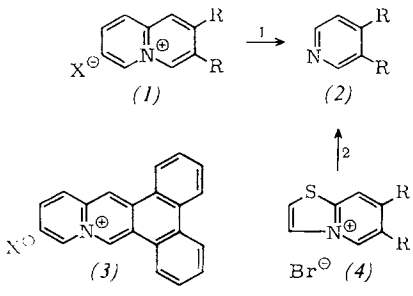
Aromatic and Heterocyclic 3,4-Disubstituted Pyridines[**]

By *O. Westphal, G. Feix*, and *A. Joos*[*]

Pyridine derivatives containing the same aromatic or heterocyclic substituent on C-3 and C-4 are difficultly accessible, and thus little is known about them. We have found that they can be readily prepared from 2,3-disubstituted quinolizinium salts[1] (Method 1) or from 6,7-disubstituted thiazolo[3,2-*a*]-pyridinium salts[2,2a] (Method 2). Since these salts are synthesized from 2-picoline[3] or 2-methylthiazole[2], respectively, a 2-substituted pyridine or thiazole is here formally transformed into a 3,4-disubstituted pyridine.

In method 1, the quinolinium salt *(1)* is converted by partial, catalytic hydrogenation[4] into its tetrahydro derivative, which is degraded by oxidation with, *e.g.*, potassium permanganate, to the 4,5-disubstituted 2-pyridinecarboxylic acid, and this is decarboxylated to give the 3,4-disubstituted pyridines *(2)*. Correspondingly, 2-azatriphenylene is obtained from the phenanthro[9,10-*b*]quinolizinium salt *(3)* by way of the tetrahydro derivative and carboxylic acid.

In method 2, 6,7-disubstituted thiazolo[3,2-*a*]pyridinium salts *(4)*[***] are converted into 3,4-disubstituted pyridines *(2)* by heating them with Raney nickel in 90 % ethanol.



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

	R	Method	Yield (%)	M.p. (°C)	Color, shape
(2a)	C_6H_5	1	25	114	Colorless cubes
(2a)	C_6H_5	2	88	114	Colorless cubes
(2b)	2-Pyridyl	2	35–40	101	Colorless prisms
(2c)	2-Furyl	2	40–50	59–60	Pale yellow prisms
2-Azatriphenylene		1	20–30	169–171	Colorless needles

3,4-Diphenylpyridine *(2a)* is obtained directly from *(4a)* in 45 % yield; about an equal amount of 1-ethyl-3,4-diphenylpyridinium bromide is isolated, which is converted almost quantitatively into *(2a)* on heating with CaO[5]. The group R is to some extent hydrogenated during desulfurization of *(4b)* and *(4c)* by freshly prepared Raney nickel, but the crude *(2b)* thus obtained can be dehydrogenated smoothly to 3,4-di-(2-pyridyl)pyridine by hot concentrated sulfuric acid[6]. However, partially hydrogenated *(2c)* cannot be thus dehydrogenated without at least partial decomposition. In this case the undesired hydrogenation can be avoided by using aged Raney nickel (kept for four weeks under ethanol).

Except for *(2a)*[7], the pyridines prepared are new; their constitution is proved by elemental analyses and IR and NMR measurements.

3,4-Di-(2-furyl)pyridine (2c) by Method 2:

Compound *(4c)* (3.48 g) was heated under reflux with aged Raney nickel (20 g; previously kept for 4 weeks under ethanol at room temperature) in 80% ethanol (200 ml), with stirring, for 12 h. The mixture was filtered whilst hot and the filtrate was taken to dryness in a rotatory evaporator. The residue was taken up in acetone (70 ml) and filtered. The filtrate was concentrated to *ca.* 15 ml, treated with methyl iodide (5 ml), and set aside at 0 °C for 12 h. The pyridinium iodide that separated was filtered off, dried, mixed with finely powdered CaO (15 g), and sublimed at 200 °C/0.1 torr, yielding pale yellow crystals of *(2c)* (0.95 g, 45%) of m.p. 59–60 °C.

Received: November 14, 1968 [Z 905b IE]
German version: Angew. Chem. *81*, 85 (1968)

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

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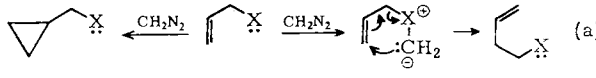
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Catalyzed Reactions of Diazomethane with Vinyloxirane

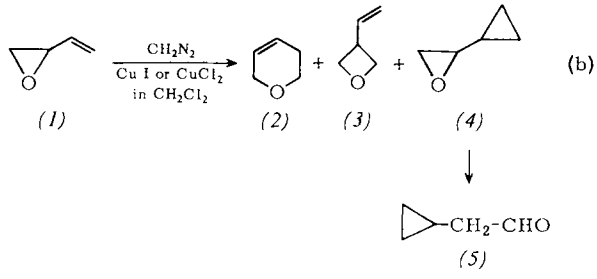
By *M. Kapps* and *W. Kirmse*[*]

In the presence of a copper salt as catalyst, diazomethane and allyl halides[1], ethers, or sulfides[2] yield cyclopropane and 3-butenyl derivatives [cf. (a)].



(a)

Analogous treatment of vinyloxirane (butadiene monoxide) *(1)*[3] affords three primary products: 5,6-dihydro-2*H*-pyran *(2)* (7%), 3-vinyloxetane *(3)* (29%), and cyclopropyloxirane *(4)* (64%). The sensitive product *(4)* rearranges readily to cyclopropylacetaldehyde *(5)*.



(b)

Compounds *(2)*[4], *(4)*[5], and *(5)*[6] were identified by comparison with authentic material; the structure of *(3)* was found from its NMR spectrum (δ = 6.16, 5.16, and 4.92 ppm, each due to a vinyl-H, M; δ = 4.71, 4.43 ppm, each due to two α-H, double doublet; δ = 3.6 ppm, β-H, M) and its catalytic hydrogenation to the known 3-ethyloxetane[7].

Compounds *(2)* and *(4)* were the products to be expected from eq. (a); formation of *(3)* is the first example known to us of a carbenoid insertion of CH_2 into a C–O bond.

If reaction (b) is carried out with bis[allylpalladium(II) chloride][8] as catalyst, *(3)* is not found among the products; *(2)* (14%) and *(4)* (86%) arise in proportions similar to those given above and in addition considerable amounts of *trans*-2-butenal (crotonaldehyde) and *trans*-2-buten-1-ol (crotyl alcohol) are obtained by isomerization and reduction of *(1)*. These compounds are produced only in traces if a copper salt is used as catalyst.

Received: November 16, 1968 [Z 906a IE]
German version: Angew. Chem. *81*, 86 (1969)

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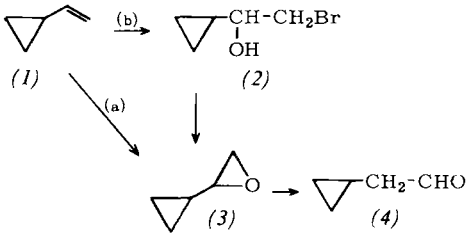
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Cyclopropyloxirane

By *W. Kirmse* and *Brigitte Kornrumpf*[*]

Cyclopropyloxirane *(3)*, which is produced by reaction of diazomethane with vinyloxirane in the presence of a copper salt as catalyst[1], has been prepared from vinylcyclopropane

(1) by an independent method. Suitable methods are: (a) oxidation with peracetic acid in dichloromethane in the presence of sodium carbonate[2]; (b) preparation of the bromohydrin *(2)* by *N*-bromosuccinimide in aqueous-ethereal solution[3] and removal of HBr by sodium hydroxide.



The compound *(3)* is also formed from cyclopropanecarbaldehyde and dimethylsulfonium methylide[4]. The action of diazomethane on cyclopropanecarbaldehyde affords cyclopropyl methyl ketone and *(3)* in the ratio 5:1.

The product *(3)* is rearranged by Lewis acids (BF_3, $SnCl_4$, $ZnCl_2$, CdI_2). The concentration of *(4)*, measurable by the NMR signal of the aldehydic hydrogen, soon decreases, however, owing to secondary reactions. As the initial rate shows, *(3)* reacts under catalysis by CdI_2 faster than does styrene oxide, which was the most reactive oxetane previously known[5].

Cyclopropyloxirane (3)

a) 40% Peracetic acid (5.1 g; pre-treated with anhydrous sodium acetate) is added dropwise to vinylcyclopropane *(1)*[6] (1.82 g) and anhydrous sodium carbonate (8.5 g) in dichloromethane (400 ml) at 15–20 °C. After being stirred for 4 days at room temperature the mixture is filtered, most of the solvent is distilled off through a 50-cm packed column, and the residue is fractionated through a 1-m spinning band column (Teflon band). Yield: 1.2 g (53%) of *(3)*, b.p. 39 °C/72 torr, with a trace of *(4)* as impurity (weak carbonyl bands in the IR spectrum).

b) *N*-Bromosuccinimide (13.8 g) and vinylcyclopropane (6.0 g) in ether (16 ml) are added dropwise to ether (6.5 ml) and water (9.5 ml) at 15 °C; the mixture is stirred for 1–2 days at room temperature and then extracted three times with 15-ml portions of ether. The combined ether extracts are dried over magnesium sulfate and distilled under vacuum. Yield: 6.2–6.9 g (48–53%) of *(2)*, b.p. 84–86 °C/20 torr. NMR spectrum (60 MHz, in CCl_4, chemical shifts in ppm with respect to TMS): 0.23–0.56 (4H), M, and 0.6–1.2 (1H, cyclopropane-H), 3.08–3.33 (1H, α-H), M, 2.96 (1H, –OH), S, 3.5 (2H, $-CH_2Br$), double doublet.

Compound *(2)* (6 g) is added dropwise, with stirring, to a solution of sodium hydroxide (8.8 g) in water (13 ml). After 2 h the upper phase is separated off, dried over NaOH, and distilled under vacuum. Yield: 2.4–2.6 g (80–86%) of *(3)*, (micro) b.p. 101 °C, $n_D^{24} = 1.4278$. NMR spectrum: 0.25–1.0 (5H, cyclopropane-H), M, 2.3–2.7 (3H, oxirane-H), M.

Received: November 16, 1968 [Z 906b IE]
German version: Angew. Chem. *81*, 86 (1969)

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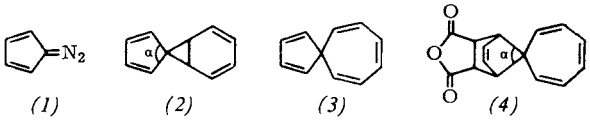
A Spiro Derivative of Norcaradiene

By *D. Schönleber*[*]

Irradiation of diazocyclopentadiene (3.0 g) *(1)*[1] in benzene (300 ml) by a Philips high-pressure lamp HPK 125 at +15 °C liberates 90% of the calculated amount of nitrogen in 3–4 h. Working up by several recrystallizations from pentane (+20 → –78 °C) gives 30–40% of a crystalline but readily polymerizable hydrocarbon, $C_{11}H_{10}$ [m.p. 25–28 °C, λ_{max} = 267 nm (log ε = 3.84)].

Surprisingly, of the pair of valence-isomeric formulas *(2)* and *(3)*, the NMR spectrum of the product unequivocally indicates formula *(2)*, that of spiro[2,4-cyclopentadiene-1,7'-norcaradiene]: apart from the signals for eight olefinic protons (τ = 3.95 m) there is a multiplet at higher field (τ = 6.40) that can only be assigned to two protons on saturated carbon atoms.

An exothermic reaction of this product *(2)* with maleic anhydride in ethyl acetate affords a 1:1 adduct of m.p. 200 to 202 °C, which according to the NMR spectrum is, however, derived, not from *(2)*, but from the tropylidene form *(3)*. The structure of *(4)* is proved by NMR spectroscopy: apart from the signals at τ = 6.75 and 6.25, whose positions correspond with those of comparable protons in the spectrum



of the cyclopentadiene-maleic anhydride adduct, there are only signals in the olefinic region (at τ = 4.54, 3.65, and 3.18 (2:2:2:4:2)[1a]).

In the above examples the position of the norcaradiene-tropylidene equilibrium[2] appears to depend on the size of the angle α: a small "counter-angle" on the spiro carbon atom favors the norcaradiene formula, and a large one favors the tropylidene formula. It is interesting that *M. Jones'* spirane[3] also has the norcaradiene structure.

An attempt to detect the equilibrium *(2)* ⇄ *(3)* at higher temperature failed because irreversible isomerizations occur at temperatures as low as 70 °C.

Received: November 6, 1968 [Z 903a IE]
German version: Angew. Chem. *81*, 83 (1969)

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[1] *W. von E. Doering* and *C. H. DePuy*, J. Amer. chem. Soc. *75*, 5955 (1953).

[1a] Instrument Varian A-60, TMS as internal reference.

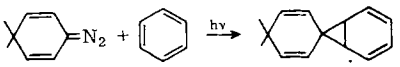
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A Stable Spironorcaradiene[1]

By *M. Jones jr.*[*][2]

It has long been recognized that an entry to the elusive norcaradiene system[3] might be gained by the reaction of a carbene with benzene. This approach has met with little success since, at least in most simple systems, the cycloheptatriene form is favored at equilibrium. To date, the 7,7-dicyanonorcaradiene prepared by *Ciganek*[4,5] remains the sole example of a norcaradiene unencumbered by bridging or benzo substitution and uncomplicated by significant amounts of the cycloheptatriene form. To this we wish to add a further example, 4,4-dimethylspiro[cyclohexadiene-1,7'-norcaradiene] *(2)*.

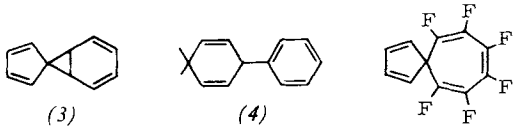


(1) (2)

In the course of an investigation of 4,4-dimethylcyclohexadienylidene[6] it became apparent that one of the products formed on photolysis of a benzene solution of the diazo compound *(1)* was the adduct *(2)*. Thus irradiation of a solution of 200 mg of *(1)* in 1 liter of degassed benzene followed by removal of the bulk of the solvent and careful gas chromatography[7] yielded *ca.* 30 mg of a low melting solid (m.p. 40–43 °C) identified as *(2)*. High resolution mass spectroscopy[8] established the elemental composition as $C_{14}H_{16}$.

The nuclear magnetic resonance spectrum[9a] is interpretable only in terms of structure *(2)*. In the region between $\tau = 3.6$ and 4.9 there appears a quartet superimposed upon a complex multiplet. The entire group integrates for eight hydrogens and, with the exception of the quartet, resembles the downfield portion of the spectrum of 7,7-dicyanonorcaradiene[9]. A six-hydrogen singlet appears at $\tau = 8.94$ and is attributable to the equivalent methyl groups. Most important, however, is the symmetrical multiplet, integrating for two hydrogens, which is centered at $\tau = 6.47$. This is very nearly the position reported for the analogous hydrogens in the dicyano compound ($\tau = 6.53$)[4] and in spiro[2,4-cyclopentadiene-1,7′-norcaradiene] *(3)* ($\tau = 6.40$)[5]. The cycloheptatriene form is therefore eliminated.

Further structural evidence is provided by the conversion of *(2)* into *(4)* on either incautious gas chromatography or heating to 100 °C for 86 min.



(3) (4) (5)

It seems noteworthy to us that *(2)* and *(3)* are in the bicyclic form while *(5)*, synthesized by us from hexafluorobenzene[10], is a cycloheptatriene. Fluorines clearly have a determining influence and actually prefer the vinyl position to the cyclopropyl. This is in accord with the observation[11] that monofluorobullvalene prefers to keep its fluorine off the three-membered ring.

Received: November 6, 1968 [Z 903b IE]
German version: Angew. Chem. *81*, 83 (1969)

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[1] Our thanks go to the National Science Foundation for support of this work through grant GP-7819.

[2] Alfred P. Sloan Research Fellow, 1967–1969.

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[5] *D. Schönleber*, Angew. Chem. *81*, 83 (1969); Angew. Chem. internat. Edit. *8*, 76 (1969), reports that cyclopentadienylidene adds to benzene to give a norcaradiene (III). We are most grateful for the communication of this result prior to publication.

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[7] A 1′, 10% FFAP on 45/60 Chromosorb W column operated at 70 °C with a flow rate of 100 ml/min was used. All other columns tried isomerized *(2)* to *(4)*.

[8] Measured on an AEI MS-9 instrument. We thank the National Science Foundation for help towards the purchase of this instrument (GP-5200). The instrument laboratory at Princeton is supported in part by Biomedical Sciences Support Grant FR-07057.

[9] *C. Ganter* and *J. D. Roberts*, J. Amer. chem. Soc. *88*, 741 (1966).

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CONFERENCE REPORTS

Cytochemistry

The Gesellschaft für Biologische Chemie (Germany) held its autumn meeting on October 2 to 4, 1968, in Münster. The following report contains summaries of some of the papers.

Structural Components of the Cell Wall of *E. coli*

By *V. Braun*[*]

The cell wall of *E. coli* contains lipoprotein and lipopolysaccharide layers which, *inter alia*, carry specific receptors for attachment of bacterial viruses and for the o-antigen groups, and also has an exclusively covalently bonded macrostructure (murein, peptidoglycan) whose size is that of the bacterial surface. This macrostructure is principally responsible for the cell form. To the interior cytoplasmic membrane are assigned the important functions of respiration, oxidative phosphorylation, and active transport.

In experiments on enzymic degradation of the cell wall by hydrolases (proteinases, glycosidases, lipases) it was found that the very specific proteinase trypsin had the strongest effect. At an enzyme:cell-wall protein ratio of 1:50 the optical density of a suspension of bacterial cell walls decreases in 2 min at room temperature to 45% of the end value, which is reached after 20 min. Other proteinases react much more slowly when used in the same molar ratio and measured each at its optimum pH: pronase 0.8%, chymotrypsin 6%, and papain 24%. This specific action of trypsin indicates a particularly trypsin-sensitive peptide bond that is of importance in holding the cell wall together. If the murein layer is isolated, after incubation, by means of sodium dodecyl sulfate, it is free from covalently bound protein. Only lysine occurs as additional amino acid, in a molar ratio of 1:10 to the other components of murein.

Even after only 3 minutes' cleavage by trypsin a protein can be isolated whose lysine:arginine ratio is 4:4 and not 5:4. From quantitative amino acid analyses it is concluded that a protein of molecular weight 7000 containing about 60 amino acids is covalently bound to, on the average, every tenth murein unit (*N*-acetylmuraminyl-*N*-acetylglucosaminyl with the side chain L-Ala-D-Glu-*meso*-DAP-D-Ala)[1].

This protein is probably a lipoprotein, as shown by the following facts: if murein containing the covalently bound protein is hydrolyzed by hydrochloric acid, an insoluble component remains which is proved to be a lipid by its solubility in organic solvents, its chromatographic behavior on silica gel, and by means of staining. Trypsin or pronase can remove the lipid together with the protein of the murein layer, but only after acid hydrolysis does this lipid become soluble in chloroform and show the R_F value of the above-mentioned sample. The name murein-lipoprotein is suggested for this macromolecule.

The rapid decrease in optical density observed on cleavage of the lysine bridge between the lipoprotein and the murein layer can also be demonstrated by electron microscopy (*K. Rehn*). In ultra-thin sections the cell wall is split into two layers by treatment with trypsin for 20 min. This investigation shows for the first time a clearly homogeneous membrane lipoprotein to which an appreciable function for stabilization of the cell wall can be attributed.

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[1] DAP = 2,6-diaminopimelic acid unit. Cf. also *W. Weidel*, Angew. Chem. *76*, 801 (1964).

Studies of the Primary Action of Phalloidin

By *M. Frimmer* (Lecturer), *H. Glossmann*, *J. Gries*, and *D. Hegner*[*]

The rapidly acting phalloidin and the more slowly acting α-amanitin play a decisive role in cases of poisoning by the bulbous leaf fungus *Amanita phalloides*. The mode of action of phalloidin can be best studied on the isolated perfused liver. The first measurable effect (noticeable after 5 min) is loss of potassium, which begins very soon, and a corresponding entry of sodium. Other metabolic changes (changes in energy relations, carbohydrate metabolism, liberation of structurally bound enzymes, *etc.*) become measurable only after some further time. The poison is taken up by the liver within a few minutes at room temperature, but extremely slowly below 10 °C. At unphysiologically low temperatures the loss of potassium and swelling of the liver do not occur or are at least much retarded.

Isolated liver-cell plasma membranes bind ^{3}H-labeled poison better than do other subcellular parts of the liver. During the first minutes of poisoning there is enrichment of the labeled phalloidin in the outer cell membrane, and it is distributed over the whole cell only later, the main portion being then bound in the inner membranes (endoplasmic reticulum).

Studies of isolated liver-cell membranes showed either a retardation or an activation of the cation-dependent ATPases, according to the experimental conditions. It is therefore unlikely that phalloidin influences active cation transport.

Electron-optical photographs of isolated liver-cell membranes show changes in the membrane structure after incubation *in vitro*; so at the beginning of poisoning the primary action is to be assumed to be on the outer protoplasmal membrane of the liver cell. With increasing enrichment of the poison in the inner cell membranes the known, morphologically visible damage to the liver cell occurs, but the change in permeability of the liver-cell plasma membrane is to be seen as the primary event of phalloidin poisoning.

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Embryonic Development of the Enzyme of Fructose Metabolism

By *F. Heinz* (Lecturer) and *F. Weiner*[*]

The embryonic and postnatal development of the enzyme of fructose metabolism has been studied in the liver of rats and chickens. The activity of the following enzymes was measured: sorbitol dehydrogenase, fructokinase, aldolase with fructose 1,6-diphosphate and fructose 1-phosphate as substrate, aldehyde-dehydrogenase with D-glyceraldehyde as substrate, and triokinase. Also measured were the activities of the NAD- and NADP-specific alcohol dehydrogenases which reduce D-glyceraldehyde to glycerol and whose importance for fructose metabolism is disputed. Comparison showed that the change in enzyme activities during embryonic and postnatal development is similar for the rat and the chicken. The enzymes can be divided into three groups: 1. Enzymes that can be detected in the liver only after birth; the sole example is fructokinase. 2. Enzymes that change their isoenzyme pattern during embryonic and postnatal development, *e.g.*, aldolase; the ratio of the experimentally found rates of cleavage of fructose 1-phosphate and fructose 1,6-diphosphate under optimal conditions changes from 10:1 in the embryo to 2.6:1 in the adult rat but only from 3.8:1 to 2.3:1 in the chicken. 3. Enzymes that can be detected in the embryo and whose activities rise steadily between the embryonic and the adult state; examples are sorbitol dehydrogenases, alcohol dehydrogenases, triokinase, and also the aldehyde-dehydrogenase that is found with high activity in the liver of even embryonic rats and chickens and which changes only slightly during further development.

Our experiments show that biosynthesis of the enzyme of fructose metabolism is not determined by a single genome. Attempts to achieve faster postnatal increase in the enzyme activity by means of fructose were unsuccessful.

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Evolution of Allosteric Enzymes

By *A. W. Holldorf*[*]

Allosteric control has been demonstrated for numerous enzymes during recent years. It has been analyzed mainly *in vitro*, and there have so far been few observations on the importance of allosteric effects in microorganisms *in vivo*. Metabolic changes can be demonstrated *in vivo* for mutants in which enzymes have lost their allosteric properties but retain their catalytic activity. Indirect evidence for the importance of allosteric mechanisms *in vivo* is provided by comparison of effective concentrations of allosteric effectors *in vitro* with the concentrations of these metabolites that occur *in vivo*.

We have compared three allosterically controlled enzymes: aspartate transcarbamylase with cytidine 5′-triphosphate as a negative effector; deoxycytidine 5′-monophosphate deaminase with thymidine 5′-triphosphate as a negative effector and with thymidine 5′-triphosphate as a positive effector; and thymidine kinase with thymidine 5′-triphosphate as a negative effector. The activities of these enzymes were measured under optimal conditions. The influence of effectors on these enzymes in cell-free extracts of microorganisms, lower plants, and animals, as well as in extracts of tissues of higher plants and animals was studied. Further, so far as analytically possible, the intracellular concentrations of the effectors were determined.

It was found that deoxycytidine 5′-monophosphate deaminase and thymidine kinase from all the organisms that contained them were influenced by effectors always at approximately the same concentrations, these concentrations being of the same order as the intracellular concentrations of the respective nucleotides. However, for aspartate transcarbamylase this behavior was observed only for some of the microorganisms; for all other organisms the effectors become efficient only in concentrations 10 to 1000 times as great as the intracellular concentration of cytidine 5′-triphosphate.

According to these results allosteric control of deoxycytidine 5′-monophosphate deaminase and of thymidine kinase may be of biological importance for all organisms, but that of aspartate transcarbamylase probably only for microorganisms. Allosteric control of aspartate transcarbamylase was probably

lost in the course of evolution and replaced by other controls, whereas it was retained for the other two enzymes in all organisms.

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Tissue Hyaluronidase and Healing of Wounds

By *W. Heller* (Lecturer) and *F. K. Mörl*[*]

We have studied the behavior of tissue hyaluronidase and of protein-bound iodine for up to seven or nine days after a goiter operation on more than fifty men and women. The content of protein-bound iodine is a well-defined measure of the thyroxine level in the blood. There is a remarkable decrease in the tissue hyaluronidase (mean curves) on the day of the operation, although it remains in the normal region; the minimum (far below the normal value) is reached only on the third day. For an exact correlation of tissue hyaluronidase and protein-bound iodine, the curves for each patient must be studied individually. After all goiter operations the amount of protein-bound iodine increases, but that of tissue hyaluronidase decreases. In the ideal case the two curves are almost the opposite of each other. Thus in almost all the patients the corresponding maxima and minima occur at the same time. The extreme values, however, depend on the nature of the goiter. This is particularly noticeable for hyperthyrosis; nevertheless, euthyrotic patients also show the course described above for both curves, but not so strikingly.

Although there is a significant relation between tissue hyaluronidase and protein-bound iodine, it is apparent that this can be only indirect, since tissue hyaluronidase can be influenced by a proteinase inhibitor whereas protein-bound iodine is not so influenced. In this way we could obtain an increase in tissue hyaluronidase that was totally independent of the level of the protein-bound iodine in the blood.

Administration of the proteinase inhibitor thus exerts a favorable therapeutic effect, since a severe fall in tissue hyaluronidase is undesirable for wound healing. The positive influence of thyroxine in wound healing is a known fact, and was confirmed in experiments *in vitro*; it explains why wounds heal so rapidly after operations for goiter.

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Allosteric Properties of Yeast Pyruvate Kinase

By *H.-J. Wieker, K.-J. Johannes* (Lecturer), and *B. Hess*[*]

In previous papers *Hess et al.*[1] demonstrated the strong cooperativity of yeast pyruvate kinase with the substrate phosphoenol pyruvate and showed that fructose 1,6-diphosphate is an allosteric activator and adenosine triphosphate (ATP) an allosteric inhibitor.

Yeast pyruvate kinase fulfils the requirements of the *Monod-Wyman-Changeux* model[1,2]. The state functions and the binding functions derived from that model, as well as the constants characterizing the enzyme, have been determined from further studies of the steady-state kinetics under the influence of fructose 1,6-diphosphate and ATP, using *Blangy, Buc*, and *Monod*'s method[3].

The number of binding sites per enzyme molecule was found to be two for the ligands phosphoenol pyruvate, fructose 1,6-diphosphate, and ATP, *i.e.*, yeast pyruvate kinase consists of two identical protomers.

An equilibrium exists between an active (R) and an inactive (T) state of the enzyme, with an equilibrium constant $[T]/[R] = L_0 = 1.5 \times 10^3$. The dissociation constants for the ligands in the R state (K_R) and in the T state (K_T) amount to $K_R = 2 \times 10^{-4}$ M, $K_T = 3.5 \times 10^{-2}$ M for phosphoenol pyruvate [non-exclusive binding coefficient $c = 6 \times 10^{-3}$], $K_R = 1 \times 10^{-4}$ M for fructose 1,6-diphosphate, and $K_T = 2 \times 10^{-3}$ M for ATP.

It can be seen from these constants that in the absence of ligands yeast pyruvate kinase is predominantly in the T state, that ATP fixes this state, and that the other two substances shift the equilibrium largely from the T to the R state.

Experiments concerning the binding of the second substrate ADP, which shows cooperativity only at phosphoenol pyruvate concentrations below 5×10^{-3} M[1], are not yet complete. Results so far indicate that binding of ADP to the enzyme-phosphoenol pyruvate complex is favored over binding to the free enzyme.

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Biogenesis of Mitochondria; Pathway of the Synthesis of Mitochondrial Phospholipids

By *B. Kadenbach*[*]

Isolated mitochondria can synthesize phosphatides only in the outer membrane[1]. The origin of the phosphatides in the inner membrane, which contains about 80% of the total phosphatides, is unknown. Experiments on incorporation of $^{32}PO_4^{3-}$ into isolated rat-liver mitochondria showed highly diverging rates of incorporation (mmoles of $^{32}PO_4^{3-}$/mole of phosphatide-phosphate in 10 min) for the phosphatides studied: phosphatidylcholine 0.08; phosphatidylethanolamine 0.29; phosphatidylserine 4.9; phosphatidylinositol 0.3; lysophosphatidylcholine 2.4. Except for lysophosphatidylcholine, these rates are less than the maximal rates of incorporation after injection of $^{32}PO_4^{3-}$ *in vivo* (8, 40, 29, 20, and 2.1, respectively).

The outer membrane, the intracristale proteins, the inner membrane, and the matrix of mitochondria labeled *in vitro* were isolated by digitonin[2] and the phosphatides were separated by two-dimensional thin-layer chromatography. The soluble fractions were obtained by one hour's centrifugation at 400000 g. They contained appreciable amounts of labeled phosphatides (nmoles of phosphatide-phosphate/mg of protein): outer membrane 660, intracristale region 195, inner membrane 345, matrix 35. For phosphatidylcholine, phosphatidylethanolamine, and phosphatidylserine + phosphatidylinositol the specific radioactivity was greatest in the outer membrane. Only lysophosphatidylcholine showed the highest activity in the intracristale region. Correspondingly their content there was greatest (2.2, as compared to 0.6–0.9).

Kinetic studies of the incorporation of $^{32}PO_4^{3-}$ *in vivo* showed rapid labeling of phosphatidylethanolamine in the microsome fraction. Only after a delay of about 10 min was the mitochondrial phosphatidylethanolamine labeled. Phosphatidylcholine in both particles was labeled only after a further delay of 10 min; as in the previous case, it was labeled more rapidly in the microsomes than in the mitochondria. *In vivo* also phosphatidylethanolamine and phosphatidylserine were labeled first in the soluble and then in the insoluble mitochondria fraction. In a further experiment the transfer of labeled phosphatides from the microsomes into the mitochondria could be demonstrated directly *in vitro*. This transfer is energy- and time-dependent, as previously shown for protein transfer[3].

The results are interpreted in the sense that most of the mitochondrial phosphatides are synthesized on the endoplasmic reticulum and transported together with newly synthesized protein as a molecular complex into the mitochondria.

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Physiological Role and Regulation of 10-Formyltetrahydrofolate:NADP Oxidoreductase

By *C. Kutzbach*[*]

The enzyme 10-formyltetrahydrofolate:NADP oxidoreductase[1], which was first found in pig liver, catalyzes reaction (1). Severe product inhibition by tetrahydrofolate makes quantitative tests difficult. The inhibition can be overcome by coupling with an excess of formate:tetrahydrofolate ligase (E.C.6.3.4.3) from *Clostridium cylindrosporum* [eq. (2)].

$$10\text{-CHO-H}_4\text{PteGlu} + \text{NADP}^+ + \text{H}_2\text{O} \rightarrow \text{CO}_2 + \text{H}_4\text{PteGlu} + \text{NADPH} + \text{H}^+ \quad (1)$$

$$\text{H}_4\text{PteGlu} + \text{HCOOH} + \text{ATP} \rightarrow 10\text{-CHO-H}_4\text{PteGlu} + \text{ADP} + \text{P} \quad (2)$$

$$\text{HCOOH} + \text{NADP}^+ + \text{ATP} + \text{H}_2\text{O} \rightarrow \text{CO}_2 + \text{NADPH} + \text{ADP} + \text{P} + \text{H}^+ \quad (3)$$

PteGlu = Pteroyl-L-glutamic acid (folic acid)

On this basis a spectrophotometric (NADPH) and a radioactive (10-^{14}CHO–H_4PteGlu or ^{14}C-formate $\rightarrow$ $^{14}CO_2$) test were developed in which formate is oxidized to CO_2 by a catalytic amount of folate in accordance with eq. (3). Oxidation of formate can occur physiologically in the same way; enzyme activities of the same order (1–5 mIU/mg) as for the enzymes for eqs. (1) and (2) are found in the cytosol from the liver and kidneys of the rabbit and rat. The activity was less or not demonstrable at all in other organs or in chicken liver. In the absence of $NADP^+$ or in the presence of 0.1 M hydroxylamine the oxidoreductase catalyzes hydrolysis of 10-formyl-H_4PteGlu to H_4PteGlu and formate at, at most, 30% of the rate of the oxidation. This indicates an active formyl compound as intermediate, but no formohydroxamate could be detected.

The K_M values are 3.5 μM for NADP and 8.2 μM for (−)-10-CHO–H_4PteGlu. The same K_m and V_{max} were found with the (±)-isomeric mixture giving only 50% conversion. Thus the inactive (+)-form does not cause inhibition. However, both isomers of the product cause severe inhibition, so that the rate of reaction amounts to only *ca.* 30% of the normal value if (±)-H_4PteGlu is used in place of CHO–H_4PteGlu in a coupled test. The inhibition constants (K_i) obtained were of the order of 12 μM [(+)-isomer] and 0.5 μM [(−)-isomer]. Inhibition is approximately, but not strictly, competitive. Inhibition is specific for H_4PteGlu; 5-CHO–H_4PteGlu, 5-CH_3–H_4PteGlu, folic acid, aminopterin, and reduced aminopterin cause no inhibition up to 5×10^{-4} M. The strong specific inhibition by product indicates regulation of the tissue concentration of unsubstituted tetrahydrofolic acid by this enzyme.

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The Point of Attack of Cortisol in the Cell Nucleus

By *M. Beato, J. Homoki,* and *C. E. Sekeris* (Lecturer)[*]

Parenteral administration of cortisol leads to a rapid stimulation of RNA polymerase activity of rat liver nuclei and to an increase in the template activity of chromatin for RNA synthesis. The same effects have been observed after incubation of cortisol with rat liver nuclei. We conclude therefore that the primary site of action of the hormone is to be found in the cell nucleus. To localize the point of attack more closely we have studied the processes occurring during the increase of the template activity of chromatin *in vitro*. Chromatin consists mainly of DNA, RNA, and protein. Since ^{3}H-cortisol is bound exclusively to nuclear protein, we have investigated the influence of the hormone on nuclear proteins *in vitro*.

It was previously postulated that chemical modifications of the basic nuclear proteins by acetylation or methylation are important for the regulation of RNA synthesis. Cortisol does not effect histone acetylation or methylation. We have established, however, an increase in the thiol content of nuclear proteins even after two minutes' incubation of the nuclei with cortisol. Both basic and acidic nuclear proteins show an increased content of thiol groups.

Our experiments indicate that cortisol can increase the template activity of chromatin by direct interaction with nuclear proteins.

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Transport of Double- and Triple-stranded Ribopolynucleotides through Cellular Membranes

By *P. L. Schell*[*]

Uptake of homologous radioactively labeled RNA into Ehrlich Ascites tumor cells was described previously[1]. It has now been shown that ^{14}C/^{3}H double-labeled poly A · U and poly A · U_2 can enter ascites cells much faster than their constituents, poly A and poly U, or RNA mentioned initially. The cells were suspended in *Hank*'s medium which contained the polymer. After incubation, the medium was removed from the cells. Then the radioactivity could be measured either in the complete cells or from the recovered polynucleotide fractions. It is remarkable that this uptake approaches 50% of maximal loading when the system was incubated at 0 °C. Even at this temperature the initial rate of loading is very fast so that a plateau is reached after incubation times of about 30 min. During this procedure the 1:1 ratio of the partners in the case of poly A · U and the 1:2 ratio in the case of poly A · U_2 was maintained. The high molecular weight ribopolynucleotides could not have been degraded during penetration of the cell wall, since this material can be phenol-extracted from the cells and exhibits a behavior identical with that of authentic poly A · U_2 when chromatographed on a G 150 Sephadex column. Actinomycin inhibits incorporation into cellular RNA of labeled poly A- or poly U-fragments. This possibility was simulated by addition of ^{14}C-AMP to a mixture of cells and poly ^{3}H-A · U_2 in *Hank*'s medium. Hardly any ^{14}C-RNA was found alongside the standard amounts of penetrated poly ^{3}H-A · U_2 when the loaded cells where extracted by phenol. Defined double- or triple strandedness is obligatory for highly efficient entry of the polymers. The method of continuous variation was employed to offer to the cells a range of media containing different ratios of poly A to poly U. The uptake of each of the partners is maximal when the ratio A · U is 1:2. The hypochromicity, *i.e.* the base pairing by H-bridges in poly A-poly U complexes, is lost when poly A is *N*-oxidized and this loss is paralleled by a sharp decrease of cellular uptake. Separation of double or triple strands during their penetration into the cell membrane has not been observed. Any dissociation of poly

[^{14}C A] [^{3}H U_2] which would have occurred would result in isotopic dilution of the labeled helix partners in the presence of added molar excesses of either non-labeled poly A or poly U or poly A U. This effect would be noticeable in the case of irreversible or reversible helix dissociation but was not observed in either case.

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Chemical and Enzymic Reactions on the Membranes of Ehrlich Ascites Tumor Cells and their Consequences for Metabolism and Permeability

By *R. Brossmer* (Lecturer), *W. Brandeis*, and *K. Kramps*[*]

In a study of the relation of chemical structure to biological function of membranes of animal cells, the cells have been modified by substances whose effect on groups in the cell surface could be defined. The effects of such modifications upon metabolism and permeability have been investigated.

Ehrlich mouse ascites tumor cells were used, but the results appear to be valid also for other types of cell.

Treating the cells with periodate (10^{-4} M to 10^{-2} M, 15 min, 37 °C) leads to changes in metabolism and permeability that vary according to the concentration employed. After treatment with 10^{-4} M periodate glycolysis is 70% of that of control cells, after 5×10^{-4} M about 50%, and after 10^{-3} M at most 5%. Similar figures are obtained for respiration.

To detect an effect on membrane function, the efflux of potassium and protein was studied in relation to periodate concentration. It was observed that the membrane became increasingly more permeable to substances of low and high molecular weight. The chemically defined action of periodate on glycoproteins and glycolipids of the cell membrane thus leads to massive changes in permeability. This is indicated also by the fact that non-permeable dyes such as Trypan Blue and Naphthalene Green V now appear within the cell. – In experiments over a long period the inhibition of metabolism caused by periodate[1] proved to be partly reversible. Thus glycolysis of the cells treated with 10^{-3} M periodate regained 45% of the control value after 5 h, and then remained constant. The diminution in metabolism thus consists of a reversible and an irreversible disturbance, in which, however, the influx of dye was the same after 5 h as at the beginning, *i.e.*, the membrane remained damaged. Transplantation of the cells became impossible only after incubation with 10^{-2} M periodate. Treatment with 0.1 M periodate (1 h, 20 °C) reduces the mobility of the cells in an electric field by 10 to 15%, and neuramidase can then cleave only little of the sialic acid (in contrast to the strong effect of the enzyme on control cells).

Whereas treating ascites cells with 0.1% of phenethyl alcohol (15 min, 37 °C) leads to only a slight diminution in metabolism, 0.5% of this alcohol reduces anaerobic glycolysis to 3% and respiration to 18% of the controls. With 0.25% of the alcohol the inhibition is wholly reversible.

A considerable disturbance of permeability is indicated by the following findings: 1. Efflux of potassium. 2. Efflux of protein. 3. Influx of dye. The cells can no longer be transplanted (0.5% of phenethyl alcohol, 15 min, 37 °C). The electrophoretic mobility is, however, unchanged.

Neither subtilisin nor lysozyme affects the metabolism or mobility; however, alkaline phosphatase reduces respiration and glycolysis by about 30%, and in this case the mobility rises by 10–15%.

The cell membrane can be modified chemically by succinylation. This not only causes positive charges to disappear but also attaches new negative charges to the cell surface. This leads experimentally to an increase of 20% in the mobility in an electric field. Cells modified in that way are morphologically intact but have special properties. Neuramidase removes about 1/3 less sialic acid than from untreated cells; metabolism is strongly inhibited.

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[1] Concentration: 10^{-3} M.

Receptors on the Surface of Human Thrombocytes

By *R. Brossmer* (Lecturer) and *H. Patscheke*[*]

Thrombocytes that have been washed once and thus freed from their complex milieu form good experimental material since they are morphologically and functionally intact. In a search for receptors for the physiologically and pathologically important process of aggregation the following were observed.

Calcium aggregates blood platelets even without further additions, and it is immaterial whether the reaction occurs in buffer solution or in plasma (with heparin). Aggregation increases with fall in temperature, reaching a maximum at 15–20 °C. For this, 5×10^{-4} M Ca^{2+} is required, *i.e.*, 1/5 of its physiological concentration in the plasma, but even 5×10^{-5} M Ca^{2+} causes appreciable aggregation. Above 3×10^{-3} M Ca^{2+} no aggregation is caused, but rather disaggregation. Qualitatively the same results are observed with magnesium (5×10^{-4} M) but the aggregation amounts only to about 40% of that caused by calcium. The aggregations induced by calcium or magnesium are reversible at increased temperatures. The cycle can be repeated several times, merely by change of temperature. Adenosine diphosphate plays no part. Thus calcium and magnesium can be considered as the simplest aggregating materials[1]. Interaction with the cells depends on simple physicochemical phenomena.

The receptor on the thrombocyte surface can be cleaved by alkaline phosphatase; there are about 10^6–10^7 phosphate groups per thrombocyte. All other calcium-dependent aggregations, including the physiologically important one caused by adenosine diphosphate, are also blocked by this enzyme. In contrast thereto, the aggregating effect of positively charged polymers[2] is unaffected in the presence of this enzyme. In this case chemically different groups act as receptors, being partly removed by neuramidase, although the action of all the calcium-dependent substances is unaffected. Thus we have proved the existence of two types of receptor for the aggregation: 1, phosphate groups, which play a special role as metal-chelating agents; and 2. sialic acid molecules.

[VB 174 IE]
German version: Angew. Chem. *81*, 37 (1969)

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Studies on Adenovirus Type 12: Relations between the Virus- and Host Genomes[**] [1]

By *W. Doerfler*[*]

The objective of the experiments described was to follow the intracellular fate of the deoxyribonucleic acid (DNA) of adenovirus type 12 (Ad 12) in the early stages after infection

of hamster cells (BHK21). It can be shown that Ad 12 does not multiply in BHK21 cells. *Strohl et al.*[2] demonstrated that BHK21 cells can be transformed by Ad 12, which belongs to the group of highly oncogenic adenoviruses.

The DNA of Ad 12 can be separated from that of BHK21 cells by equilibrium centrifugation in CsCl gradients ($\Delta\rho$ = 0.006 g × ml^{-1}). This small difference in density can be increased by culturing the BHK21 cells in a medium containing 5-bromodeoxyuridine. Such cells are infected with high multiplicities of purified Ad 12, the DNA of which had been labeled with [^{3}H]thymidine. The cells are lysed at various times after infection, and the total DNA is isolated by treatment of the lysate with pronase and phenol and by equilibrium centrifugation in CsCl. The distribution of ^{3}H between the positions of cellular and viral DNA is followed in CsCl density gradients. The position of viral DNA is determined by the addition of a small amount of ^{14}C-labeled Ad 12 DNA. Cellular DNA is found at a higher density than viral DNA.

Up to about 16 h after infection the total ^{3}H activity appears at the position of viral DNA. From 20 h after infection on, an increasing proportion of the ^{3}H activity appears in the position of cellular DNA, while the ^{3}H activity at the position of viral DNA decreases. This result can be explained by any of the following assumptions:

1) Viral DNA is replicated in the presence of 5-bromodeoxyuridine and thereby becomes heavy.

2) Viral DNA is degraded to mononucleotides by nucleases, and the [^{3}H]thymidine 5′-monophosphate liberated is converted by kinases into [^{3}H]thymidine 5′-triphosphate (TTP) and reincorporated into cellular DNA. The synthesis of cellular DNA continues after infection of BHK21 cells with Ad 12.

3) The viral genome or part of it is bound to cellular DNA (integration).

Replication of the DNA of Ad 12 in BHK21 cells is not detectable[1,3]. Thus the first of the above possibilities is excluded.

One can distinguish between possibilities 2 and 3 by comparing the CsCl density gradient profiles of DNA from infected cells in the high-polymer state (180 × 10^6 Daltons) with that of DNA that has been degraded ultrasonically to fragments of 2 × 10^6 Daltons.

As shown in Figure 1, shift of the maximum of the ^{3}H activity to the position of the density hybrid would be expected after fragmentation of the cell DNA, in case viral genes had become integrated.

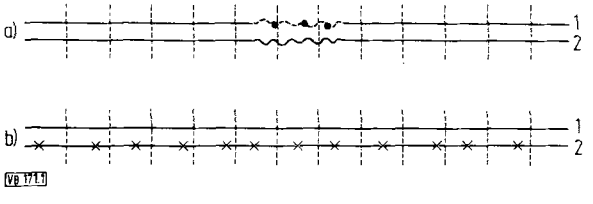


Fig. 1. a: Schematic representation of the integration of viral DNA (Ad 12) into cell DNA (BHK21). b: Uninfected control cells.

Positions at which DNA is fragmented by ultrasonication; 1, old DNA strand; 2, new DNA strand; — heavy cell DNA containing 5-bromodeoxyuridine; ~~~ heavy viral DNA containing 5-bromodeoxyuridine; .·.·.·.·. light viral DNA containing thymidine; • [^{3}H]thymidine; × [^{3}H]-5-bromodeoxyuridine.

This shift, which is due to separation of the integrated viral genes (density hybrid) from the heavy cellular DNA, would not be expected if [^{3}H]TTP had been reincorporated.

Experimentally, such a shift of the maximum of the ^{3}H activity is found after fragmentation of the DNA of 5-bromodeoxyuridine-BHK21 cells that have been infected with ^{3}H-labeled Ad 12. The shift is not observed (Figure 1b) for the DNA of uninfected control cells.

This result is consistent with the assumption that viral genes have been integrated into the DNA of BHK21 cells. The integration probably occurs by covalent linkage, since the ^{3}H activity at the position of higher density is retained also in alkaline CsCl solution (pH > 12).

Lecture at Göttingen (Germany) on July 2, 1968
German version: Angew. Chem. *81*, 87 (1969) [VB 171 IE]

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[**] These investigations were supported by the United States Public Health Service, grant No. AI-03445.

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Studies on the Mode of Action, Coenzyme Binding, and Structure of Yeast Pyruvate Decarboxylase

By *J. Ullrich*[*]

In enzymatic pyruvate decarboxylations with thiamine pyrophosphate [TPP] as coenzyme, (−)-2-α-hydroxyethyl-TPP [HETPP] can be trapped, accumulated, and isolated[1]. The conversion of this product by apo-enzymes is much slower than that of pyruvate by the TPP-saturated holo-enzymes[1]. Due to steric hindrance[2], HETPP recombines very poorly with apo-pyruvate decarboxylase. Furthermore, removal of the α-proton of HETPP, *i.e.* restoration of the carbanion primarily arising from the decarboxylation, is achieved only with difficulty[3]. This led to the assumption that the primary α-carbanion in the active site of pyruvate decarboxylase is further converted before protons from the medium can reach it. Prior to its release, the acetaldehyde residue is transferred to the 4′-amino group of the TPP[2] and, then, probably to an ε-amino group of the protein[2]. A 4′-amino group still occupied by the previous acetaldehyde residue gives rise to acetoin formation, a regularly observed side reaction. In D_2O, the rate of base catalysis by the ND_2 group is reduced to 50%, whereas the acetoin formation is not affected. Further evidence for a transfer of the unprotonated aldehyde residue is provided by the observation[2] that a 2-hydroxymethyl group, arising from the decarboxylation of glyoxylate, is not transferred; absence of the methyl group facilitates the access of protons from the medium and these can saturate the α-carbanion before the 4′-amino group has a chance to attack.

For further elucidation, the structure of the protein has been studied more closely. Yeast pyruvate decarboxylase has a molecular weight of *ca.* 170000[4] and four binding sites for TPP and Mg^{++}. Three of them bind strongly, one weakly[4]. In 6M guanidinium chloride two subunits are produced that are not further cleaved even in the presence of 10 mM mercaptoethanol. The protein has a high content of lipophilic and of all aromatic amino acids, and of proline, but contains only a small amount of cysteine. With TPP and Mg^{++}, it reversibly forms salts with Michaelis-Menten behavior at different and independent sites[2]. Binding of both cofactors at pH 6.8 leads to a protein rearrangement into a stable ternary complex[2], the holo-enzyme, under conformational changes. These can be measured by a small decrease in the absorbances at 190 nm and at 280 nm in the specific rotation and in the Moffitt parameter b_0, and by a corresponding change in circular dichroism. The calculated total α-helix content rises from 23–25% to about 27%. The protein fluorescence, mainly due to tryptophan, is partly quenched, probably by interaction of several of the 20 tryptophan residues in the molecule with TPP. Recombination with thiochrome pyrophosphate instead of TPP leads to a strong increase of the thiochrome fluorescence[5]. 2-*p*-Toluidinylnaphthalene-6-sulfonate, a dye that is highly fluorescent only in lipophilic environment, is attached to sufficiently large lipophilic areas of proteins[6]. Half of the dye bound to apo-

pyruvate decarboxylase is irreversibly displaced by TPP and Mg^{++}; TPP or Mg^{++} alone have no effect. The other half of the dye acts as competitive inhibitor of pyruvate decarboxylation. Thus, both types of the protein-bound dye must be located at the active site or in its close vicinity. No other large lipophilic regions seem to exist at the surface of the enzyme. TPP is apparently enclosed in a lipophilic pocket, produced by the formation of the stable ternary complex (cf.[2]). The entrance to the pocket and its immediate environment appear to be lipophilic too. Thus, an important condition is fulfilled for direct conversion of the primary α-carbanion: hindered access of protons from the medium, as long as the coenzyme is occupied by substrate.

Lecture at Dortmund, on October 14, 1968
German version: Angew. Chem. *81*, 87 (1969) [VB 175]

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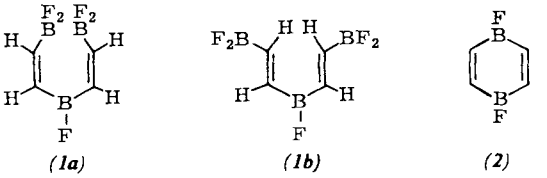
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SELECTED ABSTRACTS

The microwave spectrum of methylcyclopropane was measured by *R. G. Ford* and *R. A. Beaudet* in the frequency range 8–38 GHz. From the splitting of the rotation transitions at high quantum number the potential threshold of the intermolecular rotation was determined as 2860 ± 50 cal/mole. This value is in the expected region, in contrast to the value of the torsion-potential threshold previously determined for 1,1-difluoro-2-methylcyclopropane which at 2260 cal/mole was unusally low. From these results the authors infer preponderatingly electrostatic interaction between methyl hydrogens and hydrogen or fluorine atoms attached to the ring. The dipole moment of methylcyclopropane amounts to 0.139 ± 0.004 D. / J. chem. Physics *48*, 4671 (1968) / – Hz. [Rd 932 IE]

The absorption spectra of small polar molecules in an apolar solvent (cyclohexane) were measured by *P. Datta* and *G. M. Barrow* for the far-infrared region (down to about 40 cm^{-1}). The broad absorption bands observed, whose maxima could on occasions not be determined on the apparatus used, arise from movements of the polar molecules, of rotatory type, that are disturbed by frequent collisions with solvent molecules. From the experimental values, two parameters can be determined for each solution: one gives the energy difference between two rotation states, and the other gives the mean time between two collisions with the solvent. The second parameter amounts to about 10^{-13} sec and is relatively independent of the nature of the dissolved molecule. Thence the free path of the rotating molecule in the liquid can be estimated as about 0.5 Å. Examples of the polar molecules are HCl, NH_3, CH_3I, CH_2Cl_2, CH_3CN, C_6H_5CN, $(CH_3)_3CCl$. / J. chem. Physics *48*, 4662 (1968) / –Hz. [Rd 933 IE]

The reaction of boron monofluoride with alkynes is the subject of a report by *P. L. Timms*. BF can be obtained on a preparative scale from BF_3 and B at diminished pressure and 1800 to 2000 °C. On cocondensation (–196 °C) with acetylene it affords a yellow solid that melts and partly vaporizes when heated. The volatile fraction contains C_2H_2, BF_3, B_2F_4, and a very small amount of $C_2H_3BF_2$ [difluoro(vinyl)borane?] and $C_2H_2B_2F_4$. *(1)* and *(2)* are also isolated in a total yield of about 8%. The nuclear resonance spectra and the IR spectrum of *(1)* (m.p. –68 °C) indicate that it exists as either *(1a)* or *(1b)*. Compound *(2)*, which decomposes at 35 °C without melting and can be obtained from *(1)* by loss of BF_3, has an IR spectrum resembling that of benzoquinone. The three possible dimethyl derivatives of *(2)* are formed

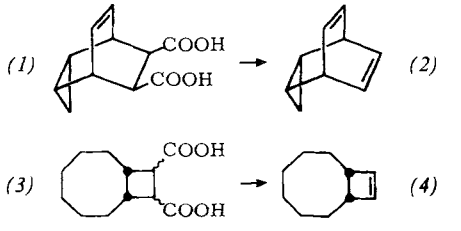


(1a) *(1b)* *(2)*

from propyne and BF, and the tetramethyl derivative is obtained from 2-butyne. / J. Amer. chem. Soc. *90*, 4585 (1968) / –Kr. [Rd 939 IE]

Conversion of liquid xenon into a metal-like state is possible by shock compression according to *M. Ross*. He reaches this conclusion because at high temperatures xenon has an abnormally large compressibility and a density that amounts to two or three times the initial value. Further, the energy difference between the valence band and the conduction band becomes rapidly smaller with increasing density. At 500 kbar and 18000 °K xenon has properties similar to those of cesium: a conduction band of 5d character is partly occupied by electrons that are supplied from the 5p valence band. / Physic. Rev. [2] *171*, 777 (1968) / –Hz. [Rd 935 IE]

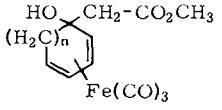
The electrolytic decarboxylation of vicinal dicarboxylic acids[1], according to *P. Radlick*, *R. Klem*, *S. Spurlock*, *J. J. Sims*, *E. E. van Tamelen*, and *T. Whitesides* as well as *H. H. Westberg* and *H. J. Dauben jr.*, is more suitable than the normal treatment with lead acetate for the introduction of a double bond, particularly into polycyclic systems. Examples: *(1)* → *(2)* (yield ≈ 35%), *(3)* → *(4)* (35%). The dicarboxylic



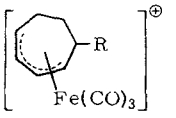
acids are readily obtainable from the anhydrides, which can be prepared by the addition of maleic anhydride to dienes. The electrolyses were carried out in aqueous pyridine in the presence of triethylamine at room temperature. / Tetrahedron Letters *1968*, 5117, 5123 / –Kr. [Rd 941 IE]

[1] *Fichter*, Helv. chim. Acta *24*, 549 (1941).

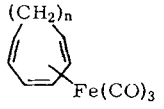
Ring expansion in organoiron compounds has been observed by *J. Lewis* and *A. W. Parkins*. The iron tricarbonyl complexes of 2,4-cyclohexadiene and 2,4-cycloheptadiene react with zinc under the conditions of the Reformatski reaction to form the hydroxy esters *(1a)* and *(1b)* respectively. These



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



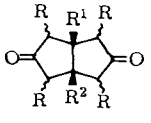
(2a), R = CO_2CH_3
(2b), R = CH_2-CO_2CH_3



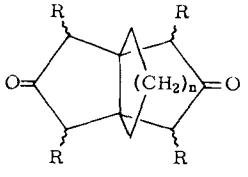
(3a), n = 1
(3b), n = 2

products are converted by trityl tetrafluoroborate into *(2a)* and *(2b)*, both cations containing seven-membered rings. The action of water on *(2a)* yields the complex *(3a)* which can be converted back into *(2a)* by protonation, whereas the reaction of *(2b)* with water results in ring expansion to form *(3b)*. / Chem. Commun. *1968*, 1194 / – Kr. [Rd 942 IE]

A one-step synthesis of pentalane and propellane ketones has been described by *U. Weiss* and *J. M. Edwards*. Dimethyl 3-oxoglutarate reacts with open-chain 1,2-diketones to form



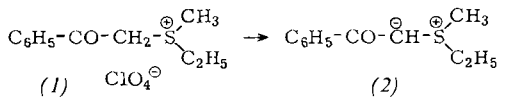
(1a), R = CO_2CH_3, R^1 = R^2 = H
(1b), R = R^1 = R^2 = H
(1c), R = CO_2CH_3, R^1 = CH_3, R^2 = H
(1d), R = R^2 = H, R^1 = CH_3



(2a), R = CO_2CH_3, n = 2
(2b), R = CO_2CH_3, n = 1
(2c), R = H, n = 2
(2d), R = H, n = 1

pentalanedione derivatives, *e.g. (1a)–(1d)*, and with cyclic 1,2-diketones to form derivatives of propellanedione *(2)*. 1,2-Cyclohexanedione and 1,2-cyclopentanedione react to form *(2a)* and *(2b)*, which can be converted into tricyclo[4.3.3.$0^{1,6}$]-dodeca-8,11-dione *(2c)*, m.p. 174 °C, yield 41%, and tricyclo[3.3.3.$0^{1,5}$]undeca-3,7-dione *(2d)*, m.p. 183 °C, yield 39%, without first being isolated. / Tetrahedron Letters *1968*, 4885 / –Kr. [Rd 943 IE]

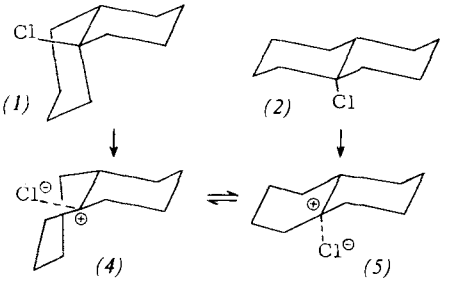
The formation and racemization of (–)-ethylmethylsulfonium phenacylide *(2)* have been described by *D. Darwish* and *R. L. Tomilson*. The reaction of optically active ethylmethylphenacylsulfonium perchlorate *(1)* with dilute NaOH led to *(2)*, which was extracted with chloroform. *(2)*, m.p. 83–85 °C, $[\alpha]_D^{25}$ –137 ° (*c* = 0.487, benzene) racemizes with first order kinetics; the half life in CCl_4 at 50 °C is ≈ 40 min. After 160 min only 5% of *(2)* had decomposed, mainly into methyl



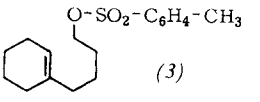
(1) $ClO_4^{\ominus}$ *(2)*

phenacyl sulfide. *(2)* racemizes about 200 times as rapidly as *(1)* in CH_3OH at 50 °C. The racemization is evidently due to inversion of the pyramidal compound. / J. Amer. chem. Soc. *90*, 5938 (1968) / –Kr. [Rd 945 IE]

Conformers of the 9-decalylium ion have been detected by *A. F. Boschung, M. Geisel*, and *C. A. Grob* during the solvolyses of *cis-(1)* and *trans*-9-chlorodecalin *(2)* and 4-(1-cyclohexenyl)-butyl *p*-toluenesulfonate *(3)*. The products obtained in



(1) *(2)* *(4)* *(5)*



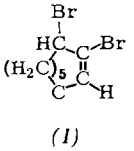
(3)

ethanol/triethylamine were as follows (in %, in the case of *(3)* based on a 55% total yield of cyclization products):

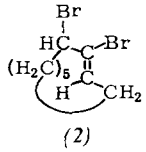
	From *(1)*	From *(2)*	From *(3)*
2,3,4,4a,5,6,7,8-Octahydronaphthalene	51	22	40.5
1,2,3,4,5,6,7,8-Octahydronaphthalene	42	78	38.5
trans-9-Decalol	5	–	6.5
cis-9-Decalol	2	–	14.5

The reaction thus does not proceed *via* a common carbonium ion. Model studies show that the replacement of the tetrahedral C-9 by a trigonal carbon would give two relatively rigid intermediates *(4)* and *(5)*, for which equilibration is slower than the formation of the products. *(3)* is thought to react *via* an intermediate similar to *(5)*. / Tetrahedron Letters *1968*, 5169 / –Kr. [Rd 944 IE]

***cis-* and *trans*-2,3-Dibromocyclononene** *(1)* and *(2)* have been obtained by *D. K. Wedegaertner* and *M. J. Millam* on addition of 1 mole of bromine to 1,2-cyclononadiene in CCl_4. In the mixture of about 40% of *(1)* and about 60% of *(2)*, only the isomer *(2)* could be highly concentrated by gas chromatography. The structures were assigned on the basis of the NMR spectrum. No allyl coupling was observed; both isomers



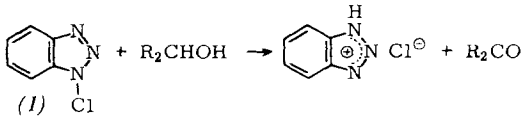
(1)



(2)

evidently prefer conformations in which the C–H bond of the methine carbon atom forms an angle close to 0 or 180 ° with the plane of the double bond. No interconversion of *(1)* and *(2)* occurs at room temperature. / J. org. Chemistry *33*, 3943 (1968) / –Kr. [Rd 946 IE]

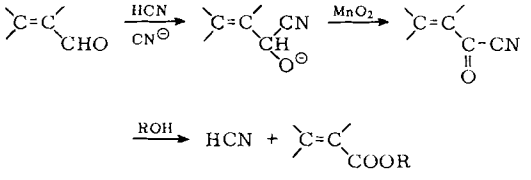
1-Chlorobenzotriazole *(1)*, a new oxidizing agent, has been described by *C. W. Rees* and *R. C. Storr. (1)*, m.p. 105 to 106 °C, which is obtained in 90% yield by the addition of aqueous Na hypochlorite to benzotriazole in 50% acetic acid, oxidizes alcohols to aldehydes or ketones and hydrazo compounds to azo compounds. The oxidations proceed in high yields under mild conditions. The reagent is converted



(1)

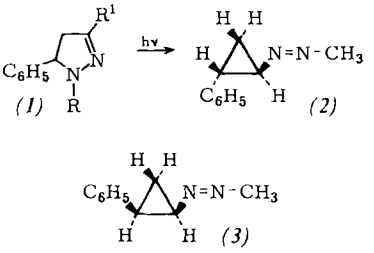
into benzotriazolium chloride. *(1)* oxidizes 1-aminobenzotriazole to dehydrobenzene, while 2-aminobenzotriazole is converted into *cis, cis*-1,4-dicyano-1,3-butadiene. / Chem. Commun. *1968*, 1305 / –Ma. [Rd 948 IE]

New methods for the oxidation of aldehydes to carboxylic acids and esters have been described by *E. J. Corey, N. W. Gilman*, and *B. E. Ganem*. Active MnO_2 oxidizes conjugated unsaturated aldehydes into methyl esters of carboxylic acids in the presence of HCN, CN^-, and methanol. The reaction may be carried out *e.g.* in acetic acid at 20–25 °C in the presence of NaCN.



Examples: benzaldehyde, cinnamaldehyde, furfural, geranial, farnesal → esters > 95, > 95, > 95, 85–95, 95% yields. The reaction proceeds without *cis-trans* isomerization of the α,β double bond. Saturated aldehydes are not converted into the esters under the same conditions. AgO gives only the carboxylic acids, even from unsaturated aldehydes. / J. Amer. chem. Soc. *90*, 5616, 1968 / –Ma. [Rd 949 IE]

Photoreactions of 5-phenylpyrazolines have been studied by *H. J. Rosenkranz* and *H. Schmid*. Irradiation of *(1)*, R = CH_3, R^1 = H, in benzene with a high-pressure Hg lamp leads to the formation, *inter alia*, of *trans*- and *cis*-1-methylazo-2-phenylcyclopropane *(2)* and *(3)*, which are converted back



(1) *(2)*

(3)

into the starting compound when heated. *(1)*, R = R^1 = CH_3, similarly form *trans*- and *cis*-1-methylazo-1-methyl-2-phenylcyclopropane, while *(1)*, R = R^1 = H gives benzaldazine and cinnamaldazine, as well as the mixed aldazine. / Helv. chim. Acta *51*, 1628 (1968) / –Ma. [Rd 950 IE]

The separation of rare earths from ceramic nuclear fuels by selective iodination is proposed by *B. Amecke* and *H. L. Scherff*. The reaction of MO_2 or M_2O_3 with carbon and iodine to form tetraiodides or triiodides and carbon monoxide is thermodynamically impossible for uranium and thorium below 1500 °K, but is possible for the rare earths up to dysprosium that are formed on nuclear fission. When an intimate mixture of rare earth oxides with carbon (prepared by carbonization of a mixture of sugar and oxide) is treated with iodine transported by a current of argon, the reaction starts at 700 °C; the yield of iodide increases with rising temperature (*e.g.* to 30–45% after 14 hours at 1100 °C). Up to 77% of the rare earths could be driven off as the iodides from an oxide mixture containing 90% of UO_2 and 5% each of La_2O_3 and CeO_2, which corresponds closely to a burnt-up nuclear fuel, after a reaction time of 55 hours at 1100 °C, whereas uranium oxide does not react. The yield increases in proportion to the partial pressure of iodine between 4 and 25 torr, and more slowly at higher pressures. It may therefore be concluded that the rate-determining step is the iodide formation at low partial pressures, and the diffusion of the rare earths in the oxide mixture at higher pressures. / Radiochim. Acta *9*, 169 (1968) / –Hz. [Rd 952 IE]

BOOK REVIEWS

Advances in Free-Radical Chemistry. Volume 2. Edited by *G. H. Williams*. Academic Press-Logos Press. London-New York 1967. 1st Edit., x, 274 pp., $ 14.00.

The purpose of progress reports is to establish cross references and to provide a forum for authors engaged in various branches of a topic to expound their views. Volume 2 of "Advances in Free-Radical Chemistry" [1] meets this demand in an exemplary manner, for alonside topics of pure organic chemistry it reports comprehensively on radicals in inorganic and macromolecular chemistry.

The topic "H- and Alkyl-containing Inorganic Radicals", which was taken up in volume 1, and which is treated hardly anywhere else in the literature, is wound up by *Friswell* and *Gowenlock*. This report should stimulate a multitude of new enquiries; systematic investigation of the field is still in its infancy. An established expert in radical chemistry, *D. H. Hey*, has written a magnificant report on the well-investigated arylation of aromatic compounds. *R. A. Abramovitch* provides an excellent summary of the difficult field of intramolecular aromatic substitutions from a mechanistic viewpoint. However, important work was published after completion of the manuscript (*T. Cohen*, 1968), mechanistic conclusions are in many cases not very conclusive, and radical 1,2-aryl migrations should have been considered.

The review by *J. I. G. Cadogan* "Radical Reactions of Phosphorus Compounds" also indicates large areas of little-explored ground and permits a first systematic assessment of the topic. The article by *A. D. Jenkins*, "The Reactivity of Polymer Radicals", is of fundamental importance. The quantitative interpretaion of the reactivity of polymeric radicals complements, and is even superior to, the corresponding theories of low-molecular chemistry concerning polar effects and the significance of radical stability for reactivity.

The editor is to be congratulated on the choice of topics; the quality of presentation is in keeping with that of volume 1.

Ch. Rüchardt [NB 746 IE]

[1] Cf. Angew. Chem. *79*, 427 (1967); Angew. Chem. internat. Edit. *6*, 475 (1967).

An Introduction to the Chemistry and Biochemistry of Fatty Acids and Their Glycerides. Edited by *F. D. Gunstone*. Chapman and Hall Ltd., London 1967. 2nd Edit., 209 pp., numerous formulas and tables, bound 63s.

The author, a student of *T. P. Hilditch*, presents the book [1] only as an introduction to the field of fatty acids. He does, however, list the representatives of this class of substances virtually completely, and discusses methods for their isolation and structure analyses with almost the same thoroughness. Long chapters are devoted to the physical and especially the chemical properties of fatty acids and their esters. The treatment is at a higher than introductory level, with many literature references to original work.

On the other hand, the chapters on the "Naturally occurring fatty acid derivatives" and on "Biosynthesis and metabolism" are presented remarkably briefly, and provide only inadequate information for the reader. Reference is made, however, to review articles, by means of which the original literature can be consulted. The literature appendix is very valuable, referring the reader both to scientific journals and to monographs. Summing up, it can be said that the book should prove very valuable to readers interested in the special problems of fatty acids. *H. Debuch* [NB 762 IE]

Dictionary of Organic Compounds, Third Supplement. By *R. Stevens*. Eyre and Spottiswoode, London, 1967, 4th Edit., 280 pp., cloth £ 10.00.

The fourth edition of the "Dictionary of Organic Compounds" was published in five volumes in 1965. To keep the work up to date, a supplement covering the recent literature and correcting errors and omissions found in earlier volumes is published every year. The entries in the third supplement, which has now appeared, refer mainly to articles published in 1966. The arrangement of the entries follows the scheme used in the main work. Additions and supplementary data relating to key words that appeared in the main work are indicated by an asterisk. A pleasing feature is the inclusion of many, carefully printed structural formulas, which always show the stereochemistry if this is known. Where practicable, the names formed according to the rules of systematic nomenclature are given for the substances listed. The entries also include the principal physicochemical properties as well as references, mainly to preparative work, but also to articles dealing with spectral data, structural investigations, isotopically labeled derivatives, *etc.* The annual supplement makes the "Dictionary of Organic Compounds" a useful addition to the organic chemist's library, and one that will always be up to date.

H. Grünewald [NB 772 IE]

The Neurosciences. A Study Program Planned and Edited by *G. C. Quarton, T. Melnechuk,* and *F. O. Schmitt*. The Rockefeller University Press, New York, 1967. 1 Edit., xx, 962 pp., numerous illustration and tables, $ 18.00.

"The human brain and the behavior correlated with its development, structure and function present a problem that is both the most complex to which man can address himself through the use of scientific methods and the most urgent from the human viewpoint". This statement taken from the foreword to the present volume, explains the foundation in 1962 of a "Neurosciences Research Program" by a group of scientists at the Massachusetts Institute of Technology. The new organization is an international and interuniversity body whose members are all indirectly or directly engaged in the study of the central nervous system and associated fields. Shortly after the foundation of the Program it was decided to hold a four-week symposium. This eventually took place at the University of Colorado in July 1966, and provided the first broad picture of contemporary knowledge of the human brain.

The 65 main papers presented at this symposium form the subject of the book under review (one paper is actually omitted, but two additional chapters are provided). This fact on its own would not justify consideration of the book in the present journal. The work is important to us because the lectures, both in their original and in their revised form, are addressed principally not to specialists, who would in any case be largely acquainted with the material, but to scientists working in neighboring disciplines.

The volume is divided into seven sections: Components of the nervous system, molecular biology (with a splendid introduction by *A. L. Lehninger*), molecular biology of brain cells, neuronal physiology, brain correlates of functional behavioral states, brain correlates of learning, interdisciplinary topics. Each section begins with an introduction which outlines the subject and places it in the context of what is already known. This is followed by the individual contributions on special problems within the subjects in question. Each paper is provided with a bibliography, thus offering an initial review of the literature. Anyone interested in the study of the central nervous system, whether he is a chemist, biologist, physicist, or psychologist, will find in this book a very useful introduction, well written and excellently edited by specialists in the field. *H. Grünewald* [NB 764 IE]

Handbook of Chemistry and Physics. By *R. C. Weast* and *S. M. Selby*. The Chemical Rubber Co., Cleveland, 1967, 48th Edit., xxvi, 1920 pp., $ 20.50.

This handbook of approximately 2000 pages has appeared annually in a new edition [1] since the end of the war (with only three exceptions), which gave it a chance of being improved and supplemented every year. It can therefore be claimed, without danger of exaggeration, that we have here the most up to date handbook of its kind. Despite its title, it offers 267 pages of mathematical tables, 1200 pages of chemical tables, 189 pages of physical tables, and 264 pages of various other tables divided more or less equally between chemistry and physics. Chemistry therefore takes up by far the greater part, if only because of the inclusion of a table of the properties of organic compounds which lists more than 13500 substances. The present, 48th edition of this work again contains several new tables among which may be mentioned a survey of the ^{1}H-NMR signals of organic structures, numerous charts of the characteristic frequencies of organic and inorganic compounds over the whole range of IR and several tables of purely chemical content. At least ten tables have been revised or supplemented.

The formulas in the large organic table are as deplorable as ever. It is really too much to except that it should be necessary to study 17 1/2 printed pages of instructions before one knows what name a particular compound may be found under in the table; fortunately, there is a formula index for the same table. The editors of this handbook should think of a solution as soon as possible which would do away with the instructions and make the contents of the table more easily accessible, perhaps by anarrangement of the formula index in such a way that the empirical formula carries not only the number of the entry but also its name, which would save a lot of unnecessary searching. As before, it is urgently desirable to carry out a thorough search through the physicochemical tables, with respect to the dimensions. It is really intolerable to find "Kg. calories", Kcal", "Kilo-cals", "Cal." and such like next to one another. It is also unnecessary that a table which contains values for ΔH_f°, ΔF_f°, $\log K_f$ and S° should have a footnote to say that "all values are expressed.

[1] Cf. Angew. Chem. *71*, 144 (1959).

[1] Cf. Angew. Chem. *78*, 912 (1966); Angew. Chem. internat. Edit. *7*, 907 (1966).

as kilo-cals per gram mole", since this footnote is simply wrong. At the same time, these objections concern superficialities, which do not detract from the reliability topicality, and breadth of the information packed in this handbook.

H. Grünewald [NB 765 IE]

The Merck Index. An Encyclopedia of Chemicals and Drugs. Published by Merck & Co., Inc. Rahway, N.J./U.S.A. 8th Edit. 1968, 1728 pages, bound $ 15.00.

A new edition of the Merck Index, the eighth since it first appeared in 1889, was published a few months ago. For those who do not know this extremely useful and reliable encyclopedia, it should immediately be pointed out that it is not a list of products marketed by the American Merck Company. In addition to a 1133 page encyclopedic index of chemicals and drugs, it devotes almost 100 pages to the description of 460 name reactions, and contains a further 40 tables that are of importance to chemists in general and particularly to those employed in the drug industry.

The central part of the book is the encyclopedic section, which is, not inappropriately, headed "Monographs", and which contains entries for more than 9500 chemicals and drugs. The entries usually begin with the trivial names of the substance in question, and then list all other systematic and non-systematic names, the Chemical Abstracts nomenclature being indicated by the use of bold-face italics. The empirical formula, molecular weight, and percentage composition by elements are followed (with literature references) by data on occurrence, isolation, structural elucidation, synthesis, and the principal physical properties of the compound and of some important derivatives; information on medical use and toxicity is also given in more than 4800 cases. Structural formulas are naturally also included (almost 5000 are given altogether), and special mention should be made here of the clearly legible type.

The reviewer knows the Merck Index from years of almost daily use. A regrettable feature of earlier editions was the absence of a formula index to the encyclopedic section. This omission has now been rectified, since the eighth edition contains a formula index, as well as the comprehensive (42000 entries) cross index of names.

For those who already know the Merck Index, nothing more need be said. To those who do not yet know it, this volume must be recommended as a worthwhile addition to their library.

H. Grünewald [NB 766 IE]

Taschenbuch für Chemiker und Physiker (Handbook of Chemistry and Physics). (D'Ans/Lax), Vol. 1: Makroskopische physikalisch-chemische Eigenschaften (Macroscopic physicochemical properties). Edited by *E. Lax*, in collaboration with *C. Synowietz*. Springer-Verlag, Berlin-Heidelberg-New York, 1967. 3rd and completely revised edition, xvi, 1522 pp., bound DM 68.00 / US $ 17.00.

The familiar "D'Ans-Lax", which now appears in its third edition, is no longer in a single handbook, but is in three volumes, volume 1 of which is now ready, after the publication of volume 2 in 1964. While volume 2 contains all the data on organic compounds that are important to chemists, volume 1 is devoted to the tabulation of macroscopic physicochemical properties. (Volume 3, still in preparation, is apparently mainly for the use of physicists.)

The first volume of this work is divided into seven chapters. Chapter 1 gives a survey of systems of measurement, units and standard dimensions for macroscopic properties, and atomic quantities. Here the user will find the symbols employed further on. The second chapter contains tables in which the various macroscopic properties of the same substance are presented, the emphasis being laid on the mechanical properties. This is followed by tables of thermomechanical properties and equilibria of homogeneous (chapter 3) and heterogeneous (chapter 4) systems. Interfacial properties form the content of chapter 5, while the thermodynamic properties of elements and compounds as a function of temperature, pressure, and composition are dealt with in chapter 6. Finally, chapter 7 gives data on viscosity, diffusion, thermal conductivity, and kinetics of chemical systems.

Within a little over 1500 pages in octavo format, this volume offers all the desired information on each subject. It does so in a clearly understandable fashion that can only be called exemplary. The units are given for every measured value, and for each symbol included in tables or equations the user finds an explanation without a long search. It would be pleasant if the example set by this volume were taken as a model for tabular representations, of whatever kind and wherever printed.

H. Grünewald [NB 767 IE]

Reallexikon der Medizin und ihrer Grenzgebiete. (Practical Dictionary of Medicine and Related Subjects.) Vol. 1: A-Carfimatum. Edited by *G. Thiele* and *H. Walter*. Urban & Schwarzenberg, Munich-Berlin-Vienna 1967. 1st Edit., xix + 799 pp., loose-leaf binding with plastic cover, DM 140.–.

Urban & Schwarzenberg, whom the chemist associates with "Ullmanns Enzyclopädie der Technischen Chemie", have now embarked on the publication of a practical dictionary of medicine estimated to run to about 4800 pages and more than 200000 entries. The editors in chief are *G. Thiele* and *H. Walter*, the imposing list of external collaborators numbers almost 300 names, and in view of the publisher's lexicographic tradition the work is anticipated with big expectations.

The first instalments are now available and already provide an indication of the essential features of the lexicon. Further volumes are to follow at annual intervals, and the overall work will be a six-volume loose-leaf collection in conveniently used and very robust folders. The advantage of this arrangement is that it is possible at any time to insert addenda and revisions and to keep the work up to date without having to produce a whole new edition. As regards the contents, the editors do not wish to restrict medicine to therapeutics in the strict sense, but aim at extending the framework to include all adjoining fields of importance for medical practice and teaching (an accompanying brochure names 22!). Here, the work becomes interesting to the biochemist, particularly the worker engaged in clinical or physiological chemistry. It will not serve him as an exhaustive source of information on problems within his own specialized field, but he can hope to obtain reliable information about subjects at the fringe of related fields.

To review this book as a chemist one turns perforce to those entries that concern one's own subject in the knowledge that this cannot lead to a valid view of the whole. This approach results in the pleasant feeling of finding the information reliable. Understandably, this dictionary is tailored to the needs of the medical man, *i.e.* it is less concerned with material properties of interest to the chemist than with providing data about the biological action, metabolic properties, medicinal uses, and side effects. For this reason structural formulas have generally been omitted, although some are in fact given.

By contrast, the terminology used for the chemical compounds seems unfortunate to the reviewer. The statement, in the notes on the use of the dictionary, that "Drugs and chemical substances are where possible listed under the keywords used in the official pharmacopeia" is ominous, and this forecast is indeed borne out. Under "Acetat" the reader is referred to "Azetat", acetic acid is listed under Acidum aceticum, boron trioxide under Acidum boricum anhydric-

um (!) and of course oxalic acid under Acidum oxalicum. At the same time, Acidum oxalaceticum is dealt with under oxalacetic acid and Acidium propionicum under propionic acid. Acetyl compounds receive similar treatment in that they are all to be found under "Azetyl". However, another entry is "Azetyl-Coenzym A", which more justly and "traditionally" should be "A.-Koenzym A". This procedure becomes quite incomprehensible when one arrives at "Argininosukzinat" next to "Biocytin", followed by "zytostatisch". The reviewer is baffled why confusion has been the aim in precisely the field of chemistry that is in any case a difficult one for the medical man to master, instead of an attempt to clarify this topic.

This calamity apart, the care used and effort made by the editors to collate what is most important and most worthwhile from the mass of the medical literature and to arrange it in an attractive and clear manner are quite admirable. There is no doubt that this dictionary will be numbered among the most important new publications.

H. Grünewald [NB 768 IE]

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 24975, Telex 461855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 2
FEBRUARY 1969
PAGES 89–156

Metal Complexes of Thiophosphinic and Selenophosphinic Acids

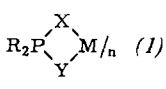
By W. Kuchen and H. Hertel[*]

The anions of thiophosphinic and selenophosphinic acids $R_2P(X)YH$ (X = S, Se; Y = O, S, Se) can act as bidentate ligands. They combine with many metals to form complexes containing a four-membered chelate ring, or to give coordination polymers in which they form ligand bridges. The preparation, properties, and reactions of these compounds, as well as the dielectric properties and analytical use of dithiophosphinato complexes, which are also of industrial interest, are described. Some thiophosphinato and selenophosphinato complexes exhibit concentration-dependent association via ligand bridges. Evidence of the chelate nature of the ligands $R_2P(X)Y^{\ominus}$ was obtained from IR spectroscopic studies. The ligand field parameters of the anion $(C_2H_5)_2P(S)S^{\ominus}$ were deduced from the electronic spectra of octahedral diethyldithiophosphinato complexes, and the position of the ligand in the spectrochemical and nephelauxetic series were determined from these parameters.

1. Introduction

Phosphinic acids $R_2P(O)OH$ differ formally from orthophosphoric acid in that two OH groups have been replaced by alkyl or aryl groups. Partial or complete replacement of the two remaining oxygen atoms by sulfur and/or selenium yields acids having the general formula $R_2P(X)YH$ (X = S, Se; Y = O, S, Se).

The anions of these acids can act as bidentate ligands. They combine with many metals to form chelates, *e.g.* of the type *(1)*, or coordination polymers in which



(1)

they function as ligand bridges. These compounds are reviewed in the present article; the dithiophosphinato complexes are discussed first, since they have been most extensively studied.

2. Complexes of the Dithiophosphinic Acids $R_2P(S)SH$

2.1. Methods of Preparation

On reaction of Grignard reagents with P_4S_{10}, *Malatesta* and *Pizzotti*[1,2] obtained a complex reaction mixture from which they were able to separate small quantities of dithiophosphinic acids *via* their Ni^{II} and Cd^{II} salts, which dissolve very readily in organic solvents.

The best method for the preparation of dithiophosphinato complexes is from the alkali metal or ammonium salts[3], according to eq. (1)[1,2,4–13], or

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[1] *L. Malatesta* and *R. Pizzotti*, Gazz. chim. ital. *76*, 167 (1946).

[2] *L. Malatesta*, Gazz. chim. ital. *77*, 509 (1947).

[3] For preparation, cf. *K. Sasse* in *Houben-Weyl-Müller*: Methoden der organischen Chemie. Thieme-Verlag, Stuttgart 1963, Vol. XII/1, p. 269ff; *L. Maier*: Topics in Phosphorus Chemistry. Interscience Publishers, New York 1965, Vol. II, p. 43.

[4] *A. W. v. Hofmann* and *F. Mahla*, Ber. dtsch. chem. Ges. *25*, 2436 (1892).

[5] *W. Kuchen* and *J. Metten*, Angew. Chem. *72*, 584 (1960).

[6] *M. M. Rauhut, H. A. Currier*, and *V. P. Wystrach*, J. org. Chemistry *26*, 5133 (1961).

[7] *P. E. Newallis, J. P. Chupp*, and *L. C. D. Groenweghe*, J. org. Chemistry *27*, 3829 (1962).

[8] Brit. Pat. 902802 (Dec. 11, 1959), American Cyanamid Co.

[9] *W. Kuchen* and *J. Metten*, German Pat. 1137732 (April 25, 1963), Chemische Fabriken Kalk.

[10] *W. Kuchen, J. Metten*, and *A. Judat*, Chem. Ber. *97*, 2306 (1964).

[11] *J. P. Milionis* and *F. I. Arthen*, German Pat. 1233134 (July 27, 1967), American Cyanamid Co.

[12] *W. Kuchen, A. Judat*, and *J. Metten*, Chem. Ber. *98*, 3981 (1965).

[13] *W. Kuchen* and *A. Judat*, Chem. Ber. *100*, 991 (1967).

$$n\,R_2P(S)S^{\ominus} + M^{n\oplus} \rightarrow [R_2P(S)S]_nM \quad (1)$$

from the free acids [3] and metal compounds, *e.g.* the oxides (or carbonates), as shown in eq. (2) [10, 25]

$$2\,R_2P(S)SH + MO \rightarrow [R_2P(S)S]_2M + H_2O \quad (2)$$

The method of eq. (2) has proved particularly useful for aromatic dithiophosphinic acids, which can be readily obtained *e.g.* by reaction of aromatic hydrocarbons with P_4S_{10} in the presence of $AlCl_3$ [3]. To prepare the complexes, the dithiophosphinic acids are then allowed to react either *in situ* [14] or after isolation in an organic solvent with the oxide or carbonate of the metal [15].

In the method of eq. (1) the dithiophosphinato complexes are precipitated by addition of the complexing agent to an aqueous solution of a salt of the metal. In some cases, however, it is preferable to reflux a suspension of the complexing agent and a metal halide in an organic solvent and to isolate the resulting complex from the solution after the sodium halide has been filtered off. This procedure is useful when the metal halide is extensively hydrolyzed in aqueous solution (*e.g.* $AsCl_3$, $SbCl_3$, R_2SnCl_2) or when the hydrated cation (*e.g.* $Cr^{III} \cdot aq$) cannot form complexes with dithiophosphinic acids [10].

Another variant of the method is the use of the thallium(I) complex of the dithiophosphinic acid instead of the alkali metal salt, this complex being allowed to react with the metal halide in organic solvents such as chloroform, dioxane, or isopropanol [16], *e.g.* according to:

$$2\,R_2P(S)STl + MX_2 \rightarrow [R_2P(S)S]_2M + 2\,TlX \quad (3)$$

The thallium(I) complexes are soluble in more organic solvents than the anhydrous sodium dithiophosphinates, which are also strongly hygroscopic. This variant is therefore preferred when it is desirable to carry out the reaction in the complete absence of water.

Dithiophosphinato complexes have also been prepared by direct reaction of tetraorganodiphosphine disulfides with metals and sulfur or with metal sulfides and sulfur.

Thus bis(dipropyldithiophosphinato)zinc(II) was obtained in a yield of about 35%, together with other products, on zinc dust distillation of tetrapropyldiphosphine disulfide. On the other hand, if the disulfides are allowed to react with metal powder and sulfur in the stoichiometric ratio in accordance with eq. (4)

$$R_2P(S)-P(S)R_2 + M + {}^2/_8\,S_8 \rightarrow [R_2P(S)S]_2M \quad (4)$$

$R = C_2H_5, C_3H_7, C_4H_9, C_5H_{11}$; M = Zn, Cd, Hg, *etc.*

the yields can be increased to 70–90%. Reaction of tetraorganodiphosphine disulfides with metal sulfides and sulfur for 3 hours at 200 °C yields bis(dialkyldithiophosphinato) complexes in yields of up to 84% [5, 10, 17] (eq. (5)).

$$R_2P(S)-P(S)R_2 + MS + {}^1/_8\,S_8 \rightarrow [R_2P(S)S]_2M \quad (5)$$

$R = C_2H_5, C_3H_7$; M = Zn, Cd

2.2. Properties and Reactions

Many complexes $[R_2P(S)S]_nM$, *e.g.* with $M = Al^{III}$, In^{III}, Tl^{I}, Pb^{II}, As^{III}, Sb^{III}, Bi^{III}, Cr^{III}, Fe^{III}, Co^{II}, Co^{III}, Ni^{II}, Zn^{II}, Cd^{II}, and Hg^{II} and $R = CH_3$, C_2H_5, C_3H_7, C_4H_9, C_5H_{11}, C_8H_{17}, $C_{12}H_{25}$, and C_6H_5, have been prepared by one or more of the above methods [1, 2, 5–17, 25]. Some other complexes are listed in Table 1.

Table 1. Complexes $[(C_2H_5)_2P(S)S]_nM$ of the platinum metals [18].

M	Color	M.p. (°C)	μ_{eff} (B.M.)
Ru^{III}	black	135–136	1.93 (294 °K)
Rh^{III}	dark brown	141–142	diamagnetic
Ir^{III}	brown	146–147	diamagnetic
Pd^{II}	dark red	137–138	diamagnetic
Pt^{II}	orange-red	144–145	diamagnetic

These complexes all crystallize well. Some of them are deeply colored, and most melt sharply without decomposing. They can often be kept for months in sealed tubes.

Bis(diethyldithiophosphinato)zinc(II) and bis(dipropyldithiophosphinato)zinc(II) are so stable thermally that they can be distilled without much decomposition even at 250–300 °C.

The complexes of dithiophosphinic acids are not wetted by water, though the Ni^{II} and Co^{II} complexes gradually dissolve. They are not affected by dilute non-oxidizing acids even when heated; on the other hand, most of them dissolve in dilute alkali when shaken vigorously. Some of the compounds, *e.g.* the zinc, cadmium, and bismuth complexes, can be reprecipitated from these solutions by acidification.

Special mention should be made of the ready solubility of dialkyldithiophosphinato complexes in organic solvents, particularly aromatic and chlorinated hydrocarbons. The complexes of aromatic dithiophosphinic acids, on the other hand, are generally less soluble.

Molecular weight determinations show that the Zn^{II} Cd^{II}, and Hg^{II} complexes of some dialkyldithiophosphinic acids exhibit concentration-dependent association in these solvents (cf. Section 4).

The nature of the Tl^{I} compounds has not yet been established. Owing to their low solubility, molecular weight determinations are possible only over a narrow concentration range, but the results obtained do show that $R_2P(S)STl$ ($R = C_2H_5$, C_6H_5) are slightly associated in benzene and chloroform [19]. It does not therefore seem justifiable to formulate these

[14] *W. G. Craig*, US-Pat. 2809979 (Jan. 26, 1954), The Lubrizol Corp.

[15] German Pat. 1014989 (Feb. 6, 1958), The Lubrizol Corp.

[16] *W. Kuchen, B. Knop*, and *H. Hertel*, unpublished.

[17] *W. Kuchen* and *J. Metten*, German Pat. 1166191 (Oct. 8, 1964), Chemische Fabriken Kalk.

[18] *W. Kuchen, A. Judat*, and *H. Hertel*, unpublished.

[19] *W. Kuchen* and *H. Mayatepek*, unpublished.

compounds as salts $Tl^{\oplus}R_2P(S)S^{\ominus}$, particularly since they are non-electrolytes in dimethylformamide [16].

The strongly covalent behavior and the non-electrolyte character observed in a series of complexes $[R_2P(X)Y]_nM$ suggest that they should be formulated as chelates *(1)*. On the basis of their stoichiometry and their molecular weight, a formula in which the metal has its characteristic coordination number can be given only if the ligand is assumed to be bidentate. This characteristic coordination state can be deduced for some metal complexes from magnetic measurements and the electronic spectra [13]. The IR spectra also provide evidence that both donor atoms are involved in coordinate bonding, and hence that the complexes are chelates (cf. Section 5).

Reaction of some of these dithiophosphinato complexes with Lewis bases leads to the formation of adducts, with an increase in the coordination number of the metal. Thus the tetrahedral bis(diethyldithiophosphinato)cobalt(II) reacts with pyridine and with gaseous ammonia to give the octahedral complexes $[(C_2H_5)_2P(S)S]_2CoPy_2$ and $[Co(NH_3)_6][(C_2H_5)_2P(S)S]_2$. Similar complexes are formed by the planar bis(diethyldithiophosphinato)nickel(II) which also gives bis(diethyldithiophosphinato)dithiophenonickel(II) with thiophene. These adducts are unstable, and very readily lose the additional ligands with regeneration of the original complex [13].

Cu^{I} and Au^{I} react with dithiophosphinate in accordance with eq. (1) to form oligomeric complexes $[R_2P(S)SM]_n$ (n = 4 or 2); such compounds are also obtained with Cu^{II} and Au^{III}. The reduction of the metal ions to the oxidation state +1 is accompanied by oxidation of the anions $R_2P(S)S^{\ominus}$ to bis(diorganothiophosphoryl)sulfanes $R_2P(S)-S_n-P(S)R_2$ (n = 1, 2, 3) [20]. Thus colorless diamagnetic tetrakis[dialkyldithiophosphinatocopper(I)] complexes, which are only sparingly soluble in organic solvents, are formed as follows

$$8\ R_2PS_2^{\ominus} + 4\ Cu^{2\oplus} \rightarrow [R_2PS_2Cu]_4 + 2\ R_2P(S)-S_2-P(S)R_2 \quad (6)$$

R = C_2H_5, decomp. *ca.* 290 °C
R = C_3H_7, decomp. *ca.* 240 °C

The degree of association was determined, within the concentration range suitable for investigation, by osmometric molecular weight determinations in benzene and chloroform. Bis(dialkyldithiophosphoryl)-disulfanes were detected as oxidation products. On the other hand, it has not yet been possible to determine the molecular weight of the corresponding phenyl compound (which decomposes at about 275 °C) because of its low solubility. It seems reasonable to assume that the tetramers have a structure similar to that of $[(C_2H_5)_3AsCuI]_4$.

In the latter compound four Cu atoms are arranged in the form of a tetrahedron, and each of these atoms is tetrahedrally surrounded by three iodine atoms and an arsine molecule. The halogen bridges connect the Cu atoms in groups of three [21]. In the present case, therefore, one of the two sulfur atoms of each chelate ligand would be coordinately bonded to three Cu atoms, taking the place of an iodine atom, while the other sulfur atom would take the place of the arsine molecule.

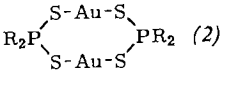
Attempts to achieve coordinative saturation with strong Lewis bases and hence to degrade the polymer structure have so far been successful only with triphenylphosphine, which gives the adduct bis(triphenylphosphine)diethyldithiophosphinatocopper(I), m.p. 184–186 °C (decomp.) [20] (186 °C [22]), as follows:

$$[(C_2H_5)_2P(S)SCu]_4 + 8\ P(C_6H_5)_3 \rightarrow 4\ (C_2H_5)_2P(S)SCu \cdot 2\ P(C_6H_5)_3 \quad (7)$$

Though the tetramers dissolve in pyridine or tertiary amines when heated, they crystallize unchanged from these solvents on cooling. In the course of several days, however, deep blue needles gradually separate from the colorless solutions of the tetrameric complexes in pyridine in the presence of air and moisture. These crystals are insoluble in the common organic solvents. Their composition corresponds to the formula $R_2P(S)S\cdot Cu(OH)\cdot Py_4$ (R = C_2H_5: m.p. 223–225 °C, μ_{eff} = 1.85 B.M. (296 °K); R = C_3H_7: m.p. 173–175 °C; R = C_6H_5: m.p. 220–221 °C). Their IR spectra all contain an absorption at 3000–3500 cm^{-1} such as is found for hydroxo complexes of copper [23, 24].

Reduction of $Au^{3\oplus}$ with dithiophosphinate leads, in accordance with eq. (8), to bis[diorganodithiophosphinatogold(I)], for which a cyclic structure *(2)* containing ligand bridges is proposed. (The molecular

$$6\ R_2P(S)S^{\ominus} + 2\ Au^{3\oplus} \rightarrow [R_2P(S)SAu]_2 + 2\ R_2P(S)-S-S-P(S)R_2 \quad (8)$$



(2)

R = C_2H_5: m.p. 153 °C; R = C_3H_7: m.p. 175 °C; R = C_6H_5: decomp. *ca.* 297 °C, colorless needles (from ligroin).

weight of the phenyl complex could not be determined with sufficient accuracy because of its low solubility.) The oxidation products isolated after reaction of the propyl and phenyl compounds according to eq. (8) were bis(diorganothiophosphoryl)disulfanes $R_2P(S)S_2P(S)R_2$, whereas the ethyl compound gave bis(diethylthiophosphoryl)monosulfane $(C_2H_5)_2P(S)-S-P(S)(C_2H_5)_2$ and bis(diethylthiophosphoryl)trisulfane $(C_2H_5)_2P(S)-S_3-P(S)(C_2H_5)_2$, presumably the dismutation products of initially formed disulfane [20].

The ions $R_2P(S)S^{\ominus}$ thus once again behave as strongly reducing ligands, which are evidently not very well suited for the stabilization of higher oxidation states of the metal in complexes of the type $[R_2P(S)S]_nM$, since even $[(C_2H_5)_2P(S)S]_3Co$ decomposes rapidly to give the trisulfane $(C_2H_5)_2P(S)-S_3-P(S)(C_2H_5)_2$ and the corresponding Co^{II} complex, and $[(C_2H_5)_2P(S)S]_3Fe$ is also unstable [13].

[20] *H. Mayatepek*, Dissertation, Technische Hochschule Aachen, 1968; *W. Kuchen* and *H. Mayatepek*, Chem. Ber. *101*, 3454 (1968).

[21] *A. F. Wells*, Z. Kristallogr., Mineralog. Petrogr., Abt. A *94*, 447 (1936).

[22] *F. Bonati*, *S. Cenini*, and *R. Ugo*, J. organometallic Chem. *9*, 395 (1967).

[23] *B. William* and *R. C. McWhinnie*, J. chem. Soc. (London) *1964*, 2959.

[24] *E. Uhlig*, *B. Borek*, and *H. Glänzer*, Z. anorg. allg. Chem. *348*, 189 (1966).

The dimeric gold(I) complexes behave in the same way as the tetrameric Cu^I complexes toward Lewis bases. Whereas they crystallize out unchanged from their solutions in pyridine, they react with triphenylphosphine to give *e.g.* bis(triphenylphosphine)dipropyldithiophosphinatogold(I) $(C_3H_7)_2P(S)SAu \cdot 2\,P(C_6H_5)_3$, m.p. 101 °C [20].

The reaction of Ag^I ions with dithiophosphinate yields complexes having the composition R_2PS_2Ag ($R = C_2H_5$ [4]: dec. approx. 262 °C; $R = C_3H_7$: dec. 285–287 °C; $R = C_4H_9$: dec. approx. 122 °C), which are very sparingly soluble in organic solvents, but separate out from large quantities of hot toluene or chloroform as colorless, matted needles, and darken in daylight within a few hours. Owing to the very low solubility of these compounds, molecular weight determinations have not yet been possible. However, the substances are probably again oligomers and polymers, in which the metal is coordinated either linearly or tetrahedrally by sulfur. A chain structure with ligand bridges $[\ldots Ag{-}S{-}PR_2{-}S{-}]_n$ would be expected in the first case and a structure similar to that of the compounds $[(CH_3)_3AsMI]_4$ ($M = Cu^I, Ag^I$ [21]) in the second. X-ray studies have shown that $[R_2P(S)SCu]_4$ and $[R_2P(S)SAg]_n$ are not isomorphous [20].

The reaction of dimethyldithiophosphinic acid with the trimethyl derivatives of aluminum, gallium, and indium according to eq. (9) yields organometal dithiophosphinates, which are sensitive to air and to moisture.

$$(CH_3)_2P(S)SH + (CH_3)_3M \rightarrow (CH_3)_2P(S)SM(CH_3)_2 + CH_4 \qquad (9)$$

These compounds are monomeric in benzene, and are coordinately saturated [25] since they do not react with triethylamine.

Whereas $Tl(NO_3)_3$ is reduced to thallium(I) by diethyl dithiophosphinate [20]

$$Tl^{3\oplus} + 3\,(C_2H_5)_2P(S)S^{\ominus} \rightarrow (C_2H_5)_2P(S)STl + (C_2H_5)_2P(S){-}S{-}S{-}P(S)(C_2H_5)_2 \qquad (10)$$

diorganothallium(III) halides R_2TlX are converted under similar conditions into the compounds $R_2P(S)STlR'_2$ ($R' = CH_3, C_6H_5$; $R = C_2H_5, C_6H_5$ [22]).

The reaction of tin(IV) halides with sodium dithiophosphinate yields dihalogenobis(dithiophosphinato)-tin(IV) [12, 22].

$$SnX_4 + 2\,R_2P(S)SNa \rightarrow [R_2P(S)S]_2SnX_2 + 2\,NaX \qquad (11)$$

$R = C_2H_5, C_6H_5$; $X = Cl, Br$

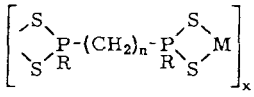
Similarly, the corresponding diorganobis(dithiophosphinato)tin(IV) complexes $[R_2P(S)S]_2SnR'_2$ are obtained from the corresponding diorganotin dihalides R'_2SnX_2 [12, 22] ($R' = CH_3, C_2H_5, C_4H_9, C_6H_5$; $R = C_2H_5, C_6H_5$) [22].

[25] *G. E. Coates* and *R. N. Mukherjee*, J. chem. Soc. (London) *1964*, 1295.

The compounds $[R_2P(S)S]_2SnR'_2$ are soluble in organic solvents, and are monomeric in benzene and in chloroform. Their stoichiometric composition suggests that the dithiophosphinato moiety again acts as a bidentate ligand, since only then does tin achieve a coordination number of six in the monomeric complexes. This is also true of the dihalogeno compounds $[R_2P(S)S]_2SnX_2$, which are non-electrolytes in dimethylformamide and nitrobenzene.

A report that bis(diethyldithiophosphinato)dichlorotin(IV) $[(C_2H_5)_2P(S)S]_2SnCl_2$ is associated [22] could not be confirmed. In agreement with earlier cryoscopic results [12], osmometric measurements in chloroform (37 °C) and in benzene (60 °C) gave molecular weight values of 504 ± 6 and 509 ± 11 respectively (averages of seven determinations each in the concentration ranges 2.858–8.446 g/l and 2.238 to 6.038 g/l), while the value calculated for the monomer is 496.1. The measurements were carried out on two samples that had been prepared exactly in accordance with the procedure given in ref. [12], and which melted at 171–172 °C (decomp.) after repeated crystallization from anhydrous toluene [19].

Finally, it should be mentioned that complexes of the type *(3)* have also been described; owing to their



(3)

M = Ni, Co; R = C_6H_5, cyclohexyl; $n = 4,5$

insolubility in organic solvents, these compounds were formulated as polymers [26, 27].

2.3. Dipole Moments

Chelates often have appreciable dipole moments, though according to the nature and steric arrangement of the ligands there should be no resultant moment.

This phenomenon, which has been studied particularly in 2,4-pentanedionatometal complexes (metal acetoacetonates), is attributed to an abnormally high atomic polarization [28, 29]. This is probably due to bending vibrations excited in the chelate rings by the alternating electric field, with deformation of molecules that are non-polar in the absence of a field [30].

It can be seen from Table 2 that dipole moments of about 1.3–2.6 D are also found for dithiophosphinato complexes [12].

This dipole moment is again probably not permanent, as is demonstrably the case in pentanedionato complexes. In the absence of an orienting polarization P_{Or}, the atomic polarization P_{At} is found from

$$P = P_{Or} + P_{At} + P_E \qquad (12)$$

[26] *K. Issleib* and *G. Döll*, Chem. Ber. *94*, 2644 (1961).

[27] *K. Issleib* and *G. Döll*, Z. anorg. allg. Chem. *324*, 259 (1963).

[28] *J. W. Smith* and *W. R. Angus*, Proc. Roy. Soc. (London), Ser. A *137*, 372 (1932).

[29] *A. E. Finn*, *G. C. Hampson*, and *L. E. Sutton*, J. chem. Soc. (London) *1938*, 1254.

[30] *I. E. Coop* and *L. E. Sutton*, J. chem. Soc. (London) *1938*, 1269.

Table 2. Dipole moments of dithiophosphinato complexes (in benzene, 20 °C).

μ^* determined from the dielectric constant and the refractive index, and μ^{**} (without taking atomic polarization into account) from the dielectric constant, the refractive index, and the density. P = polarization, P_E = electronic polarization, P_{At} = atomic polarization.

$[(C_2H_5)_2P(S)S]_nM$ M	μ^* (D)	μ^{**} (D)	P (cm^3)	P_E (cm^3)	P_{At} (%) P_E 100%	μ 70% (D)
Pb^{II}	1.94	1.97	193	112	72	
Zn^{II}	1.37	1.37	137	98	40	
Ni^{II}	1.49 [a]	1.49	146	99	47	
Co^{II}	1.43					
Bi^{III}	2.52	2.47	318	191	66	
Cr^{III}	1.38	1.43	184	142	30	
$[(C_2H_5)_2P(S)S]_2SnX_2$ X						
Cl	7.71	7.62	1331	125	70	7.3
C_6H_5	3.32					
C_4H_9	3.22					

[a] 1.66 D (benzene, 20 °C) [31].

to be $P-P_E$. Table 2 shows that the atomic polarizations found from this expression for the dithiophosphinato complexes, like those in the pentanedionato compounds, correspond to 30–70% of the measured electronic polarization P_E.

The dipole moments found for the compounds $[(C_2H_5)_2P(S)S]_2SnX_2$ (X = Cl, C_6H_5, C_4H_9) (Table 2) suggest a *cis* configuration for the substituents in the octahedral complexes. Even if allowance is made for an atomic polarization of 70% of the electronic polarization for the dichloro complex:

$$P_{Or} = P-P_E-P_{At} = 1118.5\ cm^3 \qquad (13)$$

the moment is still 7.3 D, a value of an order of magnitude such as would be expected for the *cis* form. Though corresponding calculations have not been carried out for the two diorgano compounds, it seems reasonable to assume that these two complexes, in analogy with the dichloro compounds and in agreement with the appreciable dipole moments found for them, are *cis* forms [12].

2.4. Analytical Applications [32]

The suitability of the complexing agent sodium diethyldithiophosphinate for the solvent extraction and photometric determination of metals as diethyldithiophosphinato complexes has been studied for a number of examples.

For instance Cd^{II} and Hg^{II} can be quantitatively extracted as their diethyldithiophosphinato complexes from neutral or weakly acidic solutions (pH = 6–7) with carbon tetrachloride and determined photometrically, as can Pb^{II} and Bi^{III} even from very strongly acidic solutions. On the other hand, Ni^{II}, Co^{II}, Cr^{III}, Zn^{II}, Mg^{II}, and other metals can be extracted only very incompletely or not at all from the aqueous phase. This difference in behavior has been utilized for the separation and determination of the components *e.g.* of the systems Bi^{III}/Mg^{II}, Pb^{II}/Zn^{II}, Bi^{III}/Ni^{II}, and Bi^{III}/Zn^{II}. For practical analytical work, the alkali metal dithiophosphinates should have the advantage over dithiophosphates and carbamates that they are more stable in strongly acidic, non-oxidizing media. Sodium diethyldithiophosphinate remains practically unchanged for weeks even in 15 N H_2SO_4. In the presence of nitrate, however, appreciable decomposition occurs within a few hours, depending on the acidity and the nitrate content of the solution.

2.5. Industrial Use

Several patents describe suggested industrial uses of dithiophosphinato complexes, which can be used *e.g.* as vulcanization accelerators [17], as oil additives [8,9, 14,15,17,33], as stabilizers for polyolefin molding compositions [11], and, because of their outstanding color- and light-fastness, as coloring additives for plastics [34].

3. Complexes of Other Thiophosphinic and Selenophosphinic Acids

In contrast with data on the metal complexes of dithiophosphinic acids, published information on corresponding compounds of the other thiophosphinic and selenophosphinic acids is sparse, and refers mainly to the complexes of the diethyl compounds.

The complexes listed in Table 4 were prepared by methods corresponding to equation (1) and/or (2). The complexing agents used are listed in Table 3.

Table 3. Complexing agents of the type $(C_2H_5)_2P(X)YNa \cdot nH_2O$.

	M.p. (°C)	Ref.
$(C_2H_5)_2P(S)ONa \cdot 3\ H_2O$	58–59	[35a, 35b]
$(C_2H_5)_2P(Se)ONa \cdot 4\ H_2O$	50	[36]
$(C_2H_5)_2P(Se)SNa \cdot 2\ H_2O$	124–125	[37a, 37b]
$(C_2H_5)_2P(Se)SeNa \cdot 2\ H_2O$	129–130	[37b, 37c]

These sodium salts (Table 3) are obtained by neutralization of the corresponding acids or in accordance with eq. (14) in the form of readily crystallizing, color-

$$(C_2H_5)_2P(Se)Cl \xrightarrow{2\ NaSH} (C_2H_5)_2P(Se)SNa + NaCl + H_2S \qquad (14a)$$

$$(C_2H_5)_2P(Se)Cl \xrightarrow{2\ NaSeH} (C_2H_5)_2P(Se)SeNa + NaCl + H_2Se \qquad (14b)$$

less hydrates. The complexing agents containing selenium are relatively unstable, and decompose after a time with separation of elemental selenium.

[31] *L. Malatesta*, Gazz. chim. ital. *76*, 182 (1946).

[32] *H. Meyer*, Dissertation, Technische Hochschule Aachen, 1964.

[33] *J. O. Smith* and *J. F. Kung*, US-Pat. 2929828 (March 22, 1960), Esso Research & Engineering Corp.

[34] *H. Jenkner*, German Pat. 1242857 (Dec. 14, 1967), Chemische Fabriken Kalk.

Table 4. Complexes of the type $[(C_2H_5)_2P(X)Y]_nM$.

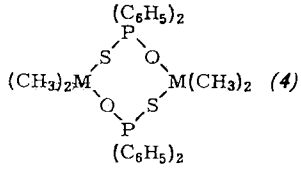
Ligand	M	Color	M.p. (°C)	Ref.
Diethylthiophosphinato $(C_2H_5)_2P(S)O^{\ominus}$	Co^{II}	deep blue	186–188	[35a, 35b]
	Zn^{II}	colorless	186–188	[35a, 35b]
	Cd^{II}	colorless	119–122	[35a, 35b]
	Pb^{II}	colorless	99–102	[35a, 35b]
	In^{III}	colorless	133	[35a, 35b]
Diethylselenophosphinato $(C_2H_5)_2P(Se)O^{\ominus}$	Co^{II}	blue	157–158	[36]
	Zn^{II}	colorless	201–203	[36]
	Cd^{II}	colorless	99–100	[36]
Diethylselenothiophosphinato $(C_2H_5)_2P(Se)S^{\ominus}$	Zn^{II}	colorless	157	[37a]
	Cd^{II}	colorless	160	[37a]
	Ni^{II}	olive green	142 (decomp.)	[37a]
	Pd^{II}	dark red	166–167	[38]
	Pb^{II}	green-yellow	132	[37a]
	Tl^{I}	colorless	139–140	[38]
	Bi^{III}	orange-red	94	[37a]
	Rh^{III}	red-brown	166–168	[39]
Diethyldiselenophosphinato $(C_2H_5)_2P(Se)Se^{\ominus}$	Zn^{II}	colorless	149–151	[37c]
	Cd^{II}	colorless	158	[37c]
	Ni^{II}	black-green	135	[38]
	Pd^{II}	dark red	196–197	[37c]
	Pb^{II}	yellow	157–158	[37c]
	Tl^{I}	pale yellow	129	[37c]
	Rh^{III}	brown-red	188–189	[39]
	In^{III}	yellow	146	[37c]
	Bi^{III}	vermilion	132	[37c]

All these compounds are readily soluble in organic solvents. The diethylthiophosphinato complexes, apart from the In^{III} compound, exhibit concentration-dependent association in solution (cf. Section 4). The same is found, though to a very much smaller degree, in the Zn^{II} and Cd^{II} complexes of the acids $(C_2H_5)_2P(S)SeH$ and $(C_2H_5)_2P(Se)SeH$. The compounds containing selenium decompose, particularly in daylight, with darkening of their color within days or weeks, depending on the metal. On the whole, they are thermally less stable than the corresponding dithio complexes; their melts decompose much more rapidly and, at lower temperatures, with separation of metal sulfide and/or selenide.

The most unstable members of this series are undoubtedly the complexes of the selenophosphinic acid $(C_2H_5)_2P(Se)OH$, of which only a few have so far been obtained in a well-defined form. For example, when heated in benzene, the blue Co^{II} complex changes into a green substance that has not yet been investigated. Attempts to prepare corresponding complexes *e.g.* of Ni^{II} and Bi^{III} and of the platinum metals always led, even under very mild conditions, merely to dark inhomogeneous decomposition products [36].

The reaction of diphenylthiophosphinic acid $(C_6H_5)_2P(S)OH$ with trimethylmetal compounds in analogy with eq. (9) yields dimeric dimethylmetal-diphenylthiophosphinato complexes *(4)* [25].

Basic dialkylthiophosphinatozinc(II) complexes having the formula $Zn_4O[R_2P(S)O]_6$ (R = C_2H_5, m.p. 273 °C;



M = Al, Ga

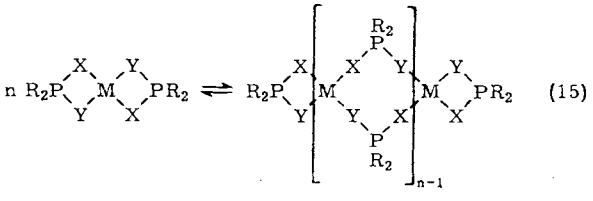
R = C_4H_9) have also been reported [40]. They are formed by the action of the free acids on zinc carbonate, a reaction that also leads to bis(diethylthiophosphinato)-zinc(II) (m.p. 186–188 °C) [35], as was mentioned above. This difference in reaction behavior is evidently due to very slight differences in the reaction conditions.

The two substances differ in their melting points and in their analytical composition. Moreover, osmometric molecular weight determinations (benzene, 37 °C) on the basic compound in the concentration range 8–20 g/l give values that correspond to the formula $Zn_4O[(C_2H_5)_2P(S)O]_6$ (1100.4). Bis(diethylthiophosphinato)zinc(II), on the other hand, exhibits concentration-dependent association under similar conditions, with molecular weights of about 4000–6500 (cf. Section 4).

According to X-ray studies the basic compounds belong to the class of tetranuclear complexes having a 4-coordinate central oxygen atom and ligand bridges between the zinc atoms [40]. This structure has been found *e.g.* in $Be_4O(CH_3COO)_6$ [41] and $Zn_4O(CH_3COO)_6$ [42].

4. Association of Phosphinato Complexes [35a, 35b]

A number of thiophosphinic and selenophosphinic acids, and particularly their zinc(II) and cadmium(II) complexes, exhibit concentration-dependent association in benzene or chloroform. This phenomenon, which was first observed in the dithiophosphinato complexes [5, 10], and which probably involves ligand bridges as shown in eq. (15), is most pronounced in



(15)

the thiophosphinato complexes $[R_2P(S)O]_nM$. Ligand bridges of this type have now also been postulated or detected in complexes of some phosphinic acids $R_2P(O)OH$ [43].

It can be seen from Figure 1, in which a number of thiophosphinato complexes have been taken as ex-

[35] a) *W. Kuchen* and *H. Hertel*, Angew. Chem. *79*, 148 (1967); Angew. Chem. internat. Edit. *6*, 175 (1967); b) Chem. Ber. *101*, 1991 (1968).

[36] *W. Kuchen, K. Schelhas*, and *K. Koch*, unpublished.

[37] a) *W. Kuchen* and *B. Knop*, Angew. Chem. *76*, 496 (1964); Angew. Chem. internat. Edit. *3*, 507 (1964); b) Chem. Ber. *99*, 1663 (1966); c) Angew. Chem. *77*, 259 (1965); Angew. Chem. internat. Edit. *4*, 244 (1965).

[38] *B. Knop*, Dissertation, Technische Hochschule Aachen, 1965.

[39] *W. Kuchen* and *B. Knop*, unpublished.

[40] *S. Meriani, G. Nardin*, and *A. Ripamonti*, Inorg. Chem. *6*, 1931 (1967).

[41] *L. Pauling* and *J. Sherman*, Proc. nat. Acad. Sci. USA *20*, 340 (1934).

[42] *H. Koyama* and *Y. Saito*, Bull. chem. Soc. Japan *27*, 112 (1954).

[43] Cf. *B. P. Block, J. Simkin*, and *L. Ocone*, J. Amer. chem. Soc. *84*, 1749 (1962); *G. E. Coates* and *D. S. Golightly*, J. chem. Soc. (London) *1962*, 2523; *C. E. Wilkes* and *R. A. Jacobsen*, Inorg. Chem. *4*, 99 (1965); *F. Giordano, L. Randaccio*, and *A. Ripamonti*, Chem. Commun. *1967*, 19; *1967*, 1239.

amples, that the *octahedral* In^{III} complex is monomeric in benzene over a wide range of concentrations, whereas the *tetrahedral* complexes are associated to varying degrees.

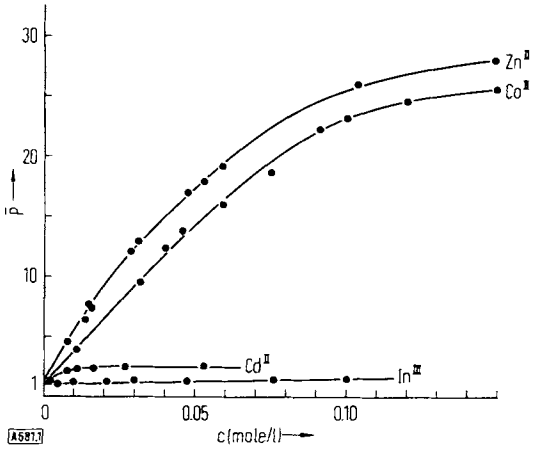


Fig. 1. Osmometrically determined average degrees of association $\bar{P}$ of complexes $[(C_2H_5)_2P(S)O]_nM$ (benzene, 37 °C).

While these compounds are evidently monomeric in very dilute solutions, their degree of association increases with concentration and tends toward a limiting value that depends on the central atom, and also on the solvent, since it decreases in the order carbon tetrachloride > benzene > chloroform [35a]. On the other hand, no temperature-dependence of the association equilibria has been detected between 37 and 60 °C.

Solutions of bis(diethylthiophosphinato)cobalt(II) and bis(diethylthiophosphinato)zinc(II) have surprisingly high viscosities, corresponding to high number average molecular weights even at low concentrations (see Fig. 1).

Viscometric measurements in benzene showed a very rapid increase in the reduced specific viscosity η_{sp}/c with increasing concentration for both complexes.

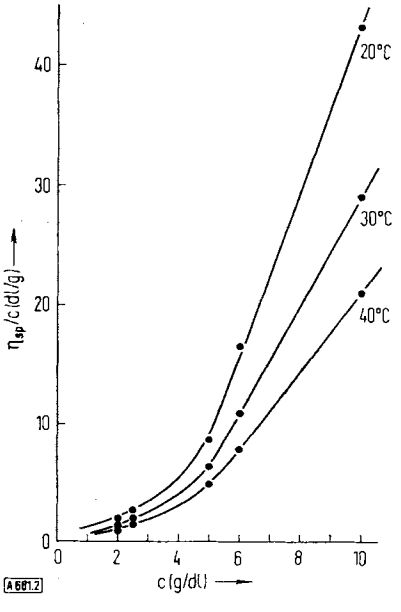


Fig. 2. Reduced specific viscosity as a function of the concentration for $[(C_2H_5)_2P(S)O]_2Co$ in benzene at various temperatures.

This observation, which is illustrated in Figure 2 for the Co^{II} compound, was also taken as evidence of an increase in association with increasing concentration [35b].

Investigations on the flow behavior of solutions of bis(diethylthiophosphinato)cobalt(II) and bis(diethylthiophosphinato)zinc(II) in benzene show no dependence of the viscosity on the shear gradient in the shear range examined (20–2500 sec^{-1}, 20 °C), and hence no structural viscosity. This behavior, like the apparently low temperature-dependence of the number average molecular weight, indicates the presence of strong bonds in the associates, such as would be expected of the postulated ligand bridges.

The nature of the donor atoms is also important to the association. Comparative measurements on Co^{II} and Cd^{II} complexes of various phosphinic acids showed that association decreases in the order

$$R_2P(O)O^{\ominus} > R_2P(S)O^{\ominus} > R_2P(S)S^{\ominus} > R_2P(Se)S^{\ominus} > R_2P(Se)Se^{\ominus}$$

The dependence of the degree of association on the size of the donor atom and on the radius and hybridization state of the metal (cf. Fig. 1) suggests that the association is mainly due to steric factors, four-membered chelate rings being replaced by less strained ligand bridges; examination of models shows that the strain in the four-membered ring  increases with decreasing radius of the central and donor atoms, whereas the formation of the four-membered ring is facilitated in the octahedral complexes by the smaller bond angle at the metal.

It can be shown *e.g.* in the case of the Co^{II} complex that the association does not tend to lead to an increase in the coordination number of the metal. Thus spectroscopic measurements show that Co^{II} is tetrahedrally coordinated in the associates, while magnetic measurements indicate that this is also the coordination state in the crystalline substance [35a, 35b].

However, factors other than steric ones must undoubtedly also be taken into account in the search for a satisfactory explanation of these association phenomena. Thus the fact that the association equilibria are at most only slightly temperature-dependent between 37 and 60 °C does not indicate that the metal-ligand bonds in the associates are energetically much more favorable. On the contrary, it suggests that entropy effects play a decisive role in the association. The importance of the part played by solvation is shown by the influence of the solvent on the degree of association.

5. IR [44] and Electronic Spectra [45]

No detailed IR spectroscopic studies, particularly normal coordinate analyses, have yet been carried out on the metal complexes of thiophosphinic and seleno-

[44] *W. Kuchen* and *G. Hägele*, unpublished.
[45] *W. Kuchen* and *H. Hertel*, unpublished.

Table 5. Stretching frequencies ν_1 and ν_2 (cm^{-1}) (averages for doublets) of phosphorus-chalcogen bonds in compounds of thiophosphinic and selenophosphinic acids. R = C_2H_5 (KBr disks).

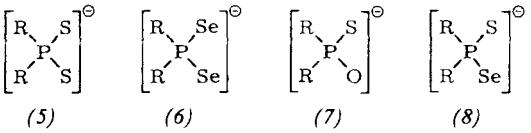
X	Y	$[R_2P(X)Y]_nM$			$[R_2P(X)Y]Na \cdot n\,H_2O$			$R_2P(X)Y-R'$			Assignment	
		ν_1	ν_2	$\nu_1-\nu_2$	ν_1	ν_2	$\nu_1-\nu_2$	ν_1	ν_2	$\nu_1-\nu_2$	ν_1	ν_2
S	O	1060–1140	548–558	*ca.* 450	1050 br	563	490	1095 [a]	564	531	PO	PS
O	S							1175 [a]	517	658	PO	PS
S	S	556–591	476–497	79–107	594	514	80	588 [b]	472	116	PS	PS
S	Se	540–560	440–454	95–115	577	496	81	583 [c]	439	144	PS	PSe
Se	Se	475–492	449–458	26–35	525	498	27	500 [c]	474	26	PSe	PSe

[a] R′ = CH_3; [b] R′ = C_3H_7; [c] R′ = C_2H_5.

phosphinic acids. However, *Coates* and *Mukherjee* [25] have investigated the IR spectra of the dimeric organometal-phosphinato complexes $[R_2P(X)YM(CH_3)_2]_2$ (R = CH_3, C_6H_5; M = Al, Ga, In, Tl; X, Y = O, S), and made assignments for the P–X and P–Y stretching vibrations.

Numerous investigations [46] have shown that the P(S) and P(Se) bonds have at most only an extremely small π component. The representation of these bonds by P–S̈: and P–S̈e:, as used in the present article, thus undoubtedly corresponds more closely to the true state of affairs than a formulation involving a conventional double bond.

Irrespective of the bond order, however, complete resonance should occur in the anions $R_2P(S)S^{\ominus}$ *(5)* and $R_2P(Se)Se^{\ominus}$ *(6)*, so that only one type of phosphorus-chalcogen bond is present; X-ray studies suggest that a similar situation exists in the analogous $[(CH_3O)_2P(S)S]^{\ominus}K^{\oplus}$ [47]. This would give C_{2v} symmetry for the anions *(5)* and *(6)*. Their IR spectra



(5) *(6)* *(7)* *(8)*

should therefore contain two absorptions, which can be assigned to an asymmetric (ν_1) and a symmetric (ν_2) stretching vibration of the phosphorus-chalcogen bond. For the anions $R_2P(S)O^{\ominus}$ *(7)* and $R_2P(S)Se^{\ominus}$ *(8)*, as well as for the esters $R_2P(X)Y-R$ (C_s symmetry), ν_1 and ν_2 correspond to the different types of phosphorus-chalcogen bonds.

As can be seen from Table 5, the metal complexes also give two characteristic absorption frequencies, which are again assigned to the above-mentioned vibrations, and are denoted by ν_1 and ν_2. They are frequently split into doublets, the degree of splitting varying up to 20 cm^{-1}. This may be due to superposition of the phosphorus-chalcogen or the metal-chalcogen stretching vibration [48], to the occurrence of synchronous and asynchronous vibrations, or to rotational isomerism [49]. Furthermore, ν_{PX} is generally smaller for the complexes than for the esters, whereas ν_{PY} is generally greater; this may be regarded as evidence that X is involved in coordination, and hence of the chelate nature of the ligand.

In the case of the diethyldithiophosphinato complexes, ν_1 is found to increase in the order Co^{II}, Hg^{II}, Bi^{III}, Sb^{III}, Pd^{II}, Pt^{II}, Ir^{III}, Rh^{III}, Ni^{II}, Pb^{II}, Tl^{I}, In^{III}, Cu^{I}, Cd^{II}, Zn^{II}, Cr^{III}.

However, it is not possible to draw conclusions from this sequence alone regarding the bond order of the PS bond, and hence also of the MS bond, in these compounds since the absorption frequency of the PS bond will depend in a complex manner on the masses, force constants, bond lengths and angles, and the symmetry of the molecule as a whole, as has been suggested for the C=S absorption frequencies of metal dithiocarbamates [48]. It is interesting to note that the differences $\nu_1-\nu_2$ for the dithio complexes lie between the corresponding values for the propyl ester (in which the two PS bonds should be different) and the sodium salt (in which the two PS bonds should be equivalent). This could be explained *e.g.* by the assumption that the chelate complexes contain both non-equivalent and equivalent PS bonds, which, owing to the coordination of the donor atom, differ only in their bond orders from their analogs in the esters and in the sodium salt.

The electronic spectra of some diethyldithiophosphinato complexes $[(C_2H_5)_2P(S)S]_nM$ show substantial agreement in the positions and intensities of the bands with those of the analogous diethyl dithiophosphato compounds $[(C_2H_5O)_2P(S)S]_nM$, in which the central atoms again have a tetrahedral, planar, or octahedral environment of four or six sulfur atoms [50a].

The ligand field parameters of the ion $(C_2H_5)_2P(S)S^{\ominus}$ have been deduced from spectra of the octahedral complexes $[(C_2H_5)_2P(S)S]_nM$ [M = Cr^{III}, Rh^{III}, Ir^{III}]

[46] Cf. *H. Siebert*, Z. anorg. allg. Chem. *275*, 210 (1954); *I. R. van Wazer*, J. Amer. chem. Soc. *78*, 5709 (1956); *L. C. Chernik, I. B. Pedley*, and *H. A. Skinner*, J. chem. Soc. (London) *1957*, 1851; *J. Goubeau*, Angew. Chem. *69*, 77 (1957); *J. Goubeau* and *W. Sawodny*, *78*, 565 (1966); Angew. Chem. internat. Edit. *5*, 567 (1966); *I. R. van Wazer, C. F. Callis, I. N. Shoolery*, and *R. C. Jones*, J. Amer. chem. Soc. *78*, 5715 (1956); *E. Fluck*: Die kernmagnetische Resonanz und ihre Anwendung in der anorganischen Chemie. Springer-Verlag, Berlin 1963, p. 268ff.; *R. F. Hudson*: Structure and Mechanism in Organophosphorus Chemistry. Academic Press, London 1965.

[47] *Ph. Coppens, C. H. MacGillavry, S. G. Hovenkamp*, and *H. Douwes*, Acta crystallogr. *15*, 765 (1962).

[48] *K. Nakamoto, J. Fujita, R. A. Condrate*, and *Y. Morimoto*, J. chem. Physics *39*, 432 (1963).

[49] *E. Steger* and *M. Kuntze*, Spectrochim. Acta A *23*, 2189 (1967); *W. W. Muelder*, *ibid. 22*, 1563 (1966); *A. H. Cowley* and *W. D. White*, *ibid. 22*, 1431 (1966).

[50] a) *C. K. Jørgensen*, J. inorg. nuclear Chem. *24*, 1571 (1962); b) Absorption Spectra and Chemical Bonding in Complexes. Pergamon Press, Oxford 1964; c) Orbitals in Atoms and Molecules. Academic Press, London 1962.

as described by *Jørgensen* [50b, 50c], using assignments made for the corresponding dithiophosphato complexes [50a] (see Table 6).

Table 6. Ligand field splitting and Racah parameters, Δ and B', and the nephelauxetic ratio $\beta = B'/B^\circ$ of octahedral diethyldithiophosphinato complexes $[(C_2H_5)_2P(S)S]_3M$.

M	Δ (cm^{-1})	B' (cm^{-1})	B° (cm^{-1})	β
Cr^{III}	13400	447	918 [50b]	0.49
Rh^{III}	20450	211	720 [50b]	0.29
Ir^{III}	24740	161	660 [50b]	0.24

This gives a relatively low ligand field strength and a considerable nephelauxetic effect for the ligand $(C_2H_5)_2P(S)S^\ominus$. It is thus situated in the immediate vicinity of the chloride ion in the spectrochemical series, and even occurs before the analogous diethyl dithiophosphate ion:

$$Br^\ominus < Cl^\ominus \approx (C_2H_5)_2P(S)S^\ominus < (C_2H_5O)_2P(S)S^\ominus < F^\ominus < H_2O < NH_3 < H_2N{-}(CH_2)_2{-}NH_2 > CN^\ominus$$

whereas its position in the nephelauxetic series is as follows:

$$F^\ominus < H_2O < NH_3 < H_2N{-}(CH_2)_2{-}NH_2 < Cl^\ominus \sim CN^\ominus < Br^\ominus < (C_2H_5)_2P(S)S^\ominus < (C_2H_5O)_2P(S)S^\ominus.$$

We are grateful to the Fonds der Chemie, the Deutsche Forschungsgemeinschaft, and the Stifterverband der Chemischen Industrie for their support of the work carried out on this topic by our own research group. W. K. thanks his co-workers named in the references for their untiring cooperation, as well as Fräulein U. Dreessen and Frau I. Haas for their conscientious help with the preparative and analytical work.

Received: March 14, 1968 [A 681 IE]
German version: Angew. Chem. *81*, 127 (1969)
Translated by Express Translation Service, London

The Catalytic Activity of Transition Metal Compounds in the Liquid-Phase Oxidation of Hydrocarbons

By N. M. Emanuel, Z. K. Maizus, and I. P. Skibida [*]

The way in which dissolved transition metal compounds affect the liquid-phase oxidation of hydrocarbons is demonstrated for compounds of cobalt, copper, and manganese. Kinetic investigations on model systems and comparisons with the non-catalyzed reaction show that the catalysts participate in all the oxidation steps.

1. Introduction

Non-catalyzed oxidation of hydrocarbons in the liquid phase may be considered to proceed by the following scheme [1, 2]:

$$RH \xrightarrow{O_2} R^\bullet \qquad \text{chain initiation} \quad (1)$$

$$R^\bullet + O_2 \rightarrow RO_2^\bullet \qquad \text{chain propagation} \quad (2)$$

$$RO_2^\bullet + RH \rightarrow ROOH + R^\bullet \qquad \text{chain propagation} \quad (3)$$

$$ROOH \rightarrow RO^\bullet + \dot{O}H \qquad \text{chain branching} \quad (4)$$

$$R^\bullet + R^\bullet \rightarrow R{-}R \qquad \text{chain termination} \quad (5)$$

$$RO_2^\bullet + R^\bullet \rightarrow ROOR \qquad \text{chain termination} \quad (6)$$

$$RO_2^\bullet + RO_2^\bullet \rightarrow ROH + R^1{-}CO{-}R^2 + O_2 \qquad \text{chain termination} \quad (7)$$

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[1] *N. N. Semenov*: Chain Reactions. Goshimizdat, Moscow 1934; Some Problems of Chemical Kinetics and Reactivity (English translation). Pergamon Press, Oxford 1958, Vol. 1, 1959, Vol. 2.

[2] *N. M. Emanuel, E. T. Denisov*, and *Z. K. Maizus*: Liquid-phase Oxidation of Hydrocarbons (English translation). Plenum Press, New York 1967.

[3] *A. A. Vichutinskii*, Doklady Akad. Nauk SSSR *157*, 150 (1964); Nature (London) *206*, 292 (1965).

In the initial stage of oxidation, free radicals are formed by interaction of the hydrocarbon and the dissolved oxygen by way of a bimolecular reaction (Equation 1) or by way of a termolecular reaction:

$$2\,RH + O_2 \rightarrow R^\bullet + H_2O_2 + R^\bullet \qquad (1')$$

The radical $R^\bullet$ so formed reacts with oxygen to form a peroxy radical $RO_2^\bullet$. This reaction usually requires no activation energy and the rate constant k_2 is about 10^7–10^8 l mole^{-1} sec^{-1}. Interaction between peroxy radicals and hydrocarbons yields hydroperoxides (Equation (3)), which are subsequently converted into alcohols, ketones, and other products (Equations (4)–(7)).

Chain termination occurs mainly by recombination of peroxy radicals $RO_2^\bullet$ (Equation (7)), since at sufficiently high oxygen concentrations all radicals $R^\bullet$ succeed in reacting with oxygen. The rate constants k_7 for recombination of $RO_2^\bullet$ have been measured for a number of hydrocarbons using the intermittent light and the photochemical after-effect techniques. k_1 can also be determined from variations in chemiluminescence [3] and by means of ESR spectroscopy [2, 4].

[4] *J. A. Howard* and *K. U. Ingold*, J. Amer. chem. Soc. *89*, 21 (1967).

Homogeneous catalysts induce essential changes in the mechanisms of all elementary steps of liquid-phase oxidation. Let us now consider these changes.

2. Chain Initiation by Radical Formation

2.1. Non-Catalyzed Radical Formation from Hydroperoxides

Decomposition of hydroperoxides yielding free radicals in the non-catalyzed oxidation of organic compounds is known to occur both by reaction (4)

$$ROOH \xrightarrow{k_4} RO^{\bullet} + \dot{O}H \qquad (4)$$

and by interaction between two saturated molecules [5, 6]. At early oxidation stages reactions (4′) and (4″) may take place.

$$ROOH + RH \xrightarrow{k_4'} RO^{\bullet} + R^{\bullet} + H_2O \qquad (4')$$

$$ROOH + ROOH \xrightarrow{k_4''} RO^{\bullet} + RO_2^{\bullet} + H_2O \qquad (4'')$$

The O–H bond in a water molecule formed by either of these reactions is very strong and has a considerably higher energy than that of the broken C–H bond in a hydrocarbon or of the O–H bond in a hydroperoxide. Consequently these reactions seem to be more advantageous from the standpoint of energetics than simple unimolecular decomposition of a hydroperoxide to free radicals according to Equation (4).

The linear dependence of the rate of radical formation on the concentration of a hydrocarbon (in an inert solvent) is evidence for reaction (4′). Measurements were made by means of the inhibitor technique. Such a mechanism of radical formation has been established, for example, for *n*-decyl-, cumyl-, and cyclododecylhydroperoxides [5–7].

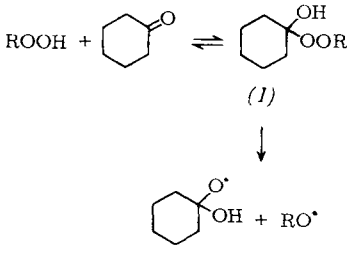
Reaction (4″) was first discovered for the oxidation of olefins [8]. Later on this reaction was studied in detail for the inhibited decomposition of hydrogen peroxide and *tert*-butyl hydroperoxide and it was found to occur through an intermediate complex involving ROOH molecules bound by hydrogen bonds [9].

Decomposition of a hydroperoxide in an olefin can lead to the formation of radicals by the following reaction [10]:

$$ROOH + \rangle C{=}C\langle \longrightarrow RO^{\bullet} + \rangle \dot{C}{-}C\langle{-}OH$$

Radicals may be formed in high yields by reaction of hydroperoxides with oxidation products, such as are obtained on oxidation of hydrocarbons. Compounds such as organic acids and alcohols form hydrogen-bonded intermediates with hydroperoxides and the rate of decomposition of such complexes to radicals appears to be higher than that of the decomposition of free hydroperoxide [11, 12]. The higher rate of radical formation accounted for by hydrogen bonds between hydroperoxides and the solvent was observed also for decomposition of methyl ethyl ketone hydroperoxide in aqueous and alcoholic solutions. Complexes of ketone hydroperoxides and these solvents decompose to radicals at a rate 10 to 20 times higher than that for a free ketone hydroperoxide.

Decomposition of a hydroperoxide in a solvent or in presence of reaction products may be accelerated not only as a result of formation of hydrogen-bonded complexes, but also because of a chemical reaction with the solvent yielding more labile hydroperoxides [2]. For instance, the higher rate of decomposition of *tert*-butyl hydroperoxide in the presence of cyclohexanone is accounted for by formation of the labile intermediate *(1)*, which readily decomposes to free radicals.



2.2. Radical Formation from Hydroperoxides in the Presence of Cobalt Catalysts

Transition metal salts accelerate the decomposition of hydroperoxides shown in equations (8) and (8′).

$$ROOH + M^{n+} \rightarrow RO^{\bullet} + OH^{-} + M^{(n+1)+} \qquad (8)$$

$$ROOH + M^{(n+1)+} \rightarrow RO_2^{\bullet} + H^{+} + M^{n+} \qquad (8')$$

This mechanism of hydroperoxide decomposition was proposed by *Haber* and *Weiss* for the decomposition of hydrogen peroxide in the presence of bivalent iron ions [13].

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^{\bullet} + OH^{-} \qquad (8'')$$

The hydroxyl radical formed initiates chain decomposition of H_2O_2. Organic hydroperoxides in aqueous solutions also decompose readily under the action of transition metals to form free alkoxy radicals [14, 15]. In a

[5] *Z. K. Maizus, I. P. Skibida,* and *N. M. Emanuel,* Doklady Akad. Nauk SSSR *131,* 880 (1960).

[6] *V. L. Antonovskii, E. T. Denisov, I. Kuznetsov, Yu. Ya. Mekhryushev,* and *L. V. Solntseva,* Kinetika i. Kataliz *6,* 815 (1965).

[7] *I. V. Berezin* and *V. G. Bykovchenko,* Neftechimija *3,* 376 (1963).

[8] *J. Bateman,* Quart. Rev. (chem. Soc., London) *8,* 147 (1954).

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[10] *E. T. Denisov* and *L. N. Denisova,* Doklady Akad. Nauk SSSR *157,* 907 (1964).

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[12] *E. T. Denisov* and *V. M. Solyanikov,* Neftechimija *4,* 458 (1964).

[13] *F. Haber* and *J. Weiss,* Naturwissenschaften *20,* 948 (1932).

[14] *J. W. Fordham* and *H. L. Williams,* J. Amer. chem. Soc. *72,* 4465 (1950); *73,* 1638 (1951).

[15] *R. G. Orr* and *H. L. Williams,* Canad. J. Chem. *30,* 985 (1952).

hydrocarbon medium the rate of reaction of transition metal salts with hydroperoxides is slower than in water; nevertheless, it is still considerably faster than the rate of thermal hydroperoxide decomposition.

It may be considered as established that, in a hydrocarbon medium, hydroperoxides form intermediate complexes with the catalyst [16–18]. However, the mechanism of decomposition of these complexes is not established; nor is there any information on the structures of such complexes or on the rates of their formation and decomposition to free radicals.

The mechanism of decomposition of *n*-decyl hydroperoxide in the presence of cobalt stearate has been investigated over the temperature range 60 to 100 °C [19,20]. It was found that hydroperoxide decomposition in such a system proceeds at a rate of 1.3×10^{-2} mole/l (see Fig. 1) irrespective of whether

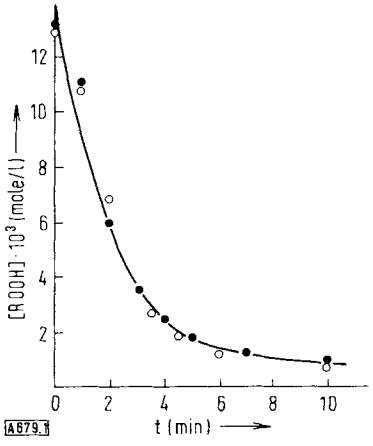


Fig. 1. Kinetics of *n*-decyl hydroperoxide (ROOH) decomposition in a flow of nitrogen at 80 °C. ○: in the presence of 1.12×10^{-3} mole/l of cobalt stearate. ●: in the presence of 1.11×10^{-3} mole/l of cobalt stearate and 8.3×10^{-2} mole/l of *N*-phenyl-β-naphthylamine. Solvent: *n*-decane.

an inhibitor (*N*-phenyl-β-naphthylamine) is present or not. Thus, it can be concluded that *n*-decyl hydroperoxide decomposes exclusively to free radicals (see Equation (4)). For this reason all further experiments on the mechanism of chain branching in *n*-decane oxidation catalyzed by cobalt stearate were conducted in the absence of an inhibitor, and the rate of formation of radicals was determined from the rate of hydroperoxide consumption. In Figure 2a the rate of free radical formation W_R in the presence of cobalt stearate is shown as a function of the initial hydroperoxide concentration $[ROOH]_0$. W_R increases linearly with hydroperoxide concentration up to the value W_{max} and then remains practically constant. This is evidence that the formation of radicals occurs *via* an intermediate hydroperoxide/cobalt stearate complex. The plot of $\log (1/W_R - 1/(2\ W_{max}))$ *versus* $\log [ROOH]_0$ is a straight line.

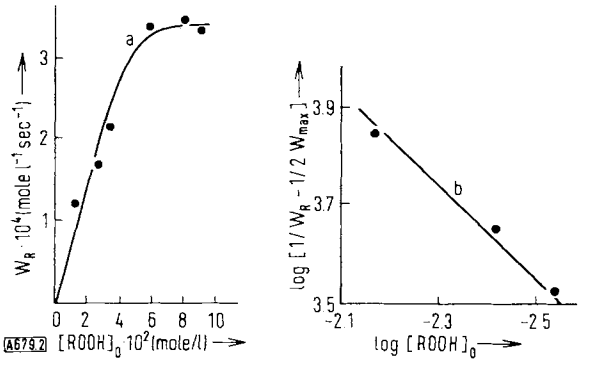


Fig. 2. a) Rate of formation W_R of radicals during the cobalt stearate catalyzed decomposition of *n*-decyl hydroperoxide (ROOH) as a function of $[ROOH]_0$. b) $\log (1/W_R - 1/(2\ W_{max}))$ as a function of $\log [ROOH]_0$. $T = 100$ °C, $[CoSt_2]_0 = 1.14 \times 10^{-3}$ mole/l. Solvent: *n*-decane.

The rate of hydroperoxide decomposition is a linear function of the square of the cobalt stearate concentration (Fig. 3). Consequently two molecules of cobalt stearate participate in the formation of radicals.

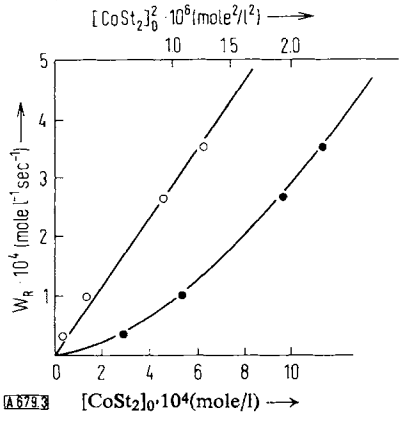


Fig. 3. Rate of decomposition of *n*-decyl hydroperoxide as a function of $[CoSt_2]_0$ (●) and $[CoSt_2]_0^2$ (○). $[ROOH]_0 = 7.5 \times 10^{-2}$ mole/l. $T = 100$ °C. Solvent: *n*-decane.

$$CoSt_2 + n\,ROOH \overset{K}{\rightleftharpoons} [CoSt_2 \cdot n\,ROOH] \quad (9)$$

$$[CoSt_2 \cdot n\,ROOH] + CoSt_2 \xrightarrow{k_4} CoSt_2(OH) + CoSt_2 + RO^{\bullet} + (n-1)\,ROOH \quad (10)$$

$$[CoSt_2 \cdot n\,ROOH] + CoSt_2(OH) \xrightarrow{k_5} 2\,CoSt_2 + H_2O + RO_2^{\bullet} + (n-1)\,ROOH \quad (11)$$

$CoSt_2$ = cobalt stearate

In this case the rate of radical formation will be

$$W_R = k_4 [CoSt_2 \cdot n\,ROOH] [CoSt_2] + k_5 [CoSt_2(OH)] [CoSt_2 \cdot n\,ROOH].$$

On substituting $[CoSt_2]$ for the $[CoSt_2(OH)]$ concentration in

$$d [CoSt_2(OH)]/dt = k_4 [CoSt_2] [CoSt_2 \cdot n\,ROOH] - k_5 [CoSt_2(OH)] [CoSt_2 \cdot n\,ROOH] = 0$$

[16] *A. J. Chalk* and *J. F. Smith*, Trans. Faraday Soc. *53*, 1214 (1957).

[17] *H. Kropf*, Liebigs Ann. Chem. *637*, 92 (1960).

[18] *V. Ya. Shlyapintokh, O. N. Karpukhin, L. M. Postnikov, I. V. Zakharov, A. A. Vichutinskii*, and *V. F. Tsepalov*: Chemiluminescence Techniques for Investigation of Slow Chemical Reactions. Izd. "Nauka", Moscow 1966.

[19] *G. M. Bulgakova, Z. K. Maizus*, and *I. P. Skibida*, Kinetika i Kataliz *7*, 332 (1966).

[20] *Z. K. Maizus, I. P. Skibida*, and *N. M. Emanuel*, Ž. fiz. Chim. *40*, 322 (1966).

we obtain

$$W_R = 2 k_4 [CoSt_2] [X] \quad (12)$$

where

$$[X] = [CoSt_2 \quad n\,ROOH]$$

Assuming that equilibrium is attained rapidly enough and is not disturbed by consumption of the complex we obtain

$$[X] = K [ROOH]^n [CoSt_2] \quad (13)$$

Since in the given case the concentration of $CoSt_2$ is always considerably lower than that of hydroperoxide, the formation of a complex reduces the hydroperoxide concentration only slightly but, at the same time, considerably reduces the concentration of cobalt stearate. From equations (12) and (13), and taking into account the conditions $[CoSt_2] = [CoSt_2]_0 - [X]$ and $[ROOH] = [ROOH]_0$, we obtain for the overall rate of hydroperoxide decomposition [*]:

$$W_R = 2 k_4 K [CoSt_2]_0^2 [ROOH]_0^n / (1 + K [ROOH]_0^n)^2 \quad (14)$$

The reaction order n based on hydroperoxide, the equilibrium constant K for complex formation, and the rate constant k_4 for the decomposition of the complex to radicals can be obtained from Equation 14 using the values given in Fig. 2.

k_4 is determined from the maximum rate of hydroperoxide decomposition. Differentiating (14), we obtain

$$[ROOH]^n = 1/K \quad (15)$$

Then the maximum decomposition rate is

$$W_{max} = k_4 [CoSt_2]_0^2 / 4 \quad (16)$$

Hence k_4 can be calculated from the known cobalt stearate concentration. It may be found also from the slope of the curve for W_R *versus* $[CoSt_2]^2$, when the rate of hydroperoxide decomposition is independent of the hydroperoxide concentration (Fig. 3). In order to determine the reaction order n and the equilibrium constant K, Equation (14) is rearranged as follows:

$$1/W_R - 1/(2 W_{max}) = 1/(k_4 K [CoSt_2]_0^2 [ROOH]_0^n) \quad (17)$$

In logarithmic form, this equation is

$$\log [1/W_R - 1/(2 W_{max})] = \log (1/k_4 K [CoSt_2]_0^2) - n \log [ROOH]_0 \quad (18)$$

The reaction order n as calculated by the least squares method from the slope of the curve $\log [1/W_R - 1/(2 W_{max})]$ *vs.* $\log [ROOH]_0$ (Fig. 2b) has a value of 0.9. Thus, the hydroperoxide/catalyst complex appears to contain one $CoSt_2$ molecule and one hydroperoxide molecule.

The rate constant k_4 for complex decomposition to radicals at 100 °C, as found from W_{max}, has a value of 1×10^3 l mole^{-1} sec^{-1}. The equilibrium constant for complex formation is $K = 10$ l/mole (at 100 °C). The temperature dependence of the constants k_4 and K between 60 and 100 °C permits an estimation of the activation energy for radical formation by interaction between the $ROOH \cdot CoSt_2$ complex and cobalt stearate ($E_4 = 24.5 \pm 0.8$ kcal/mole) and the heat of the complex formation ($\Delta H = 10 \pm 0.6$ kcal/mole). The general expression for k_1 may therefore be written as

$$k_4 = 2 \times 10^{17} \exp ((-24500 \pm 800)/RT) \text{ l mole}^{-1}$$

and that for K as

$$K = 6 \times 10^{-5} \exp ((10000 \pm 600)/RT) \text{ l/mole}^{-1}$$

The results obtained are evidence that the high catalytic efficiency of cobalt salts in the decomposition of *n*-decyl hydroperoxide to radicals is accounted for by the higher rate constant k_4. It is almost a thousand times higher than that for radical decomposition of the hydroperoxide in the absence of a catalyst.

A similar mechanism is postulated for the decomposition of ethylphenyl hydroperoxide in the presence of cobalt acetate [18], as studied by the chemiluminescence technique.

2.3. Radical Formation from Hydroperoxides in the Presence of Copper Catalysts

When *n*-decyl hydroperoxide decomposes in the presence of copper stearate the part played by the catalyst is not restricted to its participation in radical formation. If an inhibitor is introduced into such a system the rate of consumption of the inhibitor is considerably lower than that of hydroperoxide decomposition. For instance at an initial concentration of $[ROOH]_0 = 0.047$ mole/l and $[InH]_0 = 2.2 \times 10^{-4}$ mole/l the rate of ROOH decomposition is 1.2×10^{-3} mole l^{-1} min^{-1},

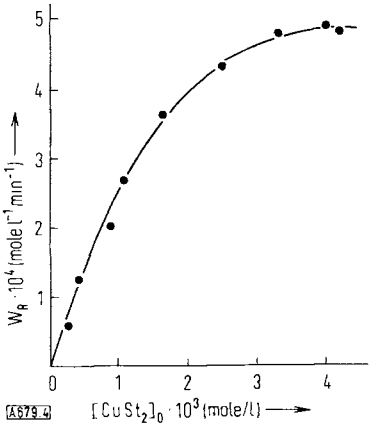


Fig. 4. Rate of formation W_R of radicals on decomposition of *n*-decyl hydroperoxide as a function of $[CuSt_2]_0$. $[ROOH]_0 = 0.047$ mole/l. $T = 80$ °C. Solvent: *n*-decane.

[*] K is the product of equilibrium constants for formation of complexes containing 1 to n hydroperoxide molecules (dimensionality l^n/mole^n).
It follows from (6) that the rate of radical formation in the presence of $CoSt_2$ will attain a certain maximum value and will then start decreasing. In the given case the region of decrease in the rate of hydroperoxide decomposition with increasing ROOH concentration was not obtained, since the hydroperoxide could not accumulate in large amounts.

and that of inhibitor consumption is 1.9×10^{-4} mole l^{-1} min^{-1}. The rate of radical formation in the presence of copper stearate was, therefore, determined from consumption of inhibitor (*N*-phenyl-β-naphthylamine). The rate of inhibitor consumption was found to be independent of concentration, *i.e.* the inhibitor reacted only with free radicals, and did not react directly either with hydroperoxides or with the other products present.

The rate of radical formation, W_R, in the presence of copper stearate, as opposed to cobalt stearate, initially increases linearly with the catalyst concentration (Fig. 4). Thus the formation of radicals is first order with respect to $CuSt_2$. Fig. 5 shows that, at low

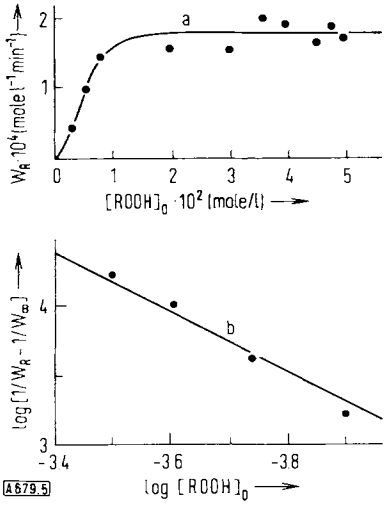


Fig. 5. a) Rate of formation W_R of the radicals on copper stearate catalyzed decomposition of *n*-decyl hydroperoxide (ROOH) as a function of [ROOH]$_0$. b) log $(1/W_R - 1/W_\infty)$ as a function of log [ROOH]$_0$. [$CuSt_2$]$_0$ = 8×10^{-4} mole/l. T = 80 °C. Solvent: *n*-decane.

hydroperoxide concentrations, W_R increases with the hydroperoxide concentration, and is independent of it at high [ROOH]$_0$ values. Thus, as in the case of decompositions catalyzed by $CoSt_2$, the formation of radicals in the presence of $CuSt_2$ occurs by decomposition of the hydroperoxide/copper stearate complex. When [$CuSt_2$] $\ll$ [ROOH] all the copper appears to be bound in a complex and any further increase in [ROOH] has no effect on the rate of radical formation.

The mechanism of *n*-decyl hydroperoxide decomposition to radicals in the presence of $CuSt_2$ may be formulated as

$$CuSt_2 + n\,ROOH \underset{2}{\overset{1}{\rightleftharpoons}} [CuSt_2 \cdot n\,ROOH] \xrightarrow{3} RO_2^{\bullet} + CuSt + HSt + (n-1)\,ROOH$$

$$CuSt + ROOH \xrightarrow{4} CuSt(OH) + RO^{\bullet}$$

Taking into account that one inhibitor molecule reacts with two free radicals and that the concentration of univalent copper remains constant we obtain

$$W_R = 2\,k_3\,[CuSt_2 \cdot n\,ROOH].$$

Assuming, as in the case of $CoSt_2$, that the equilibrium of complex formation is not disturbed by the decomposition of the complex to radicals, we find

$$W_R = k_3\,K\,[ROOH]_0^n\,[CuSt_2]_0/(1 + K\,[ROOH]_0^n) \quad (19)$$

At $1 \ll K\,[ROOH]^n$ the value W_R is independent of [ROOH]:

$$W_R = W_\infty = k_3\,[CuSt_2]_0 \quad (20)$$

It can be seen from Equation (20) that the rate constant k_3 for the decomposition of the complex to radicals may be determined from the maximum rate of the inhibitor consumption corresponding to formation of radicals (Fig. 5).

Investigation of ROOH decomposition in the presence of $CuSt_2$ over a temperature range of 60 to 100 °C yielded the following k_3 value

$$k_3 = 1.1 \times 10^7 \exp(-15500/RT)\ sec^{-1}$$

The dependence of W_R on [ROOH] in logarithmic coordinates is

$$\log(1/W_R - 1/W_\infty) = \log[1/(2\,k_3\,K\,[CuSt_2]_0)] - n \log [ROOH]_0 \quad (21)$$

From Equation (21) it is possible to determine n and K. It was found from the logarithmic anamorphose (Fig. 5a) that $n = 2$ and $K = 1.1 \times 10^9 \exp(-8000/RT)$ $l^2/mole^2$.

Investigations in the presence of copper and cobalt stearates showed that the appearance of free radicals is preceded in both cases by formation of $MSt_2 \cdot n$ ROOH complexes. Whereas the cobalt complex contains a molecule of $CoSt_2$ and one of ROOH, in the presence of copper stearate one $CuSt_2$ molecule is bound to two ROOH molecules. The mechanisms of complex decomposition are also different: the copper complex decomposes in a unimolecular manner, but the cobalt complex decomposes by a bimolecular mechanism involving a second $CoSt_2$ molecule.

Another possibility is decomposition of the peroxide in the presence of $CuSt_2$, without formation of radicals. This might be due to the cage effect, the radicals formed in the solvent cage reacting with Cu^+:

$$CuSt + R^1CH(O\dot{O})R^2 \rightarrow CuSt(OH) + R^1\text{–}C(O)\text{–}R^2$$

It has been suggested that manganese stearate acts as a catalyst in the same way [21].

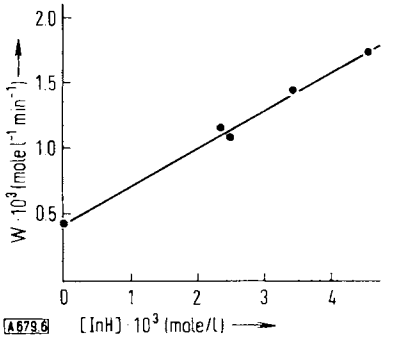


Fig. 6. Rate of decomposition W of *n*-decyl hydroperoxide as a function of the inhibitor concentration. [ROOH]$_0$ = 0.047 mole/l. T = 80 °C. Copper stearate as catalyst. Inhibitor: *N*-phenyl-β-naphthylamine. Solvent: *n*-decane.

[21] *V. M. Goldberg* and *L. K. Obukhova*, Izvest Akad. Nauk SSSR, Ser. chim. *1966*, 2217.

Introduction of an inhibitor into the *n*-decyl hydroperoxide/$CuSt_2$ system increases the rate of non-radical hydroperoxide decomposition. Fig. 6 shows that the initial rate of hydroperoxide decomposition increases linearly with the inhibitor concentration.

2.4. Radical Formation in Peroxide-Free Systems

Of great interest is the possibility of chain initiation in a system containing a hydrocarbon, dissolved oxygen, and a catalyst but no peroxides. If the metal of the catalyst is in its highest valence state, it may form free radicals by reaction with the hydrocarbon. Initiation by Co^{3+} ions in aqueous media seems to occur at high rates, as was demonstrated recently for oxidation of toluene, alcohols, and ethers by cobalt(III) perchlorate [22,23]. In a hydrocarbon medium and with cobalt(III) stearate as catalyst radical formation may occur by reaction (22).

$$CoSt_3 + RH \rightarrow CoSt_2 + HSt + R^{\bullet} \qquad (22)$$

The rate of chain initiation was found to be a linear function of tervalent cobalt concentration in the oxidation of linoleic acid in benzene [24], and of 2-methyl-2-butene in acetic acid [25] in presence of Co^{3+}.

Investigation of reactions of tervalent cobalt with olefins has shown that in acid solutions and at room temperature reaction (22) is sufficiently fast and its activation energy is 27 to 29 kcal/mole; the pre-exponential factor is 10^{20} l mole^{-1} sec^{-1} [26].

In many oxidations, reactions of type (22) seem to be of no importance since radical formation by reaction between the catalyst and the hydroperoxide occurs at a considerably higher rate. Catalysts such as cobalt or manganese salts are usually added to the hydrocarbon in a bivalent state.

Information concerning whether bivalent metal ions take part in chain initiation at the start of the reaction, or whether their initiating effect becomes possible only after appearance of peroxides is very scarce. In the absence of the hydroperoxide, the radicals may be formed by the following reactions [27,28]:

$$CoSt_2 + O_2 \rightleftharpoons CoSt_2 \cdots O_2$$
$$CoSt_2 \cdots O_2 + RH \rightarrow CoSt_2(OOH) + R^{\bullet}$$

or

$$CoSt_2 \cdots O_2 + RH \rightarrow CoSt_2(OH) + RO^{\bullet}$$

Evidence in favor of this mechanism was obtained on oxidation of methyl linoleate (RH) in benzene in the presence of cobalt stearate [28]. The rate of this reaction is independent of the hydroperoxide concentration and is found to be:

$$W = k\,[RH]\,[St_2Co].$$

A change in the polarity of the medium by addition of nitrobenzene results in a lower rate of oxidation. It may be that nitrobenzene solvates the molecules of bivalent cobalt stearate, thus preventing the formation of a complex with oxygen and, consequently, the appearance of free radicals.

The formation of radicals in the $RH/O_2/M^{2+}$ system not easy to follow since the rapid reaction of the hydroperoxide formed with M^{2+} to yield free radicals makes the study of the slower reaction involving oxygen difficult. Of great interest in this connection is the mechanism of chain initiation on oxidation of styrene in the presence of cobalt stearate [29]. The polymer peroxide formed in the oxidation of styrene is rather passive towards the catalyst. The formation of radicals was studied for the systems styrene/O_2/cobalt stearate and styrene/O_2/cobalt acetylacetonate, and in both cases the reaction rate was shown to be proportional to the styrene, oxygen, and cobalt concentrations

$$W = k\,[\text{styrene}]\,[O_2]\,[Co^{2+}] \qquad (23)$$

Equation (23) is consistent with radical formation by the termolecular reaction and by the reaction sequence (24).

$$Co^{2+} + O_2 \overset{K}{\rightleftharpoons} Co^{2+} \cdots O_2$$
$$Co^{2+} \cdots O_2 + CH_2{=}CHR \xrightarrow{k'} Co{-}O{-}O{-}CH_2{-}\dot{C}HR \qquad (24)$$

The second mechanism seems more probable. In this case the experimental constant is $k = k'K$.

The mechanism of radical formation catalyzed by pyridine-copper complexes ($Cu^{2+}(Py)_m$, $m = 1{-}4$) [30] is considerably more complicated. It was found in the oxidation of methyl ethyl ketone that the copper-pyridine complexes are very efficient enolization catalysts. This accounts for the fact that under the conditions of this reaction ketones undergo oxidation in the form of enols or enolate ions.

$$CH_3{-}CH{=}\overset{O^{\ominus}}{\overset{|}{C}}{-}CH_3 \xrightarrow{Cu^{2+}(Py)_m} CH_3{-}\overset{O^{\bullet}}{\overset{|}{C}}{=}CH{-}CH_3 \rightleftharpoons CH_3{-}\dot{C}H{-}\overset{O}{\overset{\|}{C}}{-}CH_3$$

Heterogeneous catalysts also contribute to formation of radicals in the liquid-phase oxidation of organic compounds. Thus it was found that the liquid-phase oxidation of cyclohexene and 2-methyl-2-butene in the absence of a catalyst does not start until after a rather long induction period, whereas in the presence of manganese dioxide the reaction starts immediately [31]. Similar results were obtained for liquid-phase oxidation of isobutene in the presence of MnO_2

[22] *T. A. Cooper, A. A. Clifford, D. J. Mills,* and *W. A. Waters,* J. chem. Soc. (London) B *1966,* 793.

[23] *T. A. Cooper* and *W. A. Waters,* J. chem. Soc. London B *1967,* 455, 464.

[24] *F. W. Heaton* and *N. Uri,* J. Lipid Res. *2,* 152 (1961).

[25] *C. Bawn, A. Pennington,* and *C. Tiper,* Discuss. Faraday Soc. Nr. 10, 282 (1951).

[26] *C. Bawn* and *J. Sharp,* J. chem. Soc. (London) *1957,* 1854.

[27] *E. T. Denisov* and *N. M. Emanuel,* Ž. fiz. Chim. *30,* 2499 (1956).

[28] *N. Uri,* Nature (London) *177,* 1177 (1954).

[29] *L. N. Denisova* and *E. T. Denisov,* Izvest. Akad. Nauk SSSR, Ser. chim. *1966,* 1095.

[30] *V. D. Komissarov* and *E. T. Denisov,* Neftechimija 7, 420 (1967).

[31] *J. Burger, M. C. Meyer,* and *J. C. Balaceanu,* C. R. hebd. Séances Acad. Sci. *252,* 2235 (1961).

and Cr_2O_3[32]. The composition of isobutene oxidation products in the presence of a heterogeneous catalyst is practically the same as that in the presence of azodiisobutyronitrile as initiator, suggesting that the heterogeneous catalysts studied take part in the formation of free radicals only.

3. Chain Propagation

3.1. Chain Propagation in Non-Catalyzed Reactions

The propagation of chains in a non-catalyzed reaction proceeds *via* two alternating consecutive elementary steps:

$$R^\bullet + O_2 \rightarrow RO_2^\bullet$$
$$RO_2^\bullet + RH \rightarrow ROOH + R^\bullet$$

All other oxidation products, such as alcohols, ketones, and acids, are formed from the hydroperoxide[33]. At higher conversions the peroxy radicals $RO_2^\bullet$ may react both with the initial hydrocarbon and with the oxidation products[34].

The ratio of the rate constants for the chain reaction of $RO_2^\bullet$ with hydrocarbon, hydroperoxide, and alcohol[35] are 1:9:12 for ethylbenzene oxidation, and 1:13:6.3 for *n*-decane oxidation. Thus alcohols and peroxides react with free radicals almost ten times as fast as do hydrocarbons.

Oxidation of *n*-decane affords a mixture of isomeric oxygen-containing compounds, as there is an equal probability of oxidation for each equivalent CH_2 group. It was found[36] that all isomeric decanols show practically the same reactivity in reactions with $RO_2^\bullet$.

$$RO_2^\bullet + R^1CH{=}CHR^2 \rightarrow RO^\bullet + R^1HC\!-\!\underset{\diagdown\,\diagup}{O}\!-\!CHR^2 \quad (25)$$

Alkenes can react with $RO_2^\bullet$ to form a hydroperoxide or an epoxide (oxirane) according to Eq. (25). The latter mechanism was postulated, for instance, for styrene oxidation[37]. The formation of epoxides on reaction of $RO_2^\bullet$ with olefins was recently confirmed in studies on the mechanism of conjugated oxidation (see Table 1)[39] of propene and acetaldehyde[38]. It was found that addition of an inhibitor (2,6-di-*tert*-butyl-4-methylphenol) completely stops the consumption of acetaldehyde. Some propene oxide is still formed, however, owing to occurrence of a Prilezhaev reaction (see Eq. (26) and Fig. 7).

$$ROOH + CH_2{=}CH{-}CH_3 \rightarrow ROH + H_2C\!-\!\underset{\diagdown\,\diagup}{O}\!-\!CH{-}CH_3 \quad (26)$$

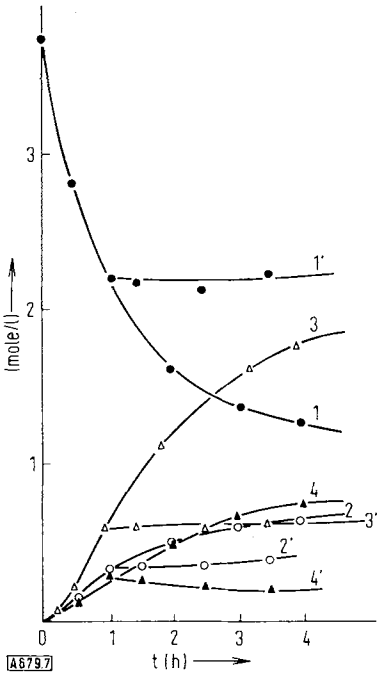


Fig. 7. Effect of the inhibitor 2,6-di-*tert*-butyl-4-methylphenol on the kinetics of acetaldehyde consumption and the accumulation of products in conjugated oxidation of propene and acetaldehyde (molar ratio 1:1) in a benzene solution at $T = 75\,^\circ C$ and p (air) = 50 atm. Figures without primes refer to experiments with no inhibitor; those with primes are for experiments with 0.02 mole/l of 2,6-di-*tert*-butyl-4-methylphenol, which was admitted 1 h after the start of the experiment. Acetaldehyde consumption (1,1'). Propene oxide (2,2'). Acetic acid (3,3'). Peroxide (4,4').

It may be seen from Table 1 that the maximum yields of propene oxide are obtained by oxidation of mixtures of propene with aldehydes and with ethyl methyl ketone involving formation of acetaldehyde as intermediate[40]. Correlating these facts with the low propene oxide yield in the absence of aldehydes, for instance in a mixture of propene and alkylaromatic

$$CH_3{-}C(=O)(-O{-}O^\bullet) + CH_2{=}CH{-}CH_3$$
$$\rightarrow CH_3{-}C(=O)(-O^\bullet) + H_2C\!-\!\underset{\diagdown\,\diagup}{O}\!-\!CH{-}CH_3$$
$$CH_3{-}C(=O)(-O^\bullet) + RH \rightarrow CH_3{-}C(=O)(-OH) + R^\bullet$$

Table 1. Examples of conjugated oxidation of propene with various other oxidizable compounds (molar ratio 2:1 for aldehydes, 1:3 for other components); yields calculated with respect to the additional components.

Additional component	Air pressure (atm)	T (°C)	Time (h)	Propene oxide in product (wt.-%)	Yield (%)
Acetaldehyde	50	60–80	1	34	70
Propionaldehyde	50	70	1	12	50
Methyl ethyl ketone	50	145	4	10	96
Butane	50	145	4	3	11
Cumene	50	130	3	3	9
Ethylbenzene	50	130	3	3	15

[32] *E.-A. Blümberg, M. G. Bulygin, L. Ya. Margolis*, and *N. M. Emanuel*, Doklady Akad. Nauk SSSR *150*, 1066 (1963).

[33] *L. S. Vartanyan, Z. K. Maizus*, and *N. M. Emanuel*, Ž. fiz. Chim. *30*, 682 (1956).

[34] *Z. K. Maizus, I. P. Skibida, N. M. Emanuel*, and *V. N. Yakovleva*, Kinetika i Kataliz *1*, 55 (1960).

[35] *I. P. Skibida, Z. K. Maizus*, and *N. M. Emanuel*, Neftechimija *4*, 82 (1964).

[36] *I. P. Skibida, Z. I. Kulitskii*, and *Z. K. Maizus*, Doklady Akad. Nauk SSSR *148*, 1358 (1963).

[37] *F. R. Mayo*, J. Amer. chem. Soc. *80*, 2465 (1958).

[38] *E. A. Blümberg* and *P. I. Valov*, Izvest. Akad. Nauk SSSR, Ser. chim. *1966*, 1334.

[39] *E. A. Blümberg, P. I. Valov, Yu. D. Norikov*, and *N. M. Emanuel*, Doklady Akad. Nauk SSSR *167*, 579 (1966).

[40] *E. A. Blümberg, M. G. Bulygin*, and *N. M. Emanuel*, Doklady Akad. Nauk SSSR *166*, 353 (1966).

hydrocarbons, the authors concluded that the structure of $RO_2^{\cdot}$ plays an important part in epoxidation and that acylperoxy radicals are particularly effective.

3.2. Chain Propagation in Catalyzed Reactions

Transition metal salts affect not only the reaction rate but also the ratio of reaction products, thus demonstrating participation of the catalysts in chain propagation. Our research on *n*-decane oxidation has indeed shown that the sequence of product formation and the mechanism of chain propagation in the presence of cobalt stearate are essentially different from those for non-catalyzed oxidation.

The sequence of oxidation product formation in the presence of homogeneous catalysts was established using the "open system" technique, *i.e.* with ideal intermixing reactors. When the reaction is conducted in an open system, the reagents are continuously introduced into the reactor and the partially reacted mixture is continuously withdrawn from it. The composition of the reacting mixture remains uniform all over the reactor due to intensive intermixing. Attainment of stationary concentrations of initial, intermediate, and end compounds is characteristic of such a system.

In a simple consecutive reaction

$$A \xrightarrow{k_1} B \xrightarrow{k_2} C$$

stationary concentrations of the initial $[\overline{A}]_i$ and intermediate compound $[\overline{B}]_i$ appear to be related by Eq. (27)

$$k_1 [\overline{A}]_i^n - k_2 [\overline{B}]_i^{n_1} - v_i [\overline{B}]_i / V = 0 \qquad (27)$$

where v_i is the volumetric velocity of the flow, V is the reactor volume. On conducting the reaction at different flows we obtain a set of equations of type (27) making possible the determination both of k_1 and k_2, and of n and n_1 [41]. For complex chain reactions involving free radicals, Eq. (27) can be written as

$$k_1 [R]_i [\overline{A}]_i - k_2 [R]_i [\overline{B}]_i - v_i [\overline{B}]_i / V = 0 \qquad (27')$$

Since a change in v_i results in a different concentration of R, determination of k_1 and k_2 using this technique appears to be impossible.

In order to measure the rates of formation and consumption of a compound in such systems it is necessary to maintain a constant radical concentration, *i.e.* a constant concentration of the initiating compound, while at the same time changing the steady-state concentration of the intermediate B [42]. This can be accomplished by feeding not only A but also B into the vessel. If v_i remains constant, the steady-state concentrations of A and R will also be constant, and the steady-state concentrations of B in experiments with and without admission of B follow Equations (28) and (29), respectively.

$$k_1 [R] [\overline{A}] - k_2 [R] [\overline{B}] - v [\overline{B}] / V = 0 \qquad (28)$$

$$k_1 [R] [\overline{A}] - k_2 [R] [\overline{B}]_1 - v [\overline{B}]_1 / V + v [B]_0 / V = 0 \qquad (29)$$

For k_2 these equations give

$$1 + V k_2 [R] / v = [B]_0 / ([\overline{B}]_1 - [\overline{B}]) \qquad (30)$$

Thus, for reactions of first order with respect to B, the k_2 [R] value and, consequently, the rate of intermediate consumption may be calculated from the slope of the curve of $([B]_1 - [B])$ *vs.* $[B]_0$. When B is consumed in a reaction of *n*-th order, Eq. (30) becomes:

$$k_2 [R] V / v = ([B]_0 + [\overline{B}]^n - [\overline{B}]_1^n) / ([\overline{B}]_1 - [\overline{B}]) \qquad (31)$$

When several isomers of B are formed, the technique permits separate determination of the rate of consumption of each isomer by analyzing only the sum of isomers formed [36].

The consumption of 2-decanol during oxidation of *n*-decane in the presence of cobalt stearate was determined by the technique described above [43]. The

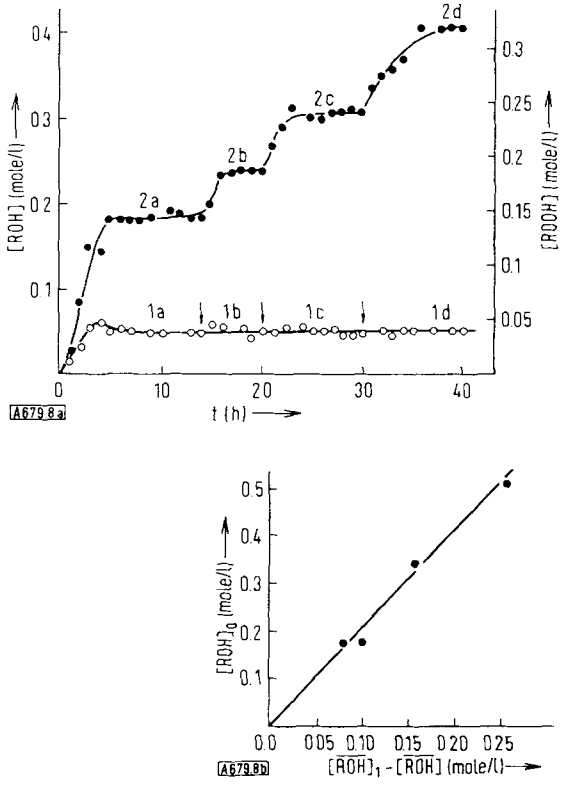


Fig. 8. a) Kinetic curves for accumulation of hydroperoxides (I) and alcohols (2) in the catalyzed oxidation of *n*-decane in an open system on successive admission of: (a) pure n-decane; (b) 0.17 mole/l of 2-decanol in *n*-decane: (c) 0.34 mole/l of 2-decanol in *n*-decane; (d) 0.51 mole/l of 2-decanol in *n*-decane.
b) $[ROH]_1 - [ROH]$ as a function of $[ROH]_0$.
$[CoSt_2]_0 = 6 \times 10^{-3}$ mole/l in the solution admitted into the reactor. $T = 130$ °C.

[41] *K. G. Denbigh* and *F. M. Page*, Discuss. Faraday Soc. Nr. 17, 145 (1954).

[42] *I. P. Skibida, Z. K. Maizus*, and *N. M. Emanuel*, Doklady Akad. Nauk SSSR *144*, 170 (1962).

[43] *I. P. Skibida, Z. K. Maizus, S. K. Ivanov*, and *N. M. Emanuel*, Doklady Akad. Nauk SSSR *167*, 1105 (1966).

steady-state concentration of the hydroperoxide, and thus of $RO_2^{\cdot}$ radicals, remained the same in all experiments (Fig. 8a). The rate and the effective rate constant for alcohol consumption were determined from the difference in steady-state concentrations of alcohol attained for different initial alcohol concentrations (Fig. 8b). The rate of alcohol formation was found from its rates of accumulation and consumption to be $W_f^{ROH} = 0.14$ mole l^{-1} h^{-1}.

In order to establish the routes of alcohol formation, the rate of alcohol formation was compared with that of hydroperoxide consumption. The latter was calculated by means of Equation (32) from the known values of k_4 and K.

$$W_d^{ROOH} = k_4 K \overline{[CoSt_2]}^2 \overline{[ROOH]}/(1 + K \overline{[ROOH]})^2 \qquad (32)$$

The rate of hydroperoxide decomposition was found to be $W_d^{ROOH} \leqslant 0.03$ mole l^{-1} h^{-1}, which is about 25 % of the rate of alcohol formation. This seemed to be evidence that the main part of the alcohol is formed directly from $RO_2^{\cdot}$. In order to obtain further confirmation the rate of hydrocarbon consumption W_c^{RH} was measured and compared with that of ROOH formation (W_f^{ROOH}):

$$W_f^{ROOH} = W_{accum.}^{ROOH} - W_d^{ROOH} \qquad (33)$$

It appeared that when $W_c^{RH} = 0.27$ mole l^{-1} h^{-1}, the value of W_f^{ROOH} is 0.044 mole l^{-1} h^{-1}, *i.e.* the rate of hydrocarbon consumption is much higher than that of hydroperoxide formation.

Moreover, $W_f^{ROOH} + W_f^{ROH} < W_c^{RH}$, thus showing that not only alcohol but also other products are formed directly from $RO_2^{\cdot}$.

The rates of formation of ketones and acids could be calculated from the steady-state concentrations of these products in experiments with and without addition of various amounts of 2-decanol (Fig. 9).

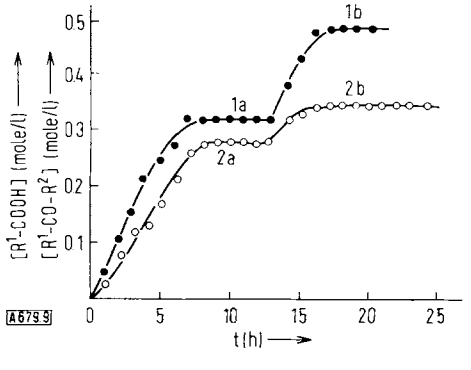


Fig. 9. Kinetic curves for accumulation of ketones (1) and acids (2) in the catalyzed oxidation of *n*-decane in an open system on successive admission of: (a) pure *n*-decane; (b) 0.51 mole/l of 2-decanol in *n*-decane. $[CoSt_2]_0 = 6 \times 10^{-3}$ mole/l in the solution admitted into the reactor. $T = 130$ °C.

Since in this case acids are the only end products of the reaction, the overall rate of their formation may be calculated from the steady-state concentration on admission of pure *n*-decane, and was found to be $W_f^{acid} = 0.095$ mole l^{-1} h^{-1}. The rate of acid formation from ketone may be established from the difference in the steady-state acid concentrations on admission of pure decane and of decane containing alcohol.

$$(W_f^{acid})_1 = K_{acid} [RO_2^{\cdot}] \overline{[B]} = \frac{(v/V)\,([\overline{A}]_1 - \overline{[A]})}{\overline{[B]}_1 - \overline{[B]}} = 0.026 \text{ mole } l^{-1} h^{-1}$$

Here $[\overline{A}]_1$ and $\overline{[B]}_1$ are steady-state concentrations of acids and ketones in experiments with admission of alcohol solutions and $[\overline{A}]$ and $\overline{[B]}$ are those for admission of pure *n*-decane. It is seen that $(W_f^{acid})_1 < W_f^{acid}$

The rates of formation of ketone from alcohol and from $RO_2^{\cdot}$ were calculated in a similar way, assuming that oxidation of ketone to acid is the only route for its consumption.

Table 2. Rates of formation and of consumption of products in the oxidation of *n*-decane catalyzed by cobalt stearate (all rates are given in mole l^{-1} h^{-1}; reaction conditions as given in Fig. 9).

	Acids	Ketones	Alcohols	Peroxides	Hydrocarbons
Overall rate of formation	0.095	0.12	0.12	0.044	—
Rate of formation from $RO_2^{\cdot}$	0.07	0.03	0.10	0.044	—
Rate of consumption	—	0.026	0.07	0.03	0.27

As shown in Table 2, the acids, alcohols, and peroxides are formed mostly from $RO_2^{\cdot}$. Formation of the main part of alcohols, ketones, and other oxidation products directly from $RO_2^{\cdot}$ in the presence of transition metal salts had previously been postulated [44–46].

Heterogeneous catalysts also contribute to chain propagation in liquid-phase oxidation [47]. Isomerization with subsequent decomposition of $RO_2^{\cdot}$, involving cleavage of the C–C or C–H bond, may occur on a solid surface, as was found earlier for gas-phase oxidation [1, 48].

Decomposition of peroxy radicals in liquid-phase oxidation was observed for *n*-butane oxidation in a metal reactor at a pressure of 50 atm over a temperature range of 100 to 200 °C; low-molecular compounds containing less than four carbon atoms were found in the oxidation products. Since 2-butyl hydroperoxide does not decompose to products containing less than four carbon atoms, it was concluded that low-molecular oxidation products, such as methanol, ethanol, formaldehyde, acetone, and CO_2, are formed directly from the 2-butyl hydroperoxy radical *(2)*, the radical

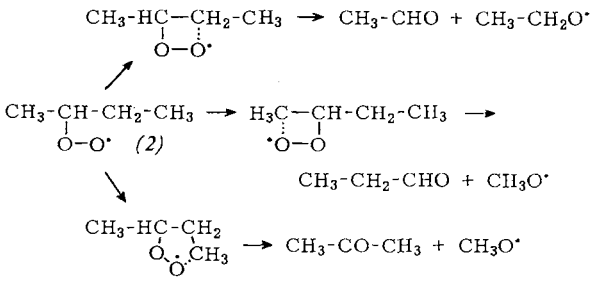
[44] *E. T. Denisov*, Ž. fiz. Chim. *32*, 1269 (1958).

[45] *P. A. S. Ravens*, Trans. Faraday Soc. *55*, 1768 (1959).

[46] *I. V. Berezin, E. T. Denisov*, and *N. M. Emanuel*: Oxidation of Cyclohexane (English translation). Pergamon Press, London 1966.

[47] *E. A. Blümberg, Yu. D. Norikov*, and *N. M. Emanuel*, Doklady Akad. Nauk SSSR *151*, 1117 (1963).

[48] *Yu. D. Norikov* and *E. A. Blümberg*, Izvest. Nauk SSSR, *1962*, 1357; *E. A. Blümberg, A. V. Bobolev*, and *Yu. D. Norikov*, *ibid.*, Ser. chim. *1964*, 826.



undergoing isomerization prior to decomposing. The $CH_3O^{\bullet}$ and $C_2H_5O^{\bullet}$ radicals carry on the chain by reacting with the initial butane to form alcohols and $\dot{C}_4H_9$ radicals. Under these conditions decomposition of $RO_2^{\bullet}$ occurs only by action of the metal surface (in this case stainless steel).

Concentrations of 2-butyl hydroperoxide 10 to 15 times higher than those obtained in metallic reactors accumulate when the reaction is conducted in a glass reactor. Methyl ethyl ketone and *sec*-butanol are formed along with the peroxide.

In glass vessels, the decomposition products of the butyl peroxy radical are formed in yields no higher than 1 % (with respect to the reacted butane). Increased yields are obtained in steel reactors. An increase in the surface of the metal reactor by packing it with stainless steel also results in a higher yield of decomposition products.

Homogeneous and heterogeneous catalysts also seem to play an important part in olefin epoxidation [49]. For instance, faster formation of propene oxide in the presence of cobalt stearate was observed for conjugated oxidation of propene and acetaldehyde. Great attention has recently been paid to a promising process for production of propene oxide, which is based on the reaction between ethylphenyl hydroperoxide and propene [50]. Addition of salts of molybdenum and other metals increases the yields considerably.

4. Chain Termination

Chain termination in liquid-phase autoxidation occurs by recombination of free radicals:

$$RO_2^{\bullet} + RO_2^{\bullet} \rightarrow \text{products}$$

This reaction may yield either a peroxide (ROOR) and oxygen, or three species: alcohol, ketone, and O_2. Similar mechanisms have also been proposed for catalyzed oxidation. However, when transition metal salts are present in the system, stable products could also be formed by interaction between free radicals and metals in a low oxidation state; this would seem to account for the inhibiting effect of transition metal salts. Thus a transition metal salt may both initiate chains by reaction with hydroperoxides and terminate them by reaction with peroxy radicals.

The inhibiting effect of cobalt, copper, and manganese salts, has been observed in some cases [2, 51–54]. The dual catalytic and inhibiting function of transition metal salts can lead to a very peculiar effect, that of abrupt transition from autoacceleration to a stationary regime on a very small change in the metal ion concentration. For instance, when *n*-decane is oxidized in the presence of increasing amount of copper stearate, the induction period first decreases and then gradually increases with the $CuSt_2$ concentration up to $[CuSt_2] = 0.06$ mole-%. When the concentration attains 0.065 mole-% the induction period abruptly increases from 30–40 min to 15 h [55]. Similar critical phenomena are observed for oxidation of *n*-decane in the presence of manganese stearate [56].

The phenomena observed were ascribed to participation of metal salts both in initiation and in termination of chains. The inhibiting effect of transition metal compounds seems to depend not only on the nature of the metal as such, but also on the structures and properties of the anion or the ligand bonded to the metal ion. Contribution by the anion to the effect of copper in the oxidation of *n*-decane was established for several copper compounds, such as copper stearate, copper acetylacetonate, and bis(trioctylamine)copper(II) at 140 °C in the presence of 20 % of chlorobenzene (used to increase the solubility of the metal compounds). It may be seen from Fig. 10 that in the case of acetylacetonate the critical transition is not so abrupt and the critical copper concentration is somewhat lower than with copper stearate.

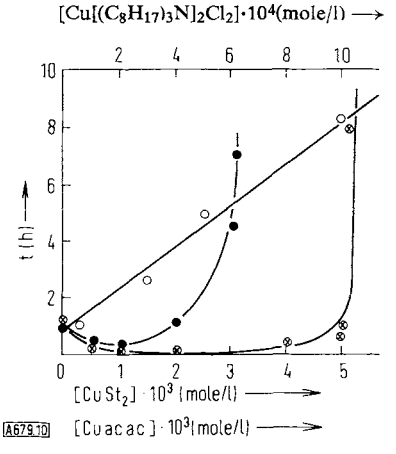


Fig. 10. The induction period for oxidation of *n*-decane/chlorobenzene (4:1) as a function of catalyst concentration. Catalysts: (⊗) copper stearate; (●) copper acetylacetonate; (○) bis(trioctylamine)copper(II)chloride. $T = 140$ °C.

[49] *E. A. Blümberg* and *T. V. Filippova*, Neftechimija *6*, 863 (1966).

[50] *R. Landau, D. Brown, J. L. Russell*, and *J. Kollar*, 7th int. Petroleum Congress, Mexico, preprints P.D. 18, p. 141.

[51] *E. T. Denisov* and *N. M. Emanuel*, Usp. Chim. *27*, 365 (1958).

[52] *K. Ingold*, Usp. Chim. *33*, 1107 (1964).

[53] *A. S. Kuz'minskii*, Vysokomolekuljarnye Soedinenija *4*, 1682 (1962).

[54] *A. T. Betts* and *N. Uri*, Makromolekulare Chem. *95*, 22 (1966).

[55] *L. G. Chuchukina, D. G. Knorre*, and *N. M. Emanuel*, Ž. fiz. Chim. *33*, 877 (1959).

[56] *V. M. Goldberg, L. K. Obukhova*, and *N. M. Emanuel*, Doklady Akad. Nauk SSSR *136*, 1130 (1962); Neftechimija *2*, 229 (1962).

The complex compound $Cu[(C_8H_{17})_3N]_2Cl_2$ showed no catalytic activity under the experimental conditions: the induction period increases linearly with the complex concentration, *i.e.* this compound inhibits oxidation.

The rate constant k in the reaction

$$RO_2^{\cdot} + Mn^{2+} \xrightarrow{k} Mn^{3+}(OH) + \text{ketone } (R = (CH_3)_2C(CN))$$

was determined by the chemiluminescence technique [57, 58]. Azodiisobutyronitrile in an inert solvent (chlorobenzene) between 60 and 80 °C was permitted to react with a stream of O_2. After attainment of a stationary radical concentration recorded by the chemiluminescence intensity, a manganese stearate solution of fixed concentration was introduced into the reactor. The luminescence intensity first dropped abruptly, and then increased again with consumption of manganese. The ratio of constants $k/\sqrt{k_7}$ was estimated from the increase in luminescence intensity, and k was determined from the known value of k_7. For manganese stearate this value appeared to be

$$k = 2.8 \times 10^8 \exp [-(4800 \pm 600)/RT] \text{ l mole}^{-1} \text{ sec}^{-1}.$$

This value is close to those for peroxy radical recombination. The reaction seems to occur *via* intermediate formation of a $St_2MnOOCHR^1R^2$ species, which subsequently decomposes to $St_2Mn(OH)$ and R_1-CO-R_2. The tervalent manganese actually appears in the reaction products as a basic salt, ketones and Mn^{3+} accumulating in equimolecular amounts.

[57] *V. M. Goldberg* and *L. K. Obukhova*, Doklady Akad. Nauk SSSR *165*, 860 (1965).

[58] *K. C. Kooyman*, J. Catalysis *4*, 626 (1965).

The corresponding rate constant for cobalt acetylacetonate was determined from the rate of Co^{2+} consumption and appeared to be 2.0×10^4 l mole^{-1} sec^{-1} [59]. The rate constant for reaction of acetylacetonate with a styrene peroxy radical, as measured in styrene, was found to be

$$k = 2.9 \times 10^9 \exp [(-7800 \pm 1500)/RT] \text{ l mole}^{-1} \text{ sec}^{-1}.$$

Ferrocene in concentrations of less than 6.7×10^{-6} mole/l was found to be an efficient inhibitor of oxidation [60]. Copper complexes containing amines also show a strong inhibiting effect on oxidation. When *n*-decane was oxidized in the presence of a mixture of copper stearate with *N*-phenyl-β-naphthylamine, it was found that after complete disappearance of the inhibitor the reaction does not go beyond the induction period for a very long time [61]. At initial concentrations $[CuSt_2]_0 = 7 \times 10^{-4}$ mole/l and $[C_{10}H_7NHC_6H_5]_0 = 0.95 \times 10^{-3}$ mole/l the inhibitor is completely consumed within two hours, whereas the induction period of oxidation lasts for ~16 hours. A similar effect is observed for mixtures of copper acetylacetonate and bis(trioctylamine)copper(II) chloride with *N*-phenyl-β-naphthylamine.

It appears from the findings described in this paper that the salts and complex compounds of transition metals play a role in all steps of oxidation.

Received: April 1, 1968 [A 679 IE]
German version: Angew. Chem. *81*, 91 (1969)

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[60] *L. M. Postnikov*, *E. M. Totschina*, and *V. Ya. Shlyapintokh*, Doklady Akad. Nauk SSSR *172*, 651 (1967).

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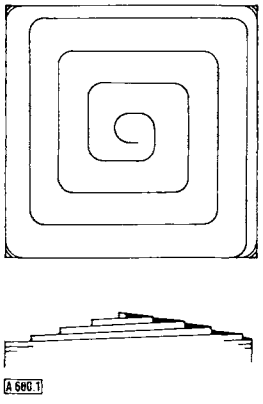
Electrocrystallization of Metals under Ideal and Real Conditions

By Hellmuth Fischer[*]

Ideal conditions during electrocrystallization, which are only approximately attainable, would lead to a perfect single crystal, whereas real conditions yield a monocrystalline or polycrystalline product containing many structural defects. The electrolytic production of quasi-ideal single crystals requires an overpotential that supplies at least the activation energy necessary for the formation of two-dimensional nuclei, since growth otherwise proceeds via screw dislocations with formation of a "real" crystal. The potential deviation in electrocrystallization under real conditions is due to electrochemical and/or crystallization overpotential, which can be determined separately. The investigation of electrocrystallization also offers possibilities for a systematic study of the formation of imperfections in real crystals.

1. Real and Ideal Crystals

The formation of solid crystalline matter is a very old and fundamental problem. In the early 1920's it was still thought (cf. [1–3]) that crystals grew only by continuously repeated formation of two-dimensional nuclei. The formation of two-dimensional nuclei, however, requires a relatively high activation energy. If this energy is not supplied, crystal growth should stop after the growth of the first lattice plane is complete. On the other hand, crystals frequently manage to grow in nature without the need for this work of nucleation. It was only in 1949 that a plausible explanation was provided in the form of the dislocation theory proposed by *Burton, Frank*, and *Cabrera* [4]. The basis of this theory is the presence of screw dislocations, which allow continuous growth of the crystal at extremely low degrees of supersaturation.



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Fig. 1. Diagram of a screw dislocation (after *Frank et al.* [4]).

This growth principle is illustrated in Figure 1.

With progressive deposition of lattice particles, the dislocation spirals out of the lattice plane with a pitch equal to the interatomic distance. This can lead to the formation *e.g.* of pyramids. The growth of such a screw dislocation proceeds as follows [5]. Starting at the emergent site D of the dislocation (Fig. 2a), the

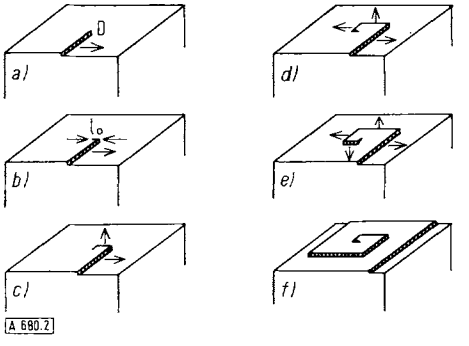


Fig. 2. Growth of a screw dislocation (after *Kaischew et al.* [5]).

edge of part of the dislocated lattice plane projects from the surface. Metal atoms are deposited on this edge in a row running parallel to it. The lattice plane step is consequently displaced perpendicular to the edge. When the side edge of the step, which simultaneously becomes longer, reaches a critical length l_0, *i.e.* the "edge length" of the two-dimensional nucleus (Fig. 2b), atoms begin to be deposited on this edge and parallel to it. This lateral step thus also moves outward perpendicular to the edge at an angle of 90° to the first step (Fig. 2c). Two further repetitions of this process complete the first turn of the screw. While all these steps continue to grow in their four directions, the second, third, fourth, *etc.* turns of the screw are formed. This leads to a very flat pyramid, the edges of which may be rounded to varying extents to reduce the edge energy.

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Screw dislocations cannot be clearly recognized even under the electron microscope. They can, however, be made visible in electro-crystallization by conversion into "growth spirals". The only difference between these and the screw dislocations is the pitch, which is no longer one interatomic distance, but several hundred to one thousand interatomic distances. Spirals, of macro-steps, which are recognizable under the optical microscope, and which were obtained *e.g.* on cathodic deposition of copper with a pulsing direct current, are shown in Figure 3 [6]. The pulses lead to the continuous formation of new dislocations at the position of the screw dislocation, which build up to form the growth spiral. The formation of growth spirals has not yet been fully explained, but appears to resemble the formation of "growth layers", which also consist of macro-steps of comparable height (see Section 4.4).

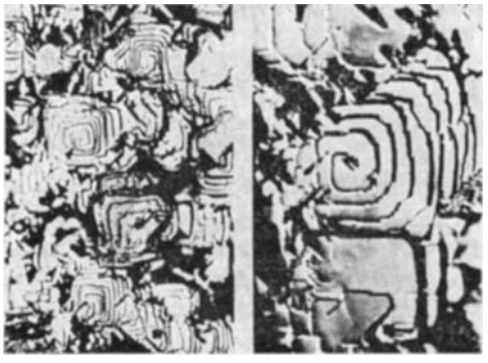


Fig. 3. Spiral growth during the electrocrystallization of copper (after *Seiter* and *Fischer* [6]).

The dislocation theory has proved extremely valuable. The more or less imperfect real crystal will therefore be compared here with the completely defect-free ideal crystal. The imperfections in a real crystal influence not only the nature of its further growth or its breakdown but also many of its physical and chemical properties. Other types of imperfections besides screw dislocations can also occur in the crystal lattice. Dimensionless imperfections, *i.e.* point defects, are where single particles have been removed from the positions that they would occupy in the ideal crystal. These defects occur either on the surface or in interstitial positions, and leave behind corresponding vacancies. Point defects, either alone or lined up to form steps, are involved in "thermal roughening" [7].

Multidimensional disorder includes edge dislocations and screw dislocations. Figure 4 shows a model of a real crystal [8] containing several types of imperfections. The point defects also include adsorbed or incorporated foreign atoms, ions, or molecules. An edge dislocation consists of a lattice plane that has been inserted between two other lattice planes, deviating from the building program of the ideal crystal. It appears on the surface of the crystal as a dislocation line. The initial stage of a screw dislocation is also shown (emergent site in the center of the left-hand side face). The atomic step of an incomplete lattice plane on the top occurs both in real and in ideal crystals.

[6] *H. Seiter* and *H. Fischer*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *63*, 249 (1959); *H. Seiter*, *H. Fischer*, and *L. Albert*, Electrochim. Acta (London) *2*, 97 (1966).

[7] *J. Frenkel*, Ž. fiz. Chim. *9*, 392 (1945).

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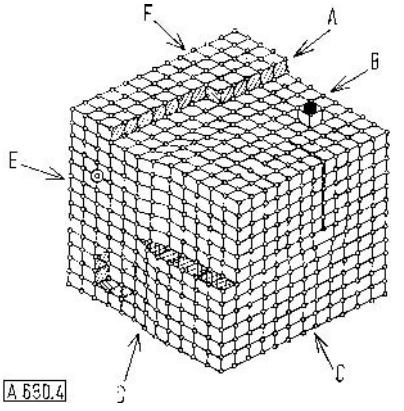


Fig. 4. Diagram of the surface of a real crystal.
A: Step; B: adsorbed ion; C: edge dislocation; D: screw dislocation; E: impurity in surface; F: kinked step (after *Gilman* in [8]).

Here we also find the kink position as "half-crystal-position". The deposition of a lattice particle here releases a particularly high deposition energy. If the row of atoms in the step is not yet complete, the incorporation of the atom leads immediately to a new kink ("repeatable step" [9]).

"Ideal" crystal growth conditions lead to a perfect structure formed in accordance with the theoretical structural plan, whereas real conditions give a structure containing many imperfections. On the basis of the habit of crystals, it is also possible to distinguish between conditions that lead to the equilibrium form of the crystal extending to infinity or to boundaries of any size even in polycrystalline aggregates that differ in their habit from the equilibrium form. Ideal conditions mean monocrystalline growth close to thermodynamic equilibrium, while real conditions lead to monocrystalline or polycrystalline growth remote from equilibrium.

It is well known that under conditions of condensation from the gas phase, the equilibrium form *e.g.* of metals having a face-centered cubic lattice, such as silver, copper, and lead, is a cube whose corners are replaced by octahedral faces and its edges by rhombododecahedral faces.

2. Electrocrystallization Compared with Condensation from the Vapor Phase

Everything that has been said so far refers to any kind of crystallization. If we now turn to the special case of the electrocrystallization of metals, phenomenological differences are clearly recognizable on comparison of its ideal course with that of a non-electric type of crystallization, *e.g.* from the vapor phase.

Figure 5 illustrates in simplified form the crystallization of a metal vapor on a solid surface of the same metal. Suppose that the surface of the substrate crystal is an equilibrium face (*e.g.* {100}) on which there is an atomic step, such as may often occur as a result of thermal roughening. A new, as yet incomplete row of atoms has been deposited on this step, with a kink

[9] See ref. [3a].

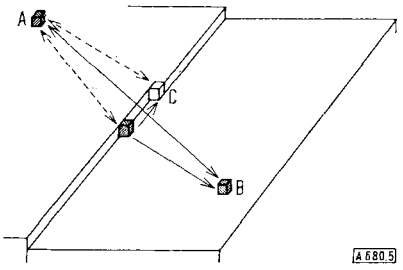


Fig. 5. Diagram of crystallization from the gas phase.
A: Metal atom in the vapor; B: adatom; C: lattice atom in the kink position.

at its end. The metal atom being transferred from the vapor phase to the solid substrate has three possibilities of reaching the energetically favorable kink position in near-equilibrium conditions: (i) it may be deposited directly in this position, (ii) it may be deposited on the step and diffuse along the edge of the step to the kink, or (iii) it may meet the surface at any point and diffuse from this point to the step and thence again to the kink.

If the position on the surface is favorable, the atom can reach the kink without first migrating to the step. In all three positions shown, the metal atom is bound less firmly to the substrate than a metal atom in the interior of the lattice. The atom situated on the surface is termed an adatom, *i.e.* it is regarded as an adsorbed metal atom. The adatom in the kink position has three nearest neighbors, and is most strongly bound in this position. The adatom on the step has two nearest neighbors, while that on the surface has only one [*].

The same simple scheme is often also used for the electrocrystallization of metals. Though the paths by which the adatom can reach the kink may be fundamentally the same [10], such a simplification can mislead one into ignoring certain differences between the two types of crystallization that are really very important.

The principal difference is undoubtedly the fact that whereas neutral metal atoms cross the metal/vapor interface in both directions during crystallization from the vapor phase, solvated or complexed metal ions (or even electrons in the other direction if *e.g.* complex anions or neutral molecules having a metal as the central atom reach the phase boundary) cross the metal/electrolyte interface in electrocrystallization. In any case the particles required for crystallization are formed at the kink or on steps or faces only after electrochemical neutralization by charge transfer.

Another important difference is that the metal surface is generally electrically charged at the metal/electrolyte interface. A condenser-like electric double layer consisting of a rigid component and a diffuse component (as in an ion cloud) is formed at this interface [11].

Thus the electrically charged metal/electrolyte interface, unlike the solid metal/metal vapor interface, is covered with oppositely charged foreign particles. Furthermore, surface-active components of the electrolyte are chemisorbed on it [12]. These foreign substances belong to the electric double layer.

Let us now follow the path taken by an initially dissolved, *e.g.* hydrated, metal ion in the greatly simplified Figure 6. The substrate is again a section of the surface

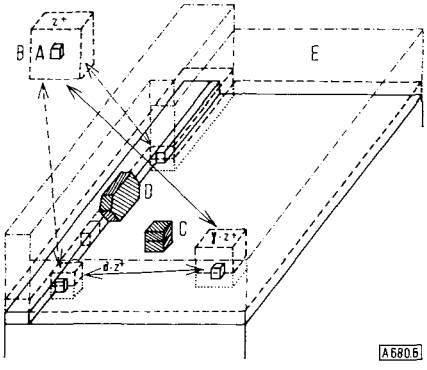


Fig. 6. Diagram of electrocrystallization.
A: Metal, B: water; C: anion; D: adsorbed organic material; E: boundary of the compact double layer.

of the crystal (same metal), *e.g.* a {100} face, with an atomic step (incomplete row of atoms) and a kink.

The hydrated metal ion follows the attraction of a strong electric field due to an externally applied DC voltage between the metal/electrolyte interface and a counter-electrode. The metal ion therefore migrates out of the electrolyte phase onto the metal phase. To reach the surface of the substrate crystal, the metal ion must pass through the electric double layer. The compact double layer (Helmholtz layer) also includes the adsorption film on the metal surface. The adsorption film will be assumed to consist mainly of water molecules, which form a largely continuous coating (only partly shown) on the metal surface. In contrast to the unhindered deposition of the metal atom from the gas phase, therefore, the metal atom must now displace one or more adsorbed water molecules from the metal surface [*] before it can enter into direct interaction with surface atoms of the metal phase.

The water film can also be partly or wholly displaced by more surface-active electrolyte components. If *e.g.* a more strongly bound organic molecule or an organic cation is adsorbed instead of a water molecule, the activation barrier for the transfer of the metal

[*] Thus we already have three energetically different states of adatoms. Their number can be greatly increased, even for the ideal crystal, if we consider the difference in their interactions with differently indexed faces, steps, and kinks. Finally the number of types of adatoms is further increased in real crystals (*e.g.* adatoms in deformed lattice regions).

[10] *W. Lorenz*, Z. physik. Chem. *202*, 275 (1953); Z. Elektrochem., Ber. Bunsenges. physik. Chem. *57*, 382 (1953).

[11] Cf. *K. J. Vetter*: Elektrochemische Kinetik. Springer, Berlin 1961, p. 68ff.

[12] *H. Fischer*: Elektrolytische Abscheidung und Elektrokristallisation von Metallen. Springer, Berlin 1954, p. 210ff.

[*] *Bockris* and *Conway* estimate that the average work required for the displacement of adsorbed water molecules is 15 to 20 kcal/mole, depending on the nature of the metal [13].

[13] *J. O'M. Bockris* and *B. E. Conway*: Modern Aspects of Electrochemistry. No. 3. Butterworth, London 1964, p. 228.

ion may be too high, so that the metal ion must go around this obstacle.

If the metal ion comes into contact with the metal phase on displacement of the solvation film, charge transfer occurs, and the hydration sheath of the ion is simultaneously split. As in crystallization from the vapor phase, the positions at which these processes can take place are fundamentally the adatom position on the crystal surface, the step position, or the kink position. In all three positions the metal ion should be more or less neutralized and dehydrated on transfer.

However, the resulting adatoms, step atoms, and kink atoms are very different from the corresponding species formed by condensation from the vapor phase. An adatom in electrocrystallization is neither completely desolvated nor completely discharged. Despite the neutralization, part of the solvation or ligand sheath remains bound to the metal atom on the electrolyte side [14, 15]. Since the remaining ligand residue of charge carriers or dipoles favors polar bonding on the (charged) metal surface, the adatoms remain partly charged. As a result of ligand coupling they are naturally more bulky than the "bare" adatoms deposited from the vapor phase, and project into the double layer. To distinguish them from the neutral adatoms formed by condensation, these partly charged types formed in electrocrystallization will be called adions.

Thus in changing into adions, the metal ions do not pass through the full possible potential difference at the interface. The adion behaves on the metal side as a metal atom and can share the electron gas of the metal substrate, while on the electrolyte side it still behaves as a solvated or complexed ion.

The step atom also possesses the characteristics of the adion, but since it is more stably bound to the substrate metal, it is probably less hydrated and carries less charge than the adion. The bonding to the substrate, the hydration, and the partial charge will vary in both cases according to the crystallographic orientation of the substrate and its surface charge. The number of types of adions and step ions will thus be significantly greater than the number of types of adatoms and step atoms in condensation.

The kink atom is the closest to the firmly incorporated lattice atom of the metal surface. It is probably almost completely neutralized and less hydrated than adions or step atoms. According to calculations by *Bockris* and *Conway* [16], the activation energy for the transfer of a completely hydrated silver ion from the electrolyte to the kink position (35 kcal) is practically the same as that for a corresponding transfer into a vacancy in the surface. The activation energy for the direct transfer of a silver ion to a step is thus about 14 kcal less, while the activation energy decreases by about 25 kcal for the transfer to the adion position.

The differences in the activation energies should be very much greater for the transfer of metal ions having significantly stronger solvation bonds, *e.g.* nickel or copper ions, to the various positions on the surface. In this case there should even be an appreciable difference between the values for transfers to kink positions and to vacancies.

The target of the metal ion in its transfer to the substrate metal is, with one exception, always the kink position. It is only by incorporation in the kink position that the growth of a screw dislocation or of a step is maintained. The exception is the filling of a vacancy in the surface, which is not associated with a "repeatable step".

Incorporation into the lattice takes longer in electrocrystallization than in crystallization from the vapor phase. Even when it is deposited directly in the kink position, the metal ion, which is losing its solvation sheath, must first displace an adsorbed water molecule or other adsorbed species. In the case of more strongly surface active adsorbed species, this is often impossible, and the kink position is then blocked.

An adion diffusing on the surface or a step atom diffusing along a step has to push the adsorbed film aside. This is not possible in the case of much more strongly surface active adsorbed species, and the path to the kink position is again blocked.

The question of whether the metal ion is incorporated directly into the kink position or has to reach this position indirectly *via* the adion position and the step position has been the subject of many discussions [17, 19]. According to recent rough calculations by *Gerischer* [18] for two models (an isolated kink position in the form of a point and a line step with kink positions lined up close together), deposition of the metal ion from sufficiently concentrated solutions close to equilibrium occurs preferentially in the kink position (*e.g.* deposition of silver from $AgNO_3$ solution).

Conversely, on deposition from very dilute solution and/or farther from equilibrium, surface diffusion from the adion or step position to the kink position seems more probable (*e.g.* deposition of nickel from $NiSO_4$ solution, deposition of metal in the presence of strongly surface active inhibiting adsorbed species).

This picture is in agreement with the views of other authors [19].

3. Electrocrystallization under Ideal and Quasi-Ideal Conditions

How can we provide ideal electrocrystallization conditions for the deposition of a perfect single crystal in the equilibrium form:

In general, an ideal metal crystal will be in equilibrium with its electrolyte if the chemical potential of the metal phase over its entire surface is equal to the chemical potential of the electrolyte. We also stipulate that the ideal crystal be in its equilibrium form and extend to infinity. Furthermore, all the steps in the conversion of the metal ion into the adion, step atom, or kink atom and all the steps in the crystallization should proceed without any hindrance.

[14] *H. Gerischer* and *R. P. Tischer*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *58*, 819 (1954); *H. Gerischer*, *ibid. 62*, 256 (1958); Analyt. Chem. *31*, 33 (1959).

[15] *B. E. Conway* and *J. O'M. Bockris*, Proc. Roy. Soc. (London) *248*, 394 (1958); Electrochim. Acta (London) *3*, 340 (1961).

[16] See ref. [13], p. 232.

[17] See ref. [12], p. 118ff., 127, 156; ref. [13], p. 224ff.

[18] *H. Gerischer*: Proc. int. Conf. Protection against Corrosion by Metal Finishing, Basel 1966. Forster-Verlag, Zürich 1967, pp. 11, 15ff.

[19] *M. Fleischmann* and *J. A. Harrison*, Electrochim. Acta (London) *11*, 749 (1966).

All these conditions should be satisfied if the equilibrium Galvani potential ε_0 prevails on all the boundary faces of the crystal. *Vetter* and *Bachmann*[20] describe this by the simple Nernst equation in the form:

$$\varepsilon_0 = E_0 + \frac{RT}{zF} \cdot \ln \frac{{}_0a_{M^{z+}}}{a_0^*} \tag{1}$$

In this equation E_0 is the standard Galvani potential, R is the gas constant, T is the absolute temperature, and z is the valency of the metal ions, ${}_0a_{M^{z+}}$ is the activity of the metal ions in the electrolyte, and a_0^* is the "surface activity" of the metal phase. a_0^*, which is the most important quantity for our purposes, has a value of 1 in the equilibrium state. In general:

$$a^* = \sum_{j=1}^{j=n} K_{j+} \cdot n_{j+} \Big/ \sum_{j=1}^{j=n} K_{j-} \cdot n_{j-} \tag{2}$$

The numerator and the denominator are summed over all the energetically distinguishable surface positions of the crystal $j = 1$ to $j = n$) for the number n_{j+} of surface states of the adions, step atoms, kink atoms, and lattice atoms and the number n_{j-} of unoccupied atomic positions (*e.g.* unoccupied kink positions, surface vacancies, *etc.*) and for the rate constants $K_{j+} > K_{j-}$ of each type of position. The positive sign denotes anodic quantities and the negative sign cathodic quantities. At equilibrium the numerator and the denominator are equal, and a^* is equal to a_0^*.

The occurrence of the predicted equilibrium form has been confirmed experimentally for crystallization from the vapor phase; however, it has not yet been possible to check whether the equilibrium form corresponding to the experimental conditions, and particularly to the electrolyte concentration, has been established in the solid metal/electrolyte system, since the theoretically possible equilibrium forms in these cases are not yet known.

In any case, the habit of these forms probably differs appreciably from that of the equilibrium form (produced from the vapor phase), since the surface states occurring at the metal/electrolyte interface are different from and much more highly differentiated than those at the metal/vapor interface.

Like any crystallization, the electrocrystallization of a metal will proceed only as long as a more or less large degree of supersaturation, *i.e.* deviation from the equilibrium state, exists. A single crystal deposited electrolytically should therefore initially differ to a greater or lesser extent in its form from the equilibrium form. The (still empirical) equilibrium form should be approximately reached only when this single crystal has been left in contact with the electrolyte for a sufficiently long time with no current passing, probably by separation and rearrangement of the external boundaries with the aid of local currents[20]. The electrode potential ε prevailing at several surfaces of the single crystal that differ in their habit or relative size from the equilibrium form will deviate from the equilibrium potential ε_0. breakdown and rearrangement proceed, ε approximates more and more closely to ε_0.

Results *e.g.* of measurements on *hkl* surfaces of copper single crystals are interesting in this connection. In a hydrogen atmosphere with complete freedom from oxygen, *Jenkins* and *Bertocci*[21] initially found potential differences not exceeding about 1.5 mV between the (110) and (100) and between the (100) and (111) faces; the value decreased within 1 hour to about 0.2 mV. The habit of the faces does not undergo any visible change. It appears that only the submicroscopic defects are in fact changed.

The difference between the Galvani potential and the equilibrium Galvani potential is known in electrochemistry as overpotential $\eta = \varepsilon - \varepsilon_0$. In electrocrystallization this overpotential can arise from two principal causes: (i) hindrance during the preceding electrochemical process of conversion of a metal ion from the electrolyte into a kink atom, a step atom, or an adion on the metal surface; the hindrance may give rise to an "electrochemical" overpotential η_e[*]; (ii) hindrance during crystallization, which leads to a crystallization overpotential η_k. This latter overpotential may be due to hindrance of incorporation in the lattice (*e.g.* as a result of surface diffusion and/or displacement of adsorbed species), formation of two-dimensional lattice-plane nuclei, or formation of three-dimensional nuclei. Direct transfer into the kink position requires practically no crystallization overpotential if only a weakly bound water molecule has to be displaced. It may, however, be hindered electrochemically.

The total overpotential of electrocrystallization can thus be written

$$\eta = \eta_e + \eta_k \tag{3}$$

In the equilibrium state there should be no inhibition of any kind, and both overpotentials should therefore be equal to zero.

As was mentioned earlier, however, the electrolytic preparation of single crystals requires a certain supersaturation, which may have a corresponding overpotential $\eta = \varepsilon - \varepsilon_0$. If the crystal is not to grow *via* screw dislocations, *i.e.* is not to become a real crystal from the outset, the overpotential must supply at least the activation energy for the formation of two-dimensional nuclei.

The electrolytic growth of a substantially perfect single crystal cannot therefore occur under strictly ideal conditions. The experiment must be carried out under electrochemical conditions which, though the system may be regarded as being close to equilibrium, are really only "quasi-ideal". Thus whereas we can still take $\eta_e = 0$, an appreciable crystallization overpotential η_k must be accepted. *Vetter* and *Bachmann*[20] define this crystallization overpotential under quasi-ideal conditions as follows:

$$\eta_k = \varepsilon - \varepsilon_0 = -(RT/zF) \ln (a^*/a_0^*) \tag{4}$$

where a^* is the surface activity, *e.g.* in the electrolytic preparation of the single crystal and a_0^* is the surface activity in the equilibrium state. This equation enables us to formulate the crystallization overpotential for all cases that can arise under quasi-ideal conditions, *e.g.* the development of non-equilibrium surfaces, the formation of a small crystal instead of one of infinite size, macroscopically rough surfaces, lattice imperfections, and two-dimensional nuclei.

[20] *K. J. Vetter* and *J. Bachmann*, Z. physik. Chem. N.F. *53*, 9 (1967).

[21] *L. H. Jenkins* and *N. Bertocci*, J. electrochem. Soc. *112*, 517 (1965).

[*] This can be further subdivided into other overpotentials (charge transfer, diffusion, and reaction overpotentials).

$\varepsilon - \varepsilon_0$ is measured in the rest state, *i.e.* with no external current flowing, so that ε should slowly change into ε_0. The η_k values that occur under these quasi-ideal conditions should be of the order of 10^{-3} to 10^{-4} V.

Over the past four decades there has been no lack of successful attempts to prepare single crystals electrolytically, though these crystals were always obtained by further electrolytic growth of a "seed crystal" that had not been prepared electrochemically.

However, the experimental conditions rarely correspond to our quasi-ideal conditions. Perhaps a known case is the deposition of silver crystals from concentrated solutions of silver salts with an anion having a relatively low surface activity, such as the nitrate ion. The electrochemical processes that precede crystallization suffer practically no inhibition in this case, and η_e is consequently negligible. Since the equilibrium current density, *i.e.* the "exchange current density" i_0 for the cathodic deposition of silver, is relatively high [*] the deviation from equilibrium is not too great if the crystal is allowed to grow at current densities $> 10^{-1}$ A/cm^2. Two-dimensional nuclei can form readily under these conditions. Finally, the silver ion is only weakly hydrated. The adion of the electrolytically deposited silver should therefore be fairly similar to the adatom of silver deposited from the vapor phase.

These quasi-ideal preparation conditions approximately prevailed in an investigation by *Kaischew, Budewski,* and *Malinowski* [22], who deposited silver from solutions of silver nitrate (3–6 N) in nitric acid at 30 °C on cathodes consisting of spherical single crystals of silver (diameter 5 to 6 mm) at current densities between 5×10^{-3} and 7.5×10^{-1} A/cm^2.

The "near-equilibrium" form deposited under these conditions does not differ much in its habit from the theoretical equilibrium form of silver deposited from the vapor phase. As in the latter case, the product is a cube whose corners have been replaced by octahedral faces, but the edges are not replaced in this case by rhombododecahedral faces. The cubic and octahedral faces are known to develop under the influence of the particularly strong interaction of nearest neighbors. The rhombododecahedral faces, on the other hand, depend on the much weaker effect of next-nearest neighbors. With decreasing supersaturation, *i.e.* with increasing proximity to equilibrium, faces that are not present in the equilibrium form appear to a small extent. These deviations could be due to the differences in the surface state of the single crystal faces prepared by the two crystallization processes. Adsorption of nitrate ions may also be important in the case of electrolytically deposited silver.

However, the crystals prepared by the above authors were undoubtedly not free from dislocations. Moreover, electrolytic deposition on spherical single crystals is open to the objection that the habit found could be influenced by a non-uniform current distribution.

This problem has very recently led to work in which the entire single crystal was no longer allowed to grow electrolytically, a special apparatus being used instead to allow the growth of only one face. It is then possible to obtain a uniform current distribution. Thus the substrate used by *Budewski, Kaischew, et al.* [23] was electrolytically deposited cubic faces of single-crystal silver that filled the cross section of a glass tube.

Initially, this single crystal face also has a relatively high dislocation density; however, the screw dislocations are eliminated in this case by pre-electrolysis with deposition of silver from an $AgNO_3$ solution. The pre-electrolysis is carried out at a voltage below the crystallization overpotential η_{k_2} (about 10 mV) required for the formation of two-dimensional nuclei. In the course of this pre-electrolysis, in which the dislocations migrate out of the surface, the current density falls to zero. The surface is then practically free from dislocations.

No current flows through a perfect single-crystal face until the nucleation overpotential (about 10 mV) is reached. Beyond this overpotential, *e.g.* with a constant direct current (galvanostatic conditions), the overpotential begins to fluctuate periodically (see Fig. 7). Each period corresponds to the nucleation of a monoatomic layer (lattice plane). The period is inversely proportional to the current density.

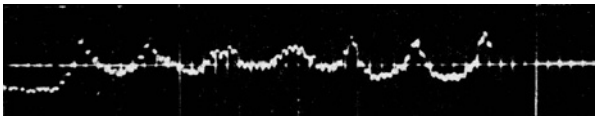


Fig. 7. Overpotential fluctuations during the growth of a dislocation-free single-crystal face ($i = 5.8 \times 10^4$ A/cm^2; abscissa: 0.2 sec/cm, ordinate: 5.2 mV/cm) (after *Budewski et al.* [23])

When the current is switched on, the corresponding adions cannot yet be incorporated. The overpotential therefore rises to a critical maximum value. It is only when this value has been reached that a nucleus of the new lattice plane can be formed from the accumulation of adions on the surface. This plane now grows by continuous addition of adions. As this lattice plane spreads out over the surface, the overpotential decreases, and reaches its lowest value when the lattice plane reaches the edges of the surface. The overpotential must rise to the critical value again before the next plane nucleus can be formed, and the process is then repeated. Thus the next nucleus is formed only when the growth of the preceding lattice plane is complete.

According to a relation found by *Volmer*, the nucleation rate, *i.e.* the number of plane nuclei formed per unit time [*], is

$$J_2 = c \exp\left(-K_{hkl}/\eta_{k_2} RT\right), \quad J_2 = 1/\tau \qquad (5)$$

where c and K_{hkl} are constants and τ is the time required for the formation of a nucleus. This relation shows that $\ln \tau$ is inversely proportional to the nucleation overpotential η_{k_2}.

[*] *Gerischer* and *Tischer* [14] found an exchange current density i_0 of 4.5 ± 0.5 A/cm^2 by the double pulse method in a 0.1 mole/l solution of $AgClO_4$.

[22] *R. Kaischew, E. Budewski,* and *S. Malinowski*, Doklady bolgarskoj Akad. Nauk *2*, 29 (1949).

[23] *E. Budewski, W. Bostanoff, T. Witanoff, Z. Stoinoff, A. Kotzewa,* and *R. Kaischew*, Electrochim. Acta (London) *11*, 1697 (1966).

[*] A different and more accurate formulation is

$J_2 = c \cdot \exp(-\pi f \varepsilon^2_{(hkl)}/ze_0 kT\eta_{k_2})$,

where f is the area occupied by an atom, $\varepsilon_{(hkl)}$ is the specific free edge energy, z is the valency, and e_0 is the unit charge.

According to *Budewski et al.*[123], one lattice plane after another can be formed as often as is desired by a continuous succession of voltage pulses (potentiostatic conditions), these pulses always exceeding the nucleation overpotential and being just sufficient for the formation of a nucleus. The measured duration of the pulses must be proportional to the nucleation time τ and inversely proportional to the nucleation rate J.

The proportionality of $\log \tau$ and $1/\eta_{1k_2}$ confirms that two-dimensional nuclei are in fact formed under these conditions.

Fig. 8 illustrates the linear relationship between the overpotential required for the formation of two-dimensional nuclei and the logarithm of the nucleation time τ.

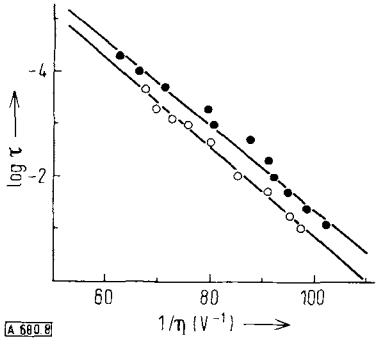


Fig. 8. Logarithm of the nucleation time τ as a function of the reciprocal of the overpotential in two-dimensional nucleation on a dislocation-free single-crystal face (after *Budewski et al.* [23]).

It was thus demonstrated for the first time that two-dimensional nuclei are in fact formed during electrocrystallization under these conditions (which are, however, special). It was thought for a long time that no such nuclei occurred in this type of crystallization. According to the data available, the work required for the formation of a two-dimensional nucleus at an overpotential of 10 mV is 8.6×10^{-13} erg.

4. Electrocrystallization under Real Conditions

4.1. Causes of Potential Deviations

As was shown earlier, it is possible, by electrolysis close to equilibrium, either to deposit single crystals having a habit that is similar to the equilibrium form, but which is by no means free from dislocations, or to form at least one equilibrium face with practically no deformations, though the latter is achieved at the cost of a nucleation overpotential.

Real conditions are characterized by a relatively large deviation from equilibrium, *i.e.* the potential ε is either very much greater or very much smaller than ε_0. Concerning the nature of the potential deviation $\varepsilon - \varepsilon_0$, which determines the nature and concentration of the adatoms, and hence also the course of the crystallization process, three cases can theoretically be distinguished. In the first case the potential deviation is due only to the crystallization, which is hindered or accelerated. This deviation will be denoted by $\varepsilon_k - \varepsilon_0$, where ε_k is the Galvani potential corresponding to the modified crystallization. This state of affairs can be achieved experimentally, though only rarely. In the second case the potential deviation is determined only by the preceding electrochemical process. The deviation from the equilibrium potential in this case is denoted by $\varepsilon_e - \varepsilon_0$, where ε_e is the Galvani potential of the modified electrochemical process.

Hindrance or acceleration of the electrochemical process nearly always leads to a change in the adion concentration on the surface of the metal, *i.e.* according to eq. (4) to a deviation of the surface activity a^* from the equilibrium activity a_0^*. This would itself lead to a crystallographic change.

With a greater deviation from equilibrium, the appreciable overpotential η_e rises above the limit below which the crystals still grow exclusively *via* dislocations. Beyond this limit, therefore, one should expect the formation of two-dimensional nuclei. This is so *e.g.* in nickel deposits formed with strong hindrance of the passage of metal ions through the electric double layer (high charge-transfer overpotential) or in very finely divided metal powders formed on strong inhibition of the transport of the metal ions to the phase boundary close to the limiting current density (high diffusion overpotential).

Inhibition of the electrochemical process without affecting the crystallization is possible only if the supply of kink positions in the crystal is so large that the transition of the metal ion still takes place only by direct incorporation into these positions from the electrolyte, *i.e.* without the formation of adions. This case is generally confined to proximity to equilibrium and special cases (see Section 4.2).

Apart from these exceptions, this second case is usually replaced by a third, the commonest case under real conditions, in which the potential deviation is determined by the electrochemical process and the crystallization. The deviation in this case is $\varepsilon_e + \varepsilon_k - \varepsilon_0$. The separation of the two effects, *i.e.* the determination of the crystallization overpotential η_k in the presence of the electrochemical overpotentials has so far proved very difficult (see Section 4.3).

4.2. Examples of Electrocrystallization

Let us consider two examples of the effect of the metal on crystallization. Whereas the conditions of the formation of two-dimensional nuclei *e.g.* during the deposition of silver on a dislocation-free substrate could be regarded as quasi-ideal so long as the preceding electrochemical process remained practically in equilibrium, this no longer seems admissible for the formation of three-dimensional nuclei, *i.e.* in the case of polycrystalline deposits. Since the formation of three-dimensional nuclei requires a much higher activation energy and overpotential, the conditions here are indisputably real.

According to *Volmer* the rate of formation of three-dimensional nuclei J_3 is given by a relation similar to

that for the rate of formation of two-dimensional nuclei [cf. eq. (5)] [*]:

$$J_3 = c' \exp(-K'/\eta_{k_3}^2 RT) \quad (6)$$

where c' and K' are constants and η_{k_3} is the overpotential required for the formation of three-dimensional nuclei.

η_{k_3} can be found experimentally with another metal as the substrate. A substrate such as platinum, tantalum, or stainless steel, generally covered with an inhibiting oxygen or oxide film, cannot simply be continued by the electrolytically deposited metal. The formation of three-dimensional nuclei from the metal deposited is therefore essential to growth.

Once formed, the nuclei grow by continuous addition of adions. The formation of three-dimensional nuclei is therefore basically only a (non-repetitive) initial process here. Quasi-ideal further growth of the polycrystalline metal deposit on a substrate of a different metal is made possible only by the intermediate layer of seed crystals adhering to the substrate.

Under deposition conditions such that no appreciable other polarizations or overpotentials can occur, an almost pure nucleation overpotential can be obtained in the initial process. In comparison with this overpotential, the overpotential that then arises during the further growth of the nuclei is relatively low. *Kaischew et al.* [24] have confirmed the validity of the Volmer relation for the initial formation of three-dimensional silver and lead nuclei on platinum single-crystal faces (which were not free from oxide). Three-dimensional nuclei of the metal were formed on another metal during a short cathodic voltage pulse with polarization. During this pulse, the nuclei formed grew into crystals that could be observed under the microscope.

The logarithm of the nucleation rate J_3 found by counting the microcrystals under an electron microscope was inversely proportional to the square of the overpotential, in agreement with the Volmer equation (6) [**].

In the quasi-ideal further growth of the nuclei there again arises the question of whether the metal ions are transferred directly from the electrolyte to the nuclei or seed crystals, or form adions only outside the nuclei. In the latter case the adions would have to make their way to the nuclei by surface diffusion.

As was shown by *Mierke* and *Schottky* [25], silver ions (from $AgNO_3$ or Ag_2SO_4 solutions of various concentrations) show a distinct preference for the first route. This was demonstrated in the example of the electrolytic formation of three-dimensional silver nuclei on platinum. According to the theory of the number of nuclei [26], the number of nuclei should show a definite dependence on the electrolyte concentration if the silver ions were deposited directly on the nuclei. If surface diffusion of the adions occurred, on the other hand, the number of nuclei should be practically independent of the electrolyte concentration. The experimental curve of the number of nuclei against the concentration agreed well with the theoretical curve.

The second example of a purely crystallization-controlled potential difference [27] is connected with changes in the corrosion potential of electrolytically deposited copper as a function of lattice imperfections. The rest Galvani potential at the metal/electrolyte interface may be regarded as a measure of corrosion resistance. As will be shown in Table 1, the rest Galvani potential changes significantly with the structure of the copper surface. Owing to the absence of external current in the rest state, the electrochemical process should be approximately in equilibrium.

Owing to their differences in structure, electrolytically deposited metals of the known structural types [27], which may be deposited *e.g.* in the presence of inhibitors with various activities, are suitable subjects for investigation. With increasing inhibition, the following structural types are obtained: the "basis-oriented reproduction type" (BR type) with its coarse crystal structure, the "field-oriented texture type" (FT type) with its fibrous structure exhibiting preferential orientation, and the "unoriented dispersion type" (UD type) with its extremely finely crystalline, randomly oriented structure.

As is shown by X-ray studies on deposits of these types [28], the sizes of coherent lattice regions decrease in the order BR, FT, UD. The densities of the subgrain boundaries, and hence the dislocation densities, increase by several orders of magnitude from the BR type to the UD type. Thus the lattice imperfections also increase in number as a result of these grain boundary effects.

If the Galvani potentials of copper of the structural types mentioned are measured in acidic $CuSO_4$ solution (in the absence of air) against the Galvani potential ε_r of a coarsely crystalline standard copper specimen whose structure has been largely re-established by annealing in a high vacuum, different reference voltages are found. The Galvani potentials measured against the same metal become increasingly negative,

[*] A different and more accurate formulation is

$J_3 = \exp -(16\pi\sigma^3 \cdot v^2 \cdot \Phi(\beta))/(3\,KT \cdot z^2 \cdot F^2 \eta_{k_3})$

where σ is the specific free surface energy, v is the molar volume, $\Phi(\beta)$ is the wetting angle of the nuclei with the substrate, z is the valency, and F is Faraday's constant.

[24] *R. Kaischew, A. Scheludko,* and *G. Bliznakow,* Ber. bulg. Akad. Wiss. physik. Ser. *1,* 137 (1950); *A. Scheludko* and *G. Bliznakow, ibid. 2,* 227 (1951); *A. Scheludko* and *M. Todorowa, ibid. 3,* 61 (1952); *B. Mutaftschiew* and *R. Kaischew, ibid. 5,* 77 (1955); Z. physik. Chem. *204,* 334 (1955).

[**] If, contrary to expectation, an appreciable electrochemical overpotential η_e had occurred (as a charge-transfer overpotential) as well as the nucleation overpotential η_{k_3}, the Volmer equation (6) could not have been confirmed so well, since instead of the observed proportionality of $\ln J_3$ to $1/\eta^2$, the hindrance of charge-transfer would have required that $\ln J_3$ be proportional to η (J_3 being proportional to the current density).

[25] *G. Mierke* and *W. F. Schottky,* Ber. Bunsenges. physik. Chem. *71,* 516 (1967).

[26] *R. Reich* and *M. Kahlweit,* Z. physik. Chem. N.F. *27,* 80 (1961); *M. Kahlweit, ibid. 28,* 245 (1961); *G. Tappe* and *M. Kahlweit, ibid. 30,* 90 (1961); *J. Osterwald,* Z. Elektrochem., Ber. Bunsenges. physik. Chem. *66,* 492 (1962).

[27] *G. Eichkorn, F. W. Schlitter,* and *H. Fischer,* Ber. Bunsenges. physik. Chem. *70,* 856 (1966).

[28] See ref. [12], p. 422ff.

i.e. decreasingly noble, with increasing imperfection density *i.e.* from the BR *via* the FT to the UD structural type.

This potential difference $\varepsilon_k - \varepsilon_r = \Delta\varepsilon_g$ may be regarded as the crystallization polarization of the electrode in the (currentless) rest state. With strong lattice imperfections in the metal (and hence also on the surface of the electrode), the imperfection-induced "activity" of the metal phase increases as a function of the density of lattice deformations.

Lattice deformations of multidimensional imperfection were examined by X-ray methods in specimens of the above type. The differences in the rest Galvani potentials $\Delta\varepsilon_g$ of various structural types can be calculated from the measured density of the lattice deformations, since it is possible, with the aid of the Nernst equation [cf. eq. (4)], to write:

$$\Delta\varepsilon_g = -(RT/zF) \ln (a_{1M}/a_{2M}) \quad (7)$$

If the imperfection-induced "activities" a_1 and a_2 of two samples of the same metal having different structures are assumed to be proportional to the relative distortions (lattice deformations) C_1 and C_2 [*], we obtain

$$\Delta\varepsilon_g = -(RT/zF) \ln (C_1/C_2) \quad (8)$$

Thus the potential difference $\Delta\varepsilon_g$ is found from the lattice deformation values C_1 and C_2 obtained by X-ray measurements. The $\Delta\varepsilon_g$ values calculated in this way for deposits M_1 and M_2 agree well with the $\Delta\varepsilon_e$ values obtained by electrochemical measurement between M_1 and M_2 (see Table 1).

Table 1. Potential differences $\Delta\varepsilon_g$ (from lattice deformations) and $\Delta\varepsilon_e$ (from electrochemical measurements) between electrolytic copper samples having different structures [29].

Structural type	C_1/C_2	$\Delta\varepsilon_g$ (mV)	$\Delta\varepsilon_e$ (mV)
M_1 UD M_2 BR	2.0	8.9	8.95
M_1 UD M_2 FT	1.68	6.6	6.6
M_1 FT M_2 BR	1.19	2.1	2.2

4.3. Determination of the Crystallization Overpotential

As was mentioned earlier, the crystallization and the preceding electrochemical process will generally both be hindered or accelerated during electrolysis. We shall now try to distinguish the characteristic results of these inhibition or acceleration phenomena, and hence the potential changes due to them. Until recently the crystallization overpotential η_k could be determined only as the difference between the total overpotential η_{tot} and all the other overpotentials, which could be determined individually (and which are referred to collectively as the electrochemical overpotential η_e in this article) plus the ohmic potential drop at the phase boundary [28]. The crystallization overpotential is thus given by

$$\eta_k = \eta_{tot} - (\eta_e + \eta_\Omega) = \eta_{tot} - (\eta_D + \eta_d + \eta_r + \eta_\Omega) \quad (9)$$

This process is relatively inaccurate and is not used much owing to its laboriousness.

Electrochemical overpotentials can be eliminated under certain conditions, if the changes in potential with time are measured in the rest state (*i.e.* with no externally applied voltage). The crystallization overpotential can be found in this way, as was shown by *Vetter* and *Bachmann* [20]. The example described by *Eichkorn* and *Fischer* [29] (see Table 1) is also based on this method. Unfortunately, however, this method cannot be used for the electrolysis.

It would be possible to solve this problem for electrolysis if one could find conditions under which the electrochemical overpotentials and the desired crystallization overpotential occurred in succession. This is so if the metal is deposited on a reproducible substrate of the same metal that has an extremely high kink concentration [29]. The deposition conditions used are such that a crystallization overpotential could be confidently expected on a substrate of the same metal with a normal (*i.e.* much lower) kink density.

On deposition of metal on the highly active substrate with a high kink concentration under the conditions mentioned, the situation should initially correspond to case 2 of Section 4.1. Thus the metal is at first mainly deposited directly in the kink positions, so that there is no crystallization overpotential. This leaves only the overpotentials of the electrochemical process and the ohmic potential drop. The substrate-dependent growth form takes several seconds or even minutes to change into an individual form, depending on the deposition conditions. The electrochemical overpotentials and the ohmic potential drop remain practically unchanged, while a crystallization overpotential also appears.

The success of this procedure must have been largely due to the choice of a suitable substrate that can be regarded as definite even in the polycrystalline state. Whereas a single-crystal surface that was practically free from dislocations was used for the further growth of a single crystal under quasi-ideal conditions, the other extreme, *i.e.* a polycrystalline substrate having a particularly high surface activity (*i.e.* dislocation density) with random crystal orientation and an extremely fine grain size, was used for the "real" conditions for the determination of the crystallization overpotential η_k in the presence of the electrochemical overpotential η_e. The substrate used in our experiments was a cathodic copper deposit of the unoriented dispersion type (UD type, see Section 4.1). A deposit of this type that has been purified in a high vacuum at 250 °C has the structure mentioned. Copper was de-

[*] Obtained by Fourier analysis of X-ray line profile measurements. This gives the mean relative lattice plane displacements, from which the relative deformations of multidimensional imperfection are obtained. They are constant over the greater part of the lattice region.

[29] *G. Eichkorn* and *H. Fischer*, Z. physik. Chem. N.F. *53*, 29 (1967).

posited on this substrate in the presence of a cathode-active foreign adsorbed substance, β-naphthoquinoline (1-azaphenanthrene). On a normal copper surface, which has a relatively low kink concentration, the copper would immediately be deposited in the "field-oriented texture type" [*] under the action of the foreign substance (concentration between 10^{-7} and 5×10^{-4} mole/l). With the highly active substrate, on the other hand, the deposit at first adapts itself to the structure of the substrate, and this structure changes into the finely fibrous FT type only on further electrolysis.

During the period in which the deposit follows the structure of the substrate, the crystallization overpotential should still be negligible. The quantity measured in this period consists only of components of the electrochemical overpotential η_e. Figure 9 shows how the overpotential changes when the current density is kept constant. The following overpotential components occur: (i) $\eta_D + \eta_\Omega$ the sum of the charge-transfer overpotential η_D and the ohmic potential drop, and (ii) η_d the diffusion overpotential reached with time.

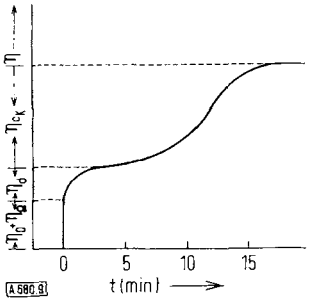


Fig. 9. Variation of the overpotential η on transition from reproduction to the individual growth form (after *Eichkorn* and *Fischer* [29]).

During a sort of incubation period, the crystal structure of the substrate is still continued in the deposit. The total polarization increases with time until a steady polarization plateau that is independent of time is reached. At this stage the deposit stops following the structure of the substrate, as can be seen under the microscope.

The preferentially oriented FT type that now occurs has a fibrous texture. It is built up uniformly from many crystal fibers, all oriented parallel to the field lines, *e.g.* perpendicular to the substrate. Each individual crystal fiber consists of numerous successive "growth layers" and each growth layer consists of a very large number of lattice planes (in the order of 1000).

4.4. Formation of the FT Structure Type

There was until now no sufficiently well founded theory of the formation of the very uniform "field-oriented texture type". The basic unit of this structure is evidently the growth layer. It was not certain whether the growth layer, and hence also the FT type, was formed *via* two-dimensional [30] or three-dimensional [31] nuclei.

As can be seen from Figure 9, the crystallization overpotential η_k corresponding to the formation of the individual layered and preferentially oriented growth form, which can be observed under the microscope, occurs above the plateau. No appreciable changes in the other types of overpotential are to be expected. The crystallization overpotential rises in an S curve with time until it reaches a steady value, which corresponds to the steady state of the substrate-independent crystallization under the deposition conditions in question. The crystallization overpotential η_{k} is thus given by the difference between the steady final overpotential and the "plateau" overpotential. The experimental S curve agrees with a calculated curve obtained by assuming that the layers are formed *via* two-dimensional nuclei [29].

On the basis of this assumption, we let the layer formation rate X, *i.e.* the number of growth layers formed per cm² per sec, be proportional to the average rate J_2 of formation of two-dimensional nuclei. On replacement of J_2 by X in the Volmer equation (5), a linear relationship between $\ln X$ and $1/\eta_{k_2}$ should be further evidence of the formation of two-dimensional nuclei.

The quantity X can be determined from the mean dimensions of the coherent lattice regions as found by X-ray analysis; these dimensions correspond to the mean dimensions of the growth layers. The average thickness of the growth layers, and hence the rate of layer formation, can be found experimentally by variation of the inhibitor concentration. This is accompanied by a change in the crystallization overpotential.

As expected, the crystallization overpotential increases with the inhibitor concentration, and reaches a value (average about 100 mV) comparable to the average electrochemical overpotential η_e. The average linear dimension of the coherent lattice regions is between 3270 and 1750 Å, depending on the inhibitor concentration. It decreases with increasing inhibitor concentration. The rate of layer formation X on the other hand, increases with increasing inhibitor concentration.

Figure 10 shows a plot of the rate of layer formation X, which is proportional to the nucleation rate, against $1/\eta_{k_2}$. It can be seen that, as expected if the

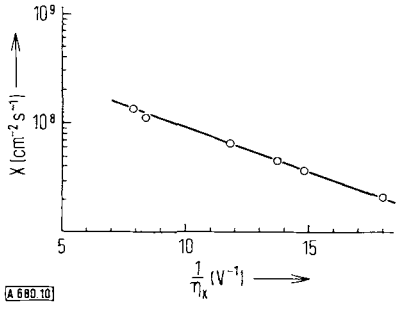


Fig. 10. Detection of the formation of two-dimensional nuclei (X = number of growth layers, η_k = nucleation overpotential) (after *Eichkorn* and *Fischer* [29]).

[*] From 1N $CuSO_4$ + 1N H_2SO_4 at 25 °C and a current density of 2×10^{-2} A/cm².

[30] See ref. [12], p. 393ff.

[31] *L. Graf*, Z. Metallkunde *42*, 336 (1951).

formation of two-dimensional nuclei is rate-determining, the relationship is linear. The activation energy found from the slope of the line is about 8×10^{-13} erg for a nucleation overpotential of 10 mV. This value agrees well with that found by *Budewski* (8.6×10^{-13} erg) for the formation of two-dimensional nuclei on silver (cf. Section 3). The two metals have the same unit cell, and dimensions are not very different.

We have thus found three pieces of evidence in favor of the formation of two-dimensional nuclei. These are the agreement of the calculated S curve with that found experimentally, the validity of the Volmer equation (5), and the agreement of the activation energies found for the formation of two-dimensional nuclei in the cases of copper and silver. It therefore seems justifiable to assume that the lattice planes in the growth layers are formed *via* two-dimensional nuclei.

The growth layer is a characteristic crystal lattice imperfection, which frequently occurs in electrocrystallization (as well as in other types of crystallization). Growth layers do not occur in the ideal crystal. In quasi-ideal growth, the formation of a new lattice plane can begin only when that of the previous plane is complete. This is confirmed by the results reported by *Budewski et al.* [23]. On the other hand, lattice plane nuclei can be formed much more frequently under real (distinctly non-equilibrium) conditions, *i.e.* they no longer have to await the completion of the previous lattice plane.

In our example the much higher nucleation frequency is partly due to the relatively high overpotential η_{le}. The activation energy for nucleation can also be further reduced by foreign adsorbed materials. In the real case, therefore, many new lattice planes will spread at short intervals over the first, as yet incomplete lattice plane (see Fig. 11, left, stage 1).

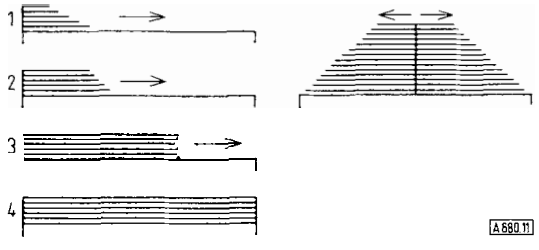


Fig. 11. Formation of growth layers and of pyramids.

The "bunching" of the individual atomic steps into a high macrostep (about 1000 atomic steps on average) (Fig. 11, left, stage 3) can be explained as follows [32]. Each of the successive lattice plane nuclei grows by deposition of metal into an atomic step extending over the substrate perpendicular to the lateral face. Metal is deposited only on the step edge with its many kinks, but not on the smooth step face parallel to the substrate, which is an equilibrium face and is therefore practically passive. There is therefore a temporarily very high local current density on the lateral face, but this must decrease very rapidly. This is ensured by the rapid increase in step edges.

[32] See ref. [12], p. 394.

The decreasing supply of metal ions and the increasing inhibition by adsorption of foreign materials slow down the growth of a given plane slightly earlier and to a greater degree than that of the next plane, so that the second plane can overtake the first. The planes then combine to form a macrostep, the growth layer. The thickness and width of the growth layer are limited by decreasing local current density (with increasing addition of atomic steps) and increasing inhibition. The decrease in the mean linear dimension of the layer due to inhibition has been confirmed experimentally (see Section 4.3).

The formation of new macrosteps is continuously repeated. This is probably how the crystal fibers of the FT type (and probably also isolated whiskers) are formed. Owing to the high nucleation frequency, very large numbers of crystal fibers are arranged in quick succession in the compact FT type, and grow parallel to one another. The number of fibers per unit area increases with the applied voltage and with inhibition.

With a combination of an adequate metal ion concentration, weak or absent inhibition, and a low current density, a given atomic step can no longer overtake those that preceded it, and macrosteps cannot be formed. The result in this case is the formation of pyramids (see Fig. 11, right).

It is in fact found that the deposition of copper from N $CuSO_4$ + N H_2SO_4 solution at 22 °C on copper having a (100) texture gives pyramids below 4×10^{-3} A/cm², whereas cubic platelets built up from growth layers are obtained at higher current densities [33]. The macrosteps of the growth spirals (see Section 1), the average height of which is comparable to that of the growth layers, are formed by a similar bunching principle. Local changes in current density on the edges of the atomic steps and different consumption rates could again enable later steps to overtake those started earlier. However, inhibition will only be slightly involved in this case, since growth spirals are readily blocked by very small quantities of inhibitors.

The fact that during growth, none of the faces on screw dislocations or spirals is exactly an equilibrium face should allow the deposition of inhibitors as well as metal ions on the faces that are not lateral faces of the steps. This may be why growth spirals do not stop growing in thickness and why they can spread out much farther than growth layers.

4.5. Formation of the UD Structural Type

The "unoriented dispersion type" (UD type), which consists of very fine, randomly oriented particles [*], is obtained when inhibition is particularly strong. Whereas the FT type is still obtained on addition of 5×10^{-4} mole/l of β-naphthoquinoline to the electrolyte, the UD type is obtained with 5×10^{-3} mole/l [34]. Preliminary experiments showed that at the higher inhibitor concentration, the overpotential no longer satisfies the Volmer equation (5), and the curve of X against $1/\eta_k$ (Fig. 10) shows a distinct deviation from linearity. This suggests that the formation of the UD type may involve three-dimensional nuclei.

[33] *H. Seiter*, *H. Fischer*, and *L. Albert*, Electrochim. Acta (London) *2*, 97 (1960), Figures 1 and 2.

[*] Average diameter about 600 Å.

[34] See ref. [12], p. 485ff.

The formation of three-dimensional nuclei has so far been detected only during the cathodic deposition of one metal on another that is covered with oxygen [24]. In the present situation, however, as in the case of the formation of two-dimensional nuclei, we are again faced with the problem of establishing the nature of the nucleus formation in the metal deposit on a substrate of the same metal in the presence of a strongly surface active inhibitor. Another difference concerns the continuity of nucleation. Whereas the formation of three-dimensional silver nuclei on platinum is only an initial process, which is stopped by the continuous growth of these first nuclei, we must expect uniform continuous nucleation, accompanied by slight growth of the nuclei, during deposition in the presence of strong inhibitors.

When copper is deposited on electrolytic copper of the BR type in the presence of a suitable quantity of inhibitor (2.5×10^{-3} to 8×10^{-3} mole/l of *o*-phenanthroline [*]), the overpotential follows the course shown in Figure 12 [35]. This curve is characteristic of deposition

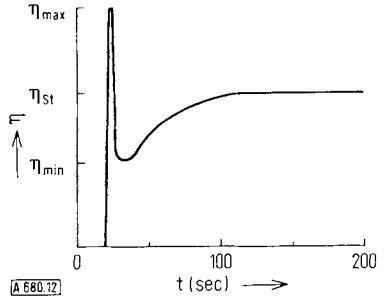


Fig. 12. Variation of the overpotential during the formation of three-dimensional nuclei (after *Eichkorn* and *Fischer* [35]).

under the conditions of formation of the fine-grain UD type on a substrate having a much coarser structure. The electrolyte was again a solution of N $CuSO_4$ + N H_2SO_4 (with added inhibitor). The adsorption of the inhibitor on the copper was allowed to reach equilibrium before deposition (25 °C, 3×10^{-2} A/cm²) was started.

At sorption equilibrium in the currentless sate, the foreign substance occupies nearly all the active sites and a large part of the inactive surface. This initial surface state leads to a high adion concentration coupled with a very rapid increase in the overpotential to the value η_{max} as soon as the current is switched on. Consequently, three-dimensional nuclei are formed everywhere almost simultaneously.

The resulting primary nucleus front, which is still controlled by the initial state, then grows out; this development is associated with a marked disturbance of the initial inhibitor adsorption equilibrium (as a result of displacement or incorporation of the inhibitor molecules in the deposit). This is accompanied by a rapid decrease in overpotential, probably because of the disappearance of the primary nucleation overpotential and part of the charge-transfer overpotential. The remaining overpotential $\eta_{i\,min}$ is the component of the charge-transfer overpotential corresponding to a steady state of inhibitor adsorption that has now been reached. This is followed at corresponding intervals by further nucleus formation and development of the nuclei. Both again reach a steady state and then proceed in a continuous manner. This corresponds to the steady overpotential $\eta_{i\,st}$.

Since the growth of the nuclei requires no appreciable overpotential, the difference $\eta_{i\,st} - \eta_{i\,min}$ must be associated with the steady nucleus formation. It increases with increasing inhibitor concentration. It is now necessary to check whether this is an overpotential η_{ik_2} or η_{ik_3}, *i.e.* whether it obeys the Volmer equation (5) or (6).

As in the detection of two-dimensional nuclei in inhibited electrocrystallization, the nucleation rate J again cannot be obtained by direct experiment. However, J can again be replaced by a quantity X, the number of particles formed per sec and per cm² (the UD type in this case). These particles correspond in size to the coherently scattering lattice regions that can be detected by X-ray measurements. It is assumed that any region of this type having an average diameter of 600 Å is derived from a single nucleation process. This is a plausible assumption.

Under the conditions of the experiment, X is given by

$$X = 1.08 \times 10^{18}/\bar{G}^3 = J \qquad (10)$$

The numerator of the fraction is the volume of copper in Å³ deposited per second and per cm² at a current density of 3×10^{-2} A/cm², and $\bar{G}^3$ is the mean volume of a coherent lattice region, $\bar{G}$ being the mean linear dimension of the region; $\bar{G}$ can be determined by X-ray measurements.

Figure 13 shows a plot of the nucleation rates J found with the aid of eq. (10) from X-ray data against the reciprocal of the square of the nucleation overpotential $1/\eta_{ik_3}^2$ for a number of inhibitor concentrations. A semilogarithmic plot gives a reproducible straight line.

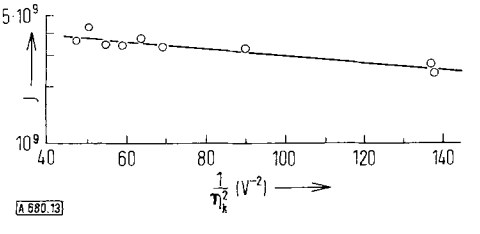


Fig. 13. Detection of the formation of three-dimensional nuclei (J = nucleation rate, η_{ik} = nucleation overpotential) (after *Eichkorn* and *Fischer* [35]).

This shows that, as was assumed, the UD type is formed *via* three-dimensional nuclei. From the data available, the work of nucleation at a nucleation overpotential $\eta_{ik_3} = 100$ mV is calculated to be 2×10^{-14} erg, while the value found for $\eta_{ik_3} = 10$ mV is 2×10^{-12} erg. These values are of the same order of magnitude as those found by other methods for the formation of three-dimensional nuclei of Ag, Pb, and Hg on platinum single crystals [24].

Received: March 8, 1968 [A 680 IE]
German version: Angew. Chem. *81*, 101 (1969)
Translated by Express Translation Service, London

[*] More suitable than β-naphthoquinoline, owing to its greater solubility.

[35] *G. Eichkorn* and *H. Fischer*, Z. physik. Chem. N.F., in press.

Reactions of Aromatic Nitro Compounds with Bases

By P. Buck[*]

Aromatic nitro compounds can react in many ways with bases. The reaction path followed depends mainly on the degree of nitration (with a sharp jump from mononitro to di- and trinitro compounds) and the base used. Redox reactions or nucleophilic aromatic substitutions predominate with mononitro compounds, whereas Meisenheimer additions together with nucleophilic aromatic substitutions are preferred by dinitro and trinitro compounds; deprotonations are less common. The bromine in nitrobromobenzenes can be replaced by metal at low temperatures. Very weak bases generally give electron donor-acceptor complexes.

1. Introduction

Nitro compounds, and particularly aromatic nitro compounds, are readily available starting materials, and are used in many syntheses involving the introduction of nitrogen atoms or in situations where it is desired to take advantage of the versatility of the amines obtained from aromatic nitro compounds. Nitrated compounds are also frequently used for investigations on reaction mechanisms. They also play a valuable role in analytical chemistry because of their great ease of crystallization and the high extinction coefficients of nitrophenyl derivatives.

Nitro compounds are generally stable in acidic media unless they also contain groups that react with acids. Reduction in acidic solution generally leads to amines. On the other hand, most aromatic nitro compounds are very sensitive to bases, with which they can react in a variety of ways. The possibilities are outlined in Table 1.

2. Reactions of the Nitro Group and Free Radical Reactions

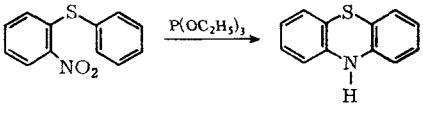
Attacks by bases on the nitro group are relatively rare, and are almost entirely confined to mononitro aromatic compounds, apart from partial reductions of the nitro group[1] in dinitro and trinitro compounds by $(NH_4)_2S$, NaHS, H_2S, and polysulfides, which are frequently also carried out in slightly basic solution.

2.1. Alkaline Reducing Agents

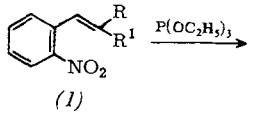
The attack of the base on the nitro group is generally associated with reduction of the nitrogen (and simultaneous oxidation of the base). Where the base is also a reducing agent (*e.g.* $Na_4[Sn(OH)_6]$[2] or $Na[BH_4]$), the reduction of the nitro group is not surprising. Thus mononitro compounds (but not dinitro or trinitro compounds, see Sections 2.2 and 2.3) whose substituents have positive Hammett σ values are reduced to azoxy compounds in very good yields by $Na[BH_4]$ in ethanol[3]. An exception is found in the case of *p*-nitrofluorobenzene, in which nucleophilic aromatic substitution by the solvent takes precedence over reduction[3].

2.2. Bases Containing Trivalent Phosphorus

Reactions with phosphorus bases such as phosphine and triethyl phosphite have recently attracted growing interest. A particularly important use of these bases is in cyclizations *e.g.* in accordance with eq. (1)[4] and eq. (2).

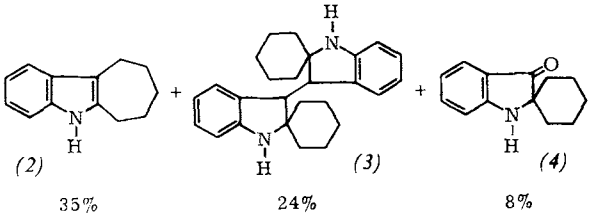


(54%) (1)



(1)

$-R-R^1- = -(CH_2)_5-$ (2)



(2) 35% *(3)* 24% *(4)* 8%

The yields of the indoles corresponding to *(2)*, which are formed by rearrangement, are generally higher if R in *(1)* is a phenyl group[5,6]. (The example of eq.

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[1] *R. Schröter* in *Houben-Weyl-Müller*: Methoden der organischen Chemie. 4th Edit., Thieme-Verlag, Stuttgart 1957, Vol. XI/1, p. 474.

[2] *O. N. Witt*, Ber. dtsch. chem. Ges. *18*, 2912 (1885).

[3] *H. Shine* and *H. E. Mallory*, J. org. Chemistry *27*, 2390 (1962).

[4] *J. I. G. Cadogan*, *R. K. MacKie*, and *M. J. Todd*, Chem. Commun. *1966*, 491.

[5] *R. J. Sundberg*, J. org. Chemistry *30*, 3605 (1965).

[6] *R. J. Sundberg* and *T. Yamazaki*, J. org. Chemistry *32*, 290 (1967).

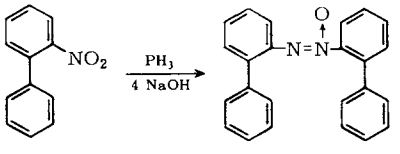
Table 1. Survey of the reactions of aromatic nitro compounds with bases.

Base \ further subst.	Mononitrobenzene			1,3-Dinitrobenzene				1,3,5-Trinitrobenzene		
	—	CH_3	*o*- or *p*-Hal	—	CH_3	4-Hal	4-OR	—	2-Hal or -OR	2,4,6-trisubst.
Alkoxides	Redox [8–11, 31]	Redox [9]	Subst [48, 49]	Add [50] Deprot [116]	CH_3-Deprot [116] Add [50]	Subst [48, 49]	Add [50] Subst [87] Deprot [116]	Add [50] Deprot [113]	Add [50, 87]	Subst [89]
Aliphatic amines			Subst [49, 92]		CH_3-Deprot [133]	Subst [48, 49]		Add [50] Deprot [114] EDA [132]	Subst [49] Add [50]	
Aromatic amines				EDA [126]		Subst [48, 49]		EDA [126]	Subst [49] EDA [126]	
Phosphites	Redox [4–6, 32, 34]	Redox [36]	(Subst) [134]							
$Na[BH_4]$	Redox [3]		Redox [3]	Add [76]	Add [76]	Add [76]		Add [75]	Add [88]	Subst NO_2^- [88]
Enolate or malonate			Subst [110]	Add [50, 63, 65, 69]	Add [50]	Add [50] Subst [49]	Add [50, 135]	Add [50, 62, 64]		
RMgX	Redox [12, 14, 42]	Redox [12]		Add [105]		Add [105]		Add [105]		
RLi	Redox [16, 17, 40]	Redox [16]	Redox and Hal-Met [18, 123]		Hal-Met [18]	Add and Hal-Met [18]			Add [18]	Hal-Met [18]

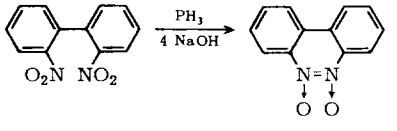
Redox = redox reaction (cf. Section 2); Add = addition to the aromatic ring; Subst = nucleophilic aromatic substitution (cf. Section 3); Deprot = deprotonation (cf. Section 4); deprotonation of the methyl group is marked. Hal-Met = halogen-metal exchange in bromine derivatives (cf. Section 5); EDA = electron donor-acceptor complex formation (cf. Section 6).

(2)[6] was chosen to show some characteristic by-products.)

The reaction with phosphine in alkaline aqueous ethanol proceeds differently[7]; the products in this case being azoxy compounds [eq. (3)]. 2,2′-Dinitrobiphenyl is only reduced to the nitroso stage [eq. (4)].



(3)



(4)

2.3. Alkoxides

Nitro groups can also be reduced by sodium ethoxide. This reaction has been known for some time[8] and has proved very useful in preparative work. In the presence of catalytic quantities (3–5%) of fluorenone or fluorenol, the reaction can also be carried out with NaOH in methanol[9]. However, the azoxy compounds formed in both cases are further reduced to hydrazo compounds by an excess of NaOH. Other alkoxides such as sodium methoxide[10] or sodium glycolate ($NaOCH_2CH_2OH$)[11] can also be used.

2.4. Organometallic Compounds

Grignard compounds and organolithium compounds also have a reducing action on mononitrobenzenes. *Gilman* and *McCracken*[12] and later *Kursanov* and *Solodkov*[13] proposed the stoichiometric equation (5) for the reaction of nitrobenzene with aryl Grignard compounds;

$$C_6H_5NO_2 + 4\,ArMgBr \rightarrow C_6H_5NH{-}Ar{-}MgBr + ArOMgBr + Ar{-}Ar + (BrMg)_2O \quad (5)$$

however, this equation can at best refer only to the principal reaction, since it gives only a very unsatisfactory description of the composition of the reaction products. The nitro group of methyl *p*-nitrobenzoate is reduced to the amino group (45% yield)[14], whereas

[7] *A. C. Bellaart*, Tetrahedron *21*, 3285 (1965).

[8] *N. Zinin*, J. prakt. Chem. (1) *36*, 93 (1845).

[9] *A. A. Sayigh*, J. org. Chemistry *25*, 1707 (1960).

[10] *Y. Ogata* and *J. Mibae*, J. org. Chemistry *27*, 2048 (1962).

[11] *W. Tadros*, *M. S. Ishak*, and *E. Bassili*, J. chem. Soc. (London) *1959*, 627.

[12] *H. Gilman* and *R. McCracken*, J. Amer. chem. Soc. *51*, 821 (1929).

[13] *D. N. Kursanov* and *P. A. Solodkov*, Ž. obšč. Chim. *5*, 1487 (1935); Chem. Abstr. *30*, 2181 (1936).

[14] *D. Y. Curtin* and *J. C. Kauer*, J. Amer. chem. Soc. *75*, 6041 (1953).

C_6H_5MgBr can add to the carbonyl group of *m*-nitrobenzaldehyde at −70 °C (77% yield) [15]. Under otherwise identical conditions, reaction at room temperature or with n-C_4H_9MgBr yields only tars [15].

Definite products such as azobenzenes and diarylamines retaining the nitrogen of the nitro compound used are generally even more difficult to obtain on reaction with organolithium bases. On the other hand, both oxygen atoms of mononitro compounds are often found quantitatively in phenols formed from the aryllithium compound [16, 17].

$$ArNO_2 \xrightarrow[2)\ H_2O]{1)\ Ar^1Li} Ar{-}N{=}N{-}Ar + Ar{-}NH{-}Ar^1 + Ar^1OH \text{ etc.} \quad (6)$$

This phenol formation is also observed in the reaction of some dinitro-bromo aromatic compounds with phenyllithium [18].

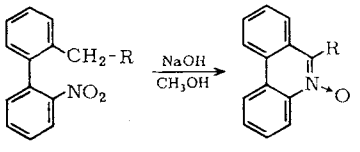
2.5. Reaction Mechanisms

How should we picture the attack of the base on the nitro group? The nitro group *(5)* formally resembles the carboxylate ion *(6)*. However, *(5)* differs from *(6)*



(5) *(6)*

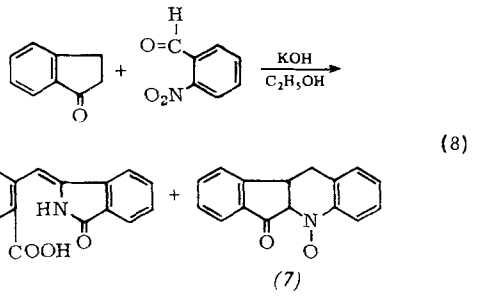
in the positive charge on the nitrogen. Because of this charge, the nitro nitrogen atom should be particularly reactive toward bases, *i.e.* it should enter into condensations similar to the Claisen ester condensation. Exactly the opposite is however found; condensations of this type are observed only in the case of biphenyl derivatives, where intramolecular condensation to form a six-membered ring is sterically favored, eq. (7) [19].



(7)

R = electron-attracting group

It is uncertain whether this is a true analog of the ester condensation, since the formation of the C–N bond need not take place with the nitro compound in its initial oxidation state. – The product *(7)* of the condensation of *o*-nitrobenzaldehyde with indanone is the only evidence of an intermolecular attack on the nitrogen of the nitro group by a carbanion [20], unless a primary condensation is assumed to occur between C-3 of the indanone and the aldehyde function.



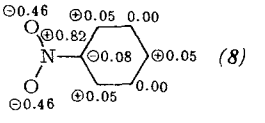
(8)

(7)

The fundamental difference between nitro compounds and carboxylic acids (or their anions) becomes clearest in $^{16}O/^{18}O$ exchange experiments: whereas carboxylic acids in $H_2{}^{18}O$ exchange ^{16}O for ^{18}O both in acidic [21] and in basic [22] solutions, no incorporation of ^{18}O into nitro compounds has so far been detected in any case [23].

This remarkable situation is probably due to the fact that the environment of the nitrogen is completely saturated with electrons, whereas the oxygen atoms suffer from an electron deficiency. Moreover, the nitrogen cannot accept further electrons from the base. Nucleophilic attack is consequently no longer possible on the nitrogen, and should occur, if at all, on the oxygen. In agreement with this view, the oxygen of the nitro group is protonated only under drastic conditions. The pK_a value of nitrobenzene [24] is −11.38, and those of dinitro and trinitro aromatic compounds are even lower [25], whereas the value for benzoic acid [26] is +4.20.

The charge distribution found by HMO calculations [27] for nitrobenzene is shown in *(8)*. The electron density evidently has more influence than the Coulomb charge



(8)

distribution [28]: It can be shown chemically that organolithium compounds attack the oxygen and not the nitrogen (see Scheme 1).

If the lithium compound attacked the nitrogen atom of the nitro group and if the resulting phenols and (hypothetical) aromatic nitroso compounds were formed from *(9)* by a sort of Meisenheimer rearrangement,

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[17] *P. Buck* and *G. Köbrich*, Tetrahedron Letters *1967*, 1563.

[18] *P. Buck*, Dissertation, Universität Heidelberg, 1967.

[19] Some examples are given in *J. D. Loudon* and *G. Tennant*, Quart. Rev. (Chem. Soc., London) *18*, 389 (1964).

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[22] *K. Mainord*, M.Sc. Thesis, University of Arkansas, 1966.

[23] a) *I. Robert*, J. chem. Physics *6*, 294 (1938); b) *I. P. Gragerov* and *A. F. Lewit*, Ž. obšč. Chim. *30*, 3726 (1960); Chem. Zbl. *1964*, 4-0732; c) *A. Fry* and *M. Lusser*, J. org. Chemistry *31*, 3422 (1966).

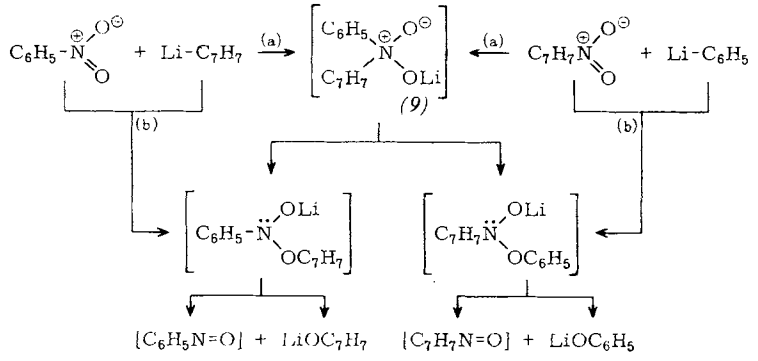
[24] *M. A. Paul* and *F. A. Long*, Chem. Reviews *57*, 1 (1957).

[25] *J. C. D. Brand*, *W. C. Horning*, and *M. B. Thornley*, J. chem. Soc. (London) *1952*, 1374.

[26] *E. S. Gould*: Mechanismus und Struktur in der organischen Chemie. 2nd Edit., Verlag Chemie, Weinheim 1964, p. 262.

[27] *A. J. Owen*, Tetrahedron *23*, 1857 (1967).

[28] This phenomenon is also found in the carbenoids [29] and the nucleophilic carbenes [30].



Scheme 1. C_7H_7 = *p*-tolyl.

the product mixture obtained would be the same whether the starting materials were nitrobenzene and *p*-tolyllithium or *p*-nitrotoluene and phenyllithium (a). If on the other hand the oxygen of the nitro group is transferred directly to the base, phenol should be formed in one case and *p*-cresol in the other (b). It is in fact found that in agreement with case (b), the only phenol formed is that corresponding to the lithium compound used [16, 17].

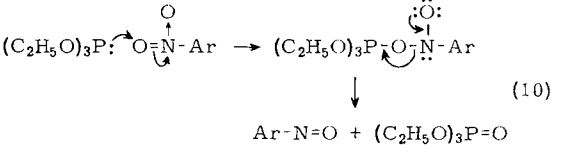
The oxygen is also found in the base in all other cases, the base being oxidized. An example is the azoxybenzene synthesis mentioned in Sections 2.2 and 2.3, in which nitrobenzene is reduced in good yields by sodium methoxide in methanol [10]; if the reaction is carried out in the absence of water, azoxybenzene and sodium formate can be isolated, each in 87% yield [calculated by the stoichiometry of eq. (9)] [31].

$$4\ C_6H_5NO_2 + 3\ CH_3ONa \rightarrow 2\ C_6H_5{-}\overset{\overset{O}{\uparrow}}{N}{=}N{-}C_6H_5 + 3\ HCOONa + 3\ H_2O \qquad (9)$$

Little is known about the course of the reaction, except that the oxygen of the nitro group is (partly) transferred to the base. It may be assumed that various reactions are involved, depending on the base.

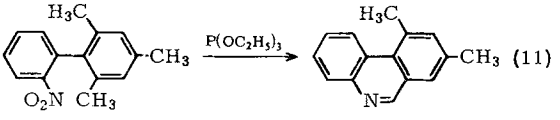
An attack on the oxygen of the nitro group by the lone electron pair of the phosphorus, eq. (10) [32], was formulated for the first time in deoxygenations by phosphorus bases.

The frequently expressed suspicion [33] that nitrene intermediates occur in reductions with phosphites has



(10)

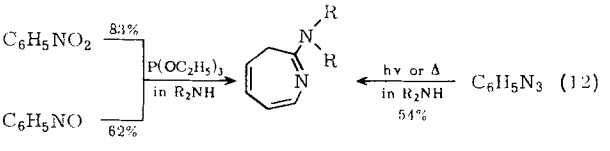
recently been confirmed. On the one hand, the distribution of products from the deoxygenation of *o*-nitrobutylbenzene [34] with triethyl phosphite is remarkably similar to that obtained on pyrolysis of *o*-azidobutylbenzene [35], and on the other, C–H insertions *e.g.* eq. (11), are occasionally also observed in cyclizations [36].



(11)

Further evidence is provided by the formation of phosphorimidates $R{-}N = P(OC_2H_5)_3$ [34, 36].

Finally, the reaction (12), which is characteristic of phenylnitrene, has recently been detected in phosphite reductions.



(12)

Reductions of both nitrobenzene [36] and nitrosobenzene [37] in a secondary aliphatic amine lead in good yields to 2-amino-3*H*-azepines, which are also observed on thermolysis [38] or photolysis [39] of phenyl azide. On the other hand, nitrosobenzene is probably not an intermediate in the reduction of nitrobenzene with phenyllithium [16].

2.6. Free Radical Reactions

Free radical reactions must also be considered in the reactions of nitrobenzene with the organometallic compounds mentioned above, particularly since an ESR signal has been observed in the reaction of nitrobenzene with *n*-butyllithium in THF/hexane (3:1) [40].

[29] *G. Köbrich*, Angew. Chem. *79*, 15 (1967); Angew. Chem. internat. Edit. *6*, 41 (1967).

[30] *H. W. Wanzlick*, Angew. Chem. *74*, 129 (1962); Angew. Chem. internat. Edit. *1*, 75 (1962).

[31] *H. S. Fry* and *J. L. Cameron*, J. Amer. chem. Soc. *49*, 864 (1927).

[32] *J. I. G. Cadogan, M. Cameron-Wood, R. K. MacKie*, and *R. J. G. Searle*, J. chem. Soc. (London) *1965*, 4831.

[33] *L. Horner* and *A. Christmann*, Angew. Chem. *75*, 707 (1963); Angew. Chem. internat. Edit. *2*, 599 (1963); *R. A. A. Abramovitch* and *B. A. Davis*, Chem. Reviews *64*, 149 (1964).

[34] *R. J. Sundberg*, Tetrahedron Letters *1966*, 477.

[35] *G. Smolinsky* and *B. I. Feuer*, J. org. Chemistry *29*, 3097 (1964).

[36] *J. I. G. Cadogan* and *M. J. Todd*, Chem. Commun. *1967*, 178.

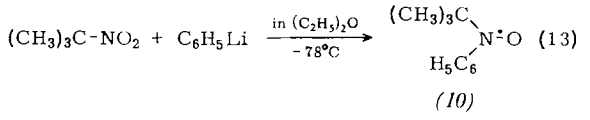
[37] *R. A. Odum* and *M. Brenner*, J. Amer. chem. Soc. *88*, 2074 (1966).

[38] *R. Huisgen, D. Vossius*, and *M. Appl*, Chem. Ber. *91*, 1 (1958).

[39] *W. von E. Doering* and *R. A. Odum*, Tetrahedron *22*, 81 (1966).

[40] *G. A. Russell, E. G. Janzen*, and *E. T. Strom*, J. Amer. chem. Soc. *86*, 1807 (1964).

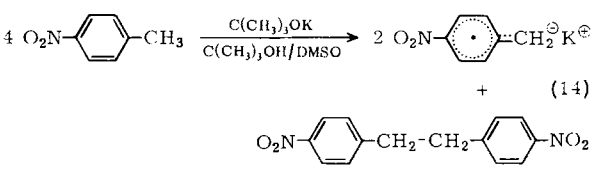
The estimated free radical concentration in this case was about 6%. Higher concentrations are obtained with tertiary aliphatic nitro compounds and organometallic compounds of alkali metals. The free radicals were identified in these cases as aminyl oxides, *e.g.* *(10)* [41].



(10)

The aminyl oxide *(10)* also occurs (together with nitrobenzene radicalanions) in the reaction of *tert*-butylmagnesium chloride with nitrobenzene [42]. It is not yet possible to establish whether these radicals are formed by direct reaction or *via* a nitroso intermediate, since nitrosobenzene also gives aminyl oxides with Grignard compounds [43], with strong bases [44], and even with olefins [45].

Free radicals have frequently also been observed in reactions with alkoxides. Thus *o*- and *p*-nitrotoluene disproportionate spontaneously in the presence of potassium *tert*-butoxide in *tert*-butanol/dimethyl sulfoxide to give *o*- and *p*-nitrotoluene radical-anions and nitrobibenzyls, eq. (14) [44].

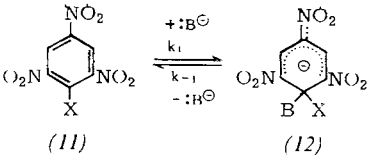


Aromatic nitro compounds without alkyl substituents do not undergo reactions of this type [46]. However, free radicals are also observed in these cases on irradiation in alcoholic methoxide solution [47].

3. Meisenheimer Compounds and Nucleophilic Aromatic Substitution

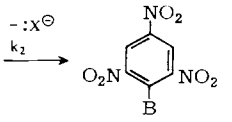
The bases that reduce the nitro group according to the last section attack only the aromatic ring if there are two or three nitro groups situated *meta* to one another. The reaction can either stop at *(12)* (Meisenheimer addition) or lead to substitution if C-4 or C-2 carries a group X that can act as a nucleofugal leaving group.

The addition and nucleophilic aromatic substitution have been fairly extensively studied and described in several reviews [48–50]. Only the fundamentals and the more recent results are discussed here.



(11) *(12)*

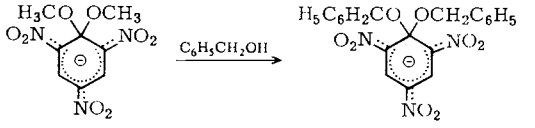
(15)



(13)

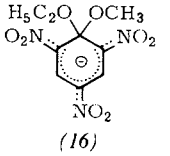
3.1. Structure of Meisenheimer Compounds

It was shown as early as the turn of the century that the addition products that can be isolated in many cases have the constitution *(12)*, *i.e.* they no longer contain an aromatic structure. Thus in 1900, *Jackson* isolated the dimethoxy compound *(14)*, which changes into the dibenzyloxy compound *(15)* on standing in benzyl alcohol [51].



(14) *(15)*

(16)



(16)

The equivalence of the two methoxy groups led *Jackson* to propose the structures *(14)* and (implicitly) *(15)*, while *Meisenheimer* found in 1902 that the adduct *(16)* is obtained both from 2,4,6-trinitroanisole and sodium ethoxide and from 2,4,6-trinitrophenetole and sodium methoxide [52]. Compounds of this type are known as Meisenheimer compounds.

According to HMO calculations, the accepted representations *(12)* and *(14)* to *(16)* are misleading. Despite the additional negative charge, the interruption of the cyclic conjugation leads to increased withdrawal of π electrons to the nitro groups [53].

NMR spectroscopy has proved a useful aid to the confirmation of the structure of many Meisenheimer

[41] *A. K. Hoffmann, A. M. Feldman,* and *E. Gelblum,* J. Amer. chem. Soc. *86,* 646 (1964).

[42] *G. Chapelet-Letourneux, H. Lemaire,* and *A. Rassat,* Bull. Soc. chim. France *1965,* 444.

[43] *K. Maruyama,* Bull. chem. Soc. Japan *37,* 1013 (1964).

[44] *G. A. Russell, E. J. Geels, F. J. Smentowski, K. Y. Chang, J. Reynolds,* and *G. Kaupp,* J. Amer. chem. Soc. *89,* 3821 (1967).

[45] *A. B. Sullivan,* J. org. Chemistry *31,* 2811 (1966).

[46] *G. A. Russell, E. G. Janzen et al.,* J. Amer. chem. Soc. *84,* 4157 (1962); *89,* 300 (1967); J. org. Chemistry *32,* 137, 821 (1967).

[47] *P. B. Ayscough, F. P. Sargent,* and *R. Wilson,* J. chem. Soc. (London) *1963,* 5418; *1966 B,* 903.

[48] *J. F. Bunnett* and *R. E. Zahler,* Chem. Reviews *49,* 273 (1951); *J. F. Bunnett,* Quart. Rev. (chem. Soc., London) *12,* 1 (1958).

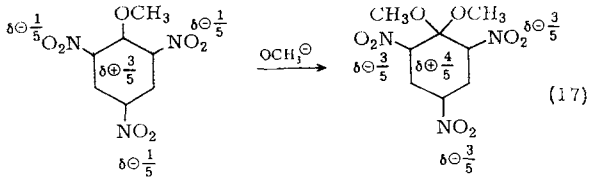
[49] *J. Sauer* and *R. Huisgen,* Angew. Chem. *72,* 294 (1960); *S. D. Ross,* Progr. physic. org. Chem. *1,* 31 (1963); *G. Illuminati,* Advances heterocyclic Chem. *3,* 285 (1964).

[50] *R. Foster* and *C. A. Fyfe,* Rev. pure appl. Chem. *16,* 61 (1966).

[51] *C. L. Jackson* and *F. H. Gazollo,* Amer. chem. J. *23,* 376 (1900).

[52] *J. Meisenheimer,* Liebigs Ann. Chem. *323,* 205 (1902).

[53] *P. Caveng, P. B. Fischer, E. Heilbronner, A. L. Miller,* and *H. Zollinger,* Helv. chim. Acta *50,* 848 (1967).



(17)

compounds [50,54]. It is not difficult to prepare these compounds as such from trinitrobenzene derivatives [55] or to record their NMR spectra in solution [54]. The same is true of corresponding compounds derived from aromatic dinitro or mononitro compounds such as *(17)* and *(18)* [56]. A compound of the type *(18)* was obtained by *Meisenheimer* [52].



(17) *(18)*

Meisenheimer compounds of dinitrobenzenes, however, are difficult to isolate, though a few have been obtained in a more or less pure state [57,58] and NMR studies have also been carried out recently [58].

3.2. Color Reactions

Dinitroaromatic compounds are used analytically in the Janovski and the Zimmermann color reactions.

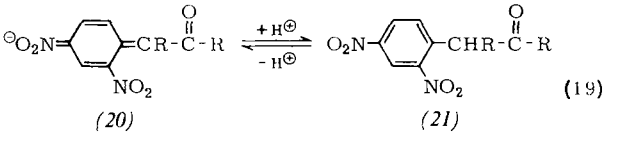
Many aromatic dinitro and trinitro compounds give a very intense blue to violet color with concentrated sodium hydroxide or sodium methoxide solution in the presence of acetone (Janovski reaction [59]). An intense violet color is also frequently obtained if the ketone is varied instead of the nitro compound. The variant with *m*-dinitrobenzene, which is known as the Zimmermann reaction [60], is particularly important in steroid chemistry, since it is a reliable test for 17-keto steroids [61].

It may be taken as certain in both reactions that a bond is formed between a carbon atom of the ketone and a carbon atom of the aromatic ring. After the reaction of 1,3,5-trinitrobenzene with acetone/KOH – the Janovski reaction is reversible – *Severin* [62] prevented the removal of the acetonyl group by reduction of the carbonyl group with $Na[BH_4]$. The compounds *(19a)* and *(19b)* were isolated.

This reaction also shows that there must be a high stationary concentration of colored Janovski complex, since 1,3,5-trinitrobenzene reacts differently with $Na[BH_4]$ [eq. (22)].

An NMR study of the Janovski reaction of *m*-dinitrobenzene indicates the structure corresponding to the formula *(19)* [63]. Janovski-Meisenheimer complexes of this type are obtained in acetone simply on addition of tertiary aliphatic amines [64].

The Zimmermann reaction, on the other hand, involves an oxidized complex *(20)*, in whose formation the nitro group itself acts as the oxidizing agent [65].



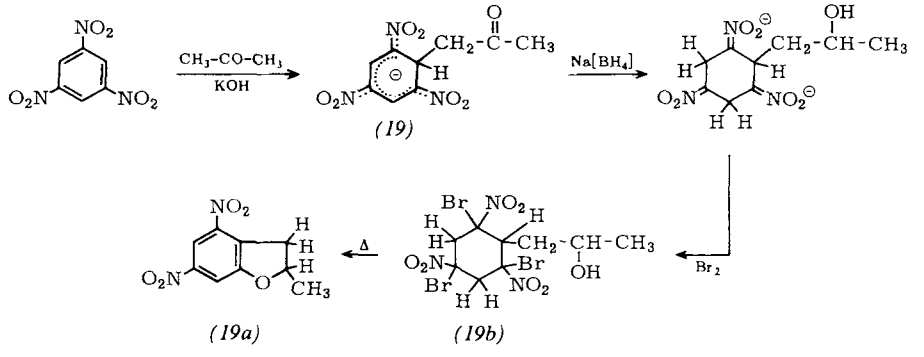
(20) *(21)*

This is also shown by spectroscopic studies, since the addition of bases to 2,4-dinitrobenzyl ketones *(21)* leads to UV absorptions that agree with those observed in correponding Zimmermann reactions [66,67].

Compounds of the types *(20)* [65,68] and *(21)* [69] have also been isolated and identified by elemental analysis [65,68] or NMR spectroscopy [69].

3.3. Site of Attack and Multiple Additions

The addition can take place on a carbon atom other than that carrying the group X (X = OCH_3, NR_2, halogen, *etc.*). Moreover, further base molecules may add to the Meisenheimer compound. Both of these possibilities are realized *e.g.* in reaction (20) [70].



(19) *(19a)* *(19b)*

(18)

[54] *M. R. Crampton* and *V. Gold*, J. chem. Soc. (London) *1964*, 4293.

[55] *L. K. Dyall*, J. chem. Soc. (London) *1960*, 5160.

[56] *R. Foster, C. A. Fyfe, P. H. Emslie*, and *M. I. Foreman*, Tetrahedron *23*, 227 (1967).

[57] *S. S. Gitis, A. J. Glaz*, and *A. Ja. Kaminskii*, Ž. obšč. Chim. *33*, 3301 (1963).

[58] *W. E. Byrne, E. J. Fendler, J. H. Fendler*, and *C. E. Griffin*, J. org. Chemistry *32*, 2506 (1967).

[59] *J. V. Janovski* and *L. Erb*, Ber. dtsch. chem. Ges. *19*, 2155 (1886).

[60] *W. Zimmermann*, Hoppe-Seylers Z. physiol. Chem. *233*, 257 (1935); *245*, 47 (1937).

[61] *A. E. Kellie*, Analyst *82*, 722 (1957).

[62] *T. Severin, R. Schmitz*, and *H. L. Temme*, Chem. Ber. *97*, 467 (1964).

[63] *C. A. Fyfe* and *R. Foster*, Chem. Commun. *1967*, 1219.

[64] *R. Foster* and *C. A. Fyfe*, J. chem. Soc. (London) *B 1966*, 53.

[65] *O. Neunhoeffer, K. Thewalt*, and *W. Zimmermann*, Hoppe-Seylers Z. physiol. Chem. *323*, 116 (1961).

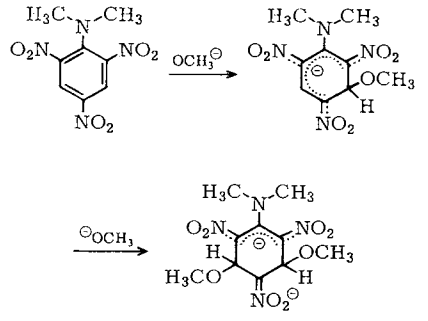
[66] *T. J. King* and *C. E. Newall*, J. chem. Soc. (London) *1962*, 367.

[67] *R. Foster* and *R. K. MacKie*, Tetrahedron *18*, 1131 (1962).

[68] *C. S. Corker, J. K. Norymberski*, and *R. Thow*, Biochem. J. *83*, 584 (1962).

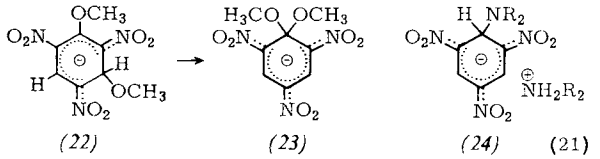
[69] *T. Nambera* and *M. Kato*, Chem. and Ind. *1967*, 1090.

[70] *M. R. Crampton* and *V. Gold*, Chem. Commun. *1965*, 256.



(20)

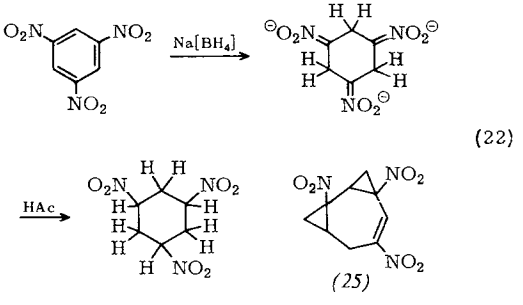
According to NMR studies, the formation of the Meisenheimer compound *(23)* in dimethyl sulfoxide also appears to be preceded by addition to C-3 to give *(22)*, which then changes rapidly into *(23)* [71].



(22) *(23)* *(24)* (21)

However, the participation of two molecules of base does not necessarily mean double addition. For example, two moles of secondary aliphatic amine react with one mole of trinitrobenzene in dimethyl sulfoxide. One amine molecule adds to give the Meisenheimer compound, which is deprotonated by the other to form *(24)*, as has been shown by NMR spectroscopy and by conductivity measurements [72, 73].

Triple additions to trinitrobenzene and picric acid are observed with diazomethane; these reactions lead to seven-membered rings such as *(25)* [74]. Trinitrobenzene is reduced to 1,3,5-trinitrocyclohexane by $Na[BH_4]$, eq. (22) [75], whereas dinitro compounds give only cyclohexene derivatives [76].



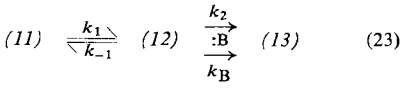
(22)

(25)

3.4. Mechanism of the Nucleophilic Aromatic Substitution

The idea that addition to the aromatic ring and nucleophilic aromatic substitution as in eq. (15) are related to each other [48] has proved extremely valuable in studies on substitution reactions of aromatic nitro compounds.

As in all two-step reactions it is necessary to distinguish two possibilities, depending on whether the ratio k_{-1}/k_2 is greater or smaller than 1. If $k_{-1} \gg k_2$ there is probably no objection to a two-step mechanism, and such a mechanism is in fact clearly indicated by kinetic studies on the base catalysis of nucleophilic aromatic substitutions on 2,4-dinitrophenyl phenyl ether [77]. The overall rate constant in this case shows a non-linear dependence on the quantity of NaOH added, as is to be expected if the decomposition of *(12)* is base catalyzed, eq. (23).



(23)

This result is confirmed by an investigation with ^{18}O-ethers [78]. On the other hand, the demonstrable existence of Meisenheimer compounds is not a conclusive argument for their occurrence as intermediates in the nucleophilic aromatic substitution; they could just as easily be products of an equilibrium side reaction [79], particularly since the addition frequently does not occur initially on the C atom to which the group X is attached, eq. (21).

Reactions in which $k_{-1} \ll k_2$ cannot yet be distinguished from those having a synchronous (*e.g.* S_N2-like) mechanism [82,83], as was shown by *Hammond* [80,81].

A third possibility, *i.e.* nucleophilic aromatic substitution by the elimination-addition (EA) mechanism, will be discussed in Section 4.2.

3.5. Electronic and Steric Effects in Addition and Substitution

The rates of nucleophilic aromatic substitution and of Meisenheimer addition increase with increasing substitution of the aromatic compound by electron-attracting groups. These may naturally be other groups than nitro groups, whose electron-attracting action is made up of two components, *i.e.* an inductive and a mesomeric component [84]. The mesomeric com-

[71] *K. L. Servis*, J. Amer. chem. Soc. *87*, 5495 (1965); *89*, 1508 (1967).

[72] *G. Briegleb*, *W. Liptay*, and *M. Cantner*, Z. physik. Chem. N.F. *26*, 55 (1960).

[73] *M. R. Crampton* and *V. Gold*, Chem. Commun. *1965*, 549.

[74] *T. J. de Boer* and *J. C. van Velzen*, Recueil Trav. chim. Pays-Bas *78*, 947 (1959); *T. J. de Boer*, Tetrahedron (Suppl. I) *20*, 339 (1964).

[75] *T. Severin* and *R. Schmitz*, Chem. Ber. *95*, 1417 (1962).

[76] *T. Severin* and *M. Adam*, Chem. Ber. *96*, 448 (1963).

[77] *J. F. Bunnett* and *R. H. Garst*, J. Amer. chem. Soc. *87*, 3879 (1965); *C. F. Bernasconi*, J. org. Chemistry *32*, 2947 (1967); *C. F. Bernasconi* and *P. Schmid*, *ibid.* *32*, 2953 (1967).

[78] *C. R. Hart* and *A. N. Bourns*, Tetrahedron Letters *1966*, 2995.

[79] *P. Caveng* and *H. Zollinger*, Helv. chim. Acta *50*, 866 (1967).

[80] *G. S. Hammond* and *R. L. Parks*, J. Amer. chem. Soc. *77*, 340 (1955).

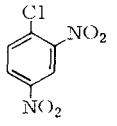
[81] See the fundamentally similar problem treated by *J. E. Leffler* and *R. D. Temple*, J. Amer. chem. Soc. *89*, 5235 (1967).

[82] *R. E. Parker* and *T. O. Read*, J. chem. Soc. (London) *1962*, 9.

[83] *M. Simonetta* and *S. Carra*, Tetrahedron (Suppl. I) *20*, 383 (1964); *S. Carra*, *M. Raimondi*, and *M. Simonetta*, Tetrahedron *22*, 2673 (1966).

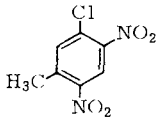
[84] For the ratio of the two components see *H. A. Staab*: Einführung in die theoretische organische Chemie. 3rd Edit., Verlag Chemie, Weinheim 1962, p. 580ff.

ponent is strongly suppressed when coplanarity of the nitro group with the ring is prevented by bulky neighboring substituents. This is clear from the relative rate constants (figures under the formulas) for the substitution of chlorine in *(26)* to *(29)* by piperidine in ethanol [85].



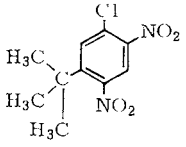
(26)

1



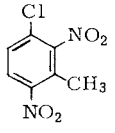
(27)

0.28



(28)

0.017



(29)

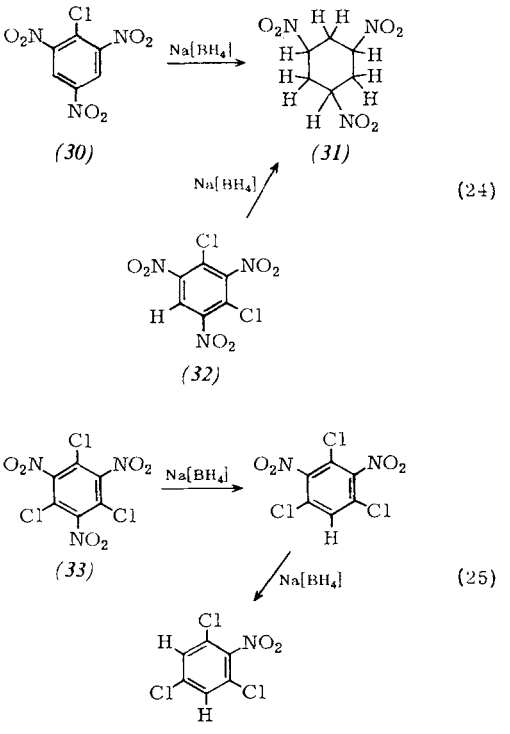
0.001

Whether the reaction stops at the stage of the Meisenheimer compound depends mainly on how effectively the negative charge of the electron-attracting groups can be absorbed. The differences in the delocalization energies between the nitro aromatic systems and the Meisenheimer compounds (4-nitrobenzenes, −8 kcal/mole; 2,4-dinitrobenzenes, 1 kcal/mole; 2,4,6-trinitrobenzenes, 10 kcal/mole), which were successfully used by *Miller* [86] for the calculation of activation parameters of nucleophilic substitutions and additions, illustrate the enormous influence of the successive introduction of mutually *meta* nitro groups.

Consequently, no Meisenheimer compounds of mononitrobenzenes are known; those of dinitro compounds are difficult to isolate as such, whereas with trinitro compounds often no substitution [87] is observed but addition.

The effect of steric hindrance on the addition, *i.e.* the suppression of the mesomeric withdrawal of electrons by the nitro groups, is impressively demonstrated by *Kaplan*'s experiments [88]. The products of hydride additions to *(30)* and *(32)* are sufficiently long-lived to allow further additions, which lead to *(31)* (the stage at which the Cl atom is removed is unknown); *(33)*, on the other hand, exhibits only nucleophilic substitution, in which NO_2^- leaves more readily than Cl^-, as is known from other investigations [82,92]. In *sym*-trinitrotrimethoxybenzene, the methoxyl group is replaced by ethoxide [89], whereas 2,4,6-trinitroanisole gives only the Meisenheimer compound *(16)*.

Poor leaving groups X also increase the life of a Meisenheimer compound such as *(12)*. The nucleophilic



(24)

(25)

aromatic substitution is therefore catalyzed by bases in particular in nitro-fluoro compounds [90] and nitrated aryl ethers [77] (cf. Section 3.4). Experiments with 2,4-dinitrophenyl phenyl ethers having electron-attracting substituents on the electrofugal group confirm this, since they show a distinct decrease in base catalysis [91]. For the same reason, most of the Meisenheimer compounds studied have H and/or OR groups attached to the sp^3 ring carbon atom.

The rate of substitution of halogenonitrobenzenes generally decreases in the order Hal = I < Br < Cl ≪ F [48,49,92]. Thus the acceptance of a negative charge by the carbon to which the halogen is attached, which facilitates the addition of the base to the ring, has a stronger effect on the reaction rate than the leaving tendency of the halide ion. The reverse order is also found occasionally [80,93]. The relevant numerical data and the extremely high reactivity of the fluorine compounds, of which practical use can be made [94], are by no means fully understood.

In nucleophilic aromatic substitution by neutral bases, *e.g.* amines, the reaction rate exhibits a definite dependence on the dielectric constant of the solvent [95,96], except in the cases of alcohol, dimethylformamide, and dimethyl sulfoxide. The relative rate constants for different substrates can also be related to the nature of the solvent [96]. The solvent dependence has not been so systematically studied in reactions of basic ions. In this case high reaction rates are found particularly in aprotic dipolar solvents (DMF, DMSO, *etc.*) [97].

[85] *B. Capon* and *N. B. Chapman*, J. chem. Soc. (London) *1957*, 600.

[86] *J. Miller*, J. Amer. chem. Soc. *85*, 1628 (1963).

[87] *J. Fendler*, Chem. and Ind. *1965*, 764.

[88] *L. A. Kaplan*, J. Amer. chem. Soc. *86*, 740 (1964).

[89] *S. S. Gitis, A. I. Glaz*, and *A. Sch. Glaz*, Ž. org. Chim. *3*, 1620 (1967).

[90] *F. Pietra* and *A. Fava*, Tetrahedron Letters *1963*, 1535; *F. Pietra, ibid. 1965*, 745, 1432; *C. Bernasconi* and *H. Zollinger, ibid. 1965*, 1083; *F. Pietra* and *D. Vitali, ibid. 1966*, 5701; *1967*, 576.

[91] *J. F. Bunnett* and *C. Bernasconi*, J. Amer. chem. Soc. *87*, 5209 (1965).

[92] *H. Suhr*, Chem. Ber. *97*, 3268 (1964).

[93] *P. J. C. Fierens* and *A. Halleux*, Bull. Soc. chim. belges *64*, 696 (1955).

[94] *F. Sanger*, Biochem. J. *39*, 507 (1945); Advances Protein Chem. *7*, 1 (1952); *H. L. Boter* and *G. R. van den Berg*, Recueil Trav. chim. Pays-Bas *85*, 919 (1966).

[95] *H. Suhr*, Ber. Bunsenges. physik. Chem. *67*, 893 (1963).

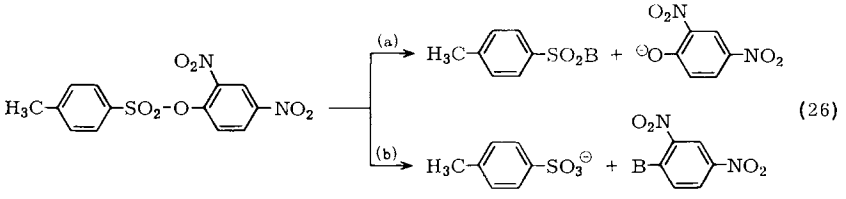
[96] *H. Suhr*, Chem. Ber. *97*, 3277 (1964).

[97] *J. Miller* and *A. J. Parker*, J. Amer. chem. Soc. *83*, 117 (1961).

Methanol[98], dimethyl sulfoxide[99], and water[100] have a strong accelerating effect when added in small quantities to other solvents.

3.6. Effect of the Base on the Nucleophilic Aromatic Substitution

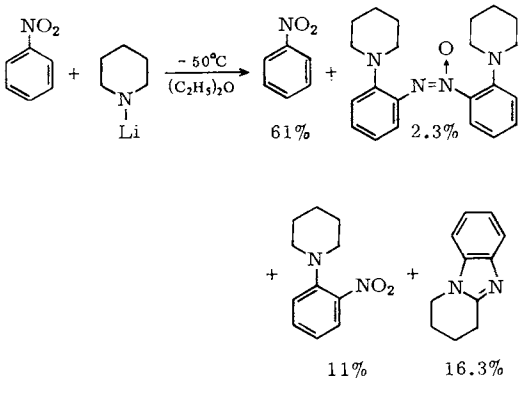
The nature of the base used is a factor of the utmost importance. As expected, faster substitutions are found with strongly nucleophilic bases whose electron cloud is readily deformed. *Pearson* and *Songstad* have applied the principle of "hard" and "soft" acids and bases to nucleophilic aromatic substitutions[101], but have not always succeeded in making correct predictions. In the hydrolysis of sulfonic esters, a change of base can even lead to a change in the course of the reaction. Whereas reaction (26) proceeds to the extent of 88 % by path (a) with sodium methoxide, the reaction with thiophenolate proceeds exclusively by path (b)[102].



(26)

Steric hindrance of the base molecule has been studied with piperidine, 2-methylpiperidine, and 2,6-dimethylpiperidine[103,104]. The ratio of their rate constants with *p*-nitrofluorobenzene[104] is 135000:26:1.

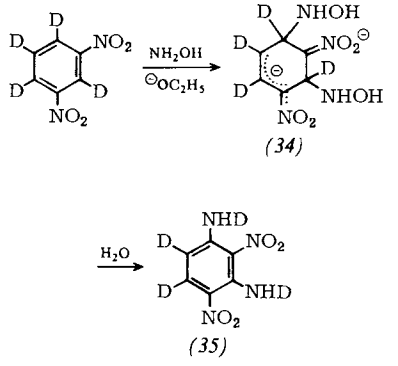
Unlike organometallic compounds, which undergo multiple addition to the aromatic ring[105], alkali metal amides react exclusively by substitution under comparable conditions, even when only poor leaving groups such as hydride are available, eq. (27)[106].



Similar substitutions (though in the *p* position) have also been observed with piperidine and sodamide[107], as well as with sodium and potassium diphenylamides[108].

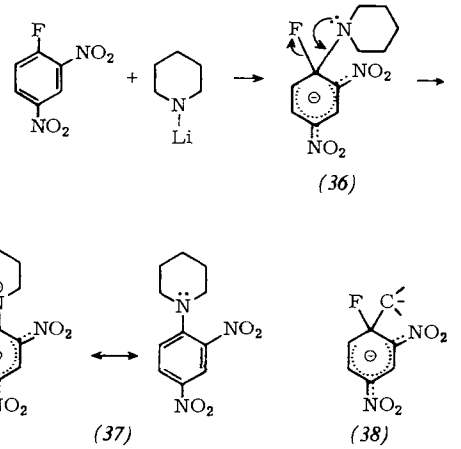
An interesting hydride substitution has been described by *Gitis et al.*[109]. [1,2,3,5-D_4]-*m*-Dinitrobenzene and hydroxylamine react in the presence of an excess of sodium ethoxide to form the intermediate *(34)*; this is decomposed by water to give *(35)*, which still contains all the deuterium originally present.

Fluorine in 2,4-dinitrofluorobenzene also undergoes more than 65 % nucleophilic substitution by lithium piperidide[16].



(28)

The striking difference between N–Li and C–Li compounds may be due to assistance of the release in the nucleofugal group by the lone pair of electrons present in all bases that



(29)

[98] *H. Zollinger* and *C. Bernasconi*, Helv. chim. Acta *49*, 103 (1966).

[99] *C. A. Kingsberg*, J. org. Chemistry *29*, 3262 (1964); *C. Bernasconi*, *M. Kaufmann*, and *H. Zollinger*, Helv. chim. Acta *49*, 2563 (1966).

[100] *R. G. Burns* and *B. D. England*, J. chem. Soc. (London) *B 1966*, 855.

[101] *R. G. Pearson* and *J. Songstad*, J. Amer. chem. Soc. *89*, 1827 (1967).

[102] *J. F. Bunnett* and *J. Y. Bassett*, J. Amer. chem. Soc. *81*, 2104 (1959).

[103] *H. Suhr*, Liebigs Ann. Chem. *689*, 109 (1965); *F. Pietra* and *F. Del Cima*, Tetrahedron Letters *1966*, 1925.

[104] *F. Pietra* and *F. Del Cima*, Tetrahedron Letters *1966*, 4453.

[105] *T. Severin* and *M. Adam*, Chem. Ber. *97*, 186 (1964); *T. Severin* and *R. Schmitz*, *ibid. 96*, 3083 (1963).

[106] *R. Huisgen* and *H. Rist*, Liebigs Ann. Chem. *594*, 159 (1955).

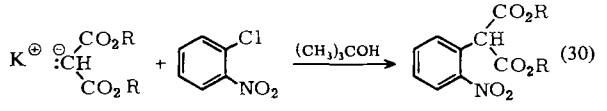
[107] *W. Bradley* and *R. Robinson*, J. chem. Soc. (London) *1932*, 1254.

[108] *F. E. Bergstrom*, *I. M. Granara*, and *V. Erickson*, J. org. Chemistry *7*, 98 (1942).

[109] *S. S. Gitis*, *A. I. Glaz*, *V. V. Grigoriev*, *A. Ja. Kaminskii*, *A. S. Martinenko*, and *P. I. Sankov*, Ž. org. Chim. *3*, 1617 (1967).

are capable of substitution. In eq. (29) the resonance stabilized 2,4-dinitrophenyl-1-piperidine *(37)* would be formed, whereas the corresponding complex *(38)* formed from a carbanion has *no* lone pair and so cannot react in the same way as *(36)*, but enters into additions instead [16].

Mononitroaromatic compounds can only rarely be nucleophilically substituted by carbanions. Substitution of *o*-nitrochlorobenzene can be achieved with potassiomalonic ester or potasioisocyanoacetic ester in *tert*-butanol, eq. (30) [110].



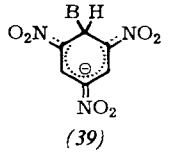
(30)

Pentafluoronitrobenzene is substituted in good yields in the *o* and *p* positions by pentafluoromagnesium bromide [111].

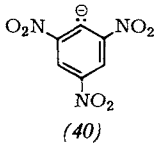
4. Deprotonation and Substitution *via* Dehydrobenzene

4.1. Deprotonation

Owing to the electron-attracting action of the nitro group, the *o*-H atoms in aromatic nitro compounds should be readily split off as protons. Few deprotonations of this type are known, however, probably because addition results in a greater energy gain. Whereas addition yields a delocalized system *(39)*, the negative charge on the carbanion *(40)* can only be stabilized inductively, and cannot be transferred to the nitro groups by resonance. The formation of Meisenheimer compounds thus occurs in preference to deprotonation, with the result that attempts to detect H/D exchange in *sym*-trinitrobenzene were for a long time unsuccessful [72, 112].



(39)



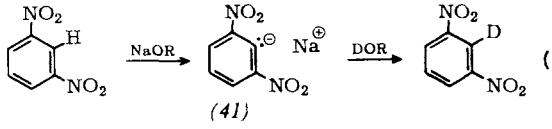
(40)

A slow H/D exchange can however be observed in a 9:1 dimethylformamide/water mixture. After 24 hours in dilute NaOD solution at room temperature, 15% of the hydrogen in *sym*-trinitrobenzene has been replaced by deuterium. At 100 °C the yield of [1,3,5-D_3]-*sym*-trinitrobenzene is 95% [113].

Other bases, both ions (*e.g.* acetate) and neutral molecules (*e.g.* 1,4-diazabicyclo[2.2.2]octane), are also effective under these conditions [114].

In *m*-dinitrobenzene, the hydrogen atom on C-2 can be exchanged under milder conditions. In addition to hydroxide [115] and methoxide [116], weaker bases are also active in this case [117], though to a smaller extent.

It has repeatedly been reported that the deep color of alkaline solutions of dinitro aromatic compounds is not due to the anion *(41)* [116]. A solution of *m*-dinitrobenzene in DMF/D_2O (0.005 M NaOD) is colorless [115]; moreover, color formation is much faster



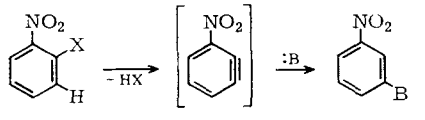
(41)

(31)

than H/D exchange [117] at high concentrations of base, so that the concentration of *(41)* must be vanishingly small. Deep colors are therefore probably due to Meisenheimer complexes. However, nitrophenyllithiums, which can be prepared by halogen-metal exchange (cf. Section 5), also have very deep colors [118].

4.2. Substitution of Halogen by the EA Mechanism

The deprotonation of aromatic nitro compounds, though possible, is relatively unfavorable (see Section 4.1); nucleophilic aromatic substitution by an elimination-addition (EA) mechanism should therefore be unlikely. This type of reaction is generally not even considered in connection with aromatic nitro compounds, though it is very frequently observed in the nitrogen heterocycles, which are often compared with aromatic nitro compounds [118].



(32)

4.3. Substitution of NO_2^-

Since NO_2^- is a relatively good leaving group [82,95,96], a dehydrobenzene intermediate could be expected on thermolysis of *o*-nitrophenyllithium (see Section 5). However, no Diels-Alder adduct with 1,3-diphenylisobenzofuran could be detected in this case [16,17], the decomposition leaving the nitro group and its bond to the ring intact [18].

The occasionally observed substitution of a *m*-nitro group in trinitro aromatic compounds, the reason for which is not immediately obvious, is also not generally explained by dehydrobenzene intermediates. For example, when *sym*-trinitrobenzene is allowed to stand

[110] *C. A. Grob* and *O. Weissbach*, Helv. chim. Acta *44*, 1748 (1961).

[111] *G. M. Brooke* and *W. K. R. Musgrave*, J. chem. Soc. (London) *1965*, 1864.

[112] *J. A. A. Ketelaar*, *A. Bier*, and *H. T. Vlaar*, Recueil Trav. chim. Pays-Bas *73*, 37 (1964).

[113] *E. Buncel* and *E. A. Symons*, Canad. J. Chem. *44*, 771 (1966).

[114] *E. Buncel* and *E. A. Symons*, Chem. Commun. *1967*, 771.

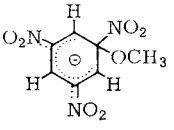
[115] *R. J. Pollitt* and *B. C. Saunders*, Proc. chem. Soc. (London) *1962*, 176; J. chem. Soc. (London) *1965*, 4615.

[116] *R. Foster* and *R. K. Mackie*, Tetrahedron *19*, 691 (1963); *M. R. Crampton* and *V. Gold*, J. chem. Soc. (London) *B 1966*, 498.

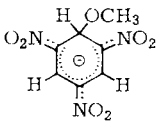
[117] *E. Buncel* and *A. W. Zabel*, J. Amer. chem. Soc. *89*, 3084 (1967).

[118] *T. Kauffmann*, Angew. Chem. *77*, 557 (1965); Angew. Chem. internat. Edit. *4*, 543 (1965); *H. J. den Hertog* and *H. C. van der Plas*, Advances heterocyclic Chem. *4*, 121 (1965).

in methanolic methoxide solution, sodium nitrite and 3,5-dinitroanisole are ultimately formed [119]. According to *Foster* and *Fyfe* [50], this substitution is due to poor delocalization of the negative charge in *(42)*, so that such a species once formed decomposes rapidly, whereas the formation of the normal Meisenheimer compound *(43)* is reversible.

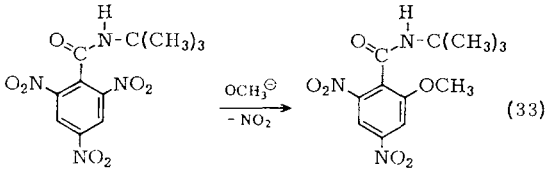


(42)



(43)

The substitution of the 2-nitro group in *(44)* by OCH_3^- or OH^- surprisingly exhibits first order kinetics (rate $=k_1$ *[(44)]*), *i.e.* it is independent of the base concentration [120].



(33)

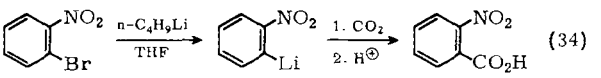
(44)

In addition to these reactions, which take place even in the dark, photochemical substitutions of the nitro group have been observed in some aromatic trinitro compounds [121], in *p*-nitrophenyl phosphate, and in *p*-nitroanisole [122].

5. Halogen-Metal Exchange in Aromatic Nitro-Bromo Compounds [123]

5.1. Mononitro Aromatic Compounds

Deprotonations are of only minor importance in nitro compounds (see Section 4.1). Halogen-metal exchange, which is made possible in the same manner by the positive nitrogen of the nitro group, and which normally proceeds very rapidly [124], is also unable to compete with other reactions at room temperature [125]. Between −100 and −110 °C, on the other hand, *o*-nitrobromobenzene is smoothly converted into *o*-nitrophenyllithium by phenyllithium or *n*-butyllithium, eq. (34).



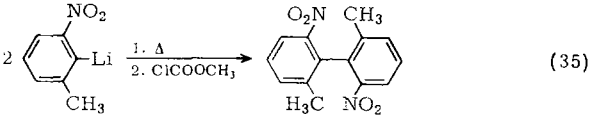
(34)

Other *o*-nitro-bromo aromatic compounds, such as 2-bromo-3-nitrotoluene, can also be converted into the lithium derivatives in this way. The yields rapidly decrease if the nitro group is *meta* or *para* to the bromine atom, since its exclusively inductive effect is then decreased (see Table 2).

Table 2. Optimum yields of carboxylic acid (from the lithium compound), bromobenzene (from halogen-metal exchange reactions), and phenol (from oxidation reactions of phenyllithium) in the reaction of nitrobromobenzenes with phenyllithium.

Substrate	Carboxylic acid yield (%)	Bromobenzene yield (%)	Phenol Yield (%)
o-Nitrobrombenzene	97	97	3
m-Nitrobrombenzene	16	42	70
p-Nitrobrombenzene	8	18	78

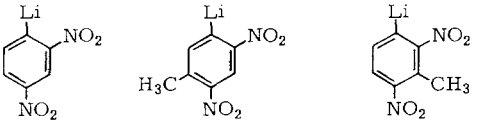
The ratio of bromine-lithium exchange to the redox reaction described in Section 2 is strongly dependent on the solvent and the reaction temperature. The redox reaction is favored by apolar solvents (ether, toluene) and high temperatures. *o*-Nitrophenyllithium decomposes exothermally at −100 °C; oxidation of the reaction products yields 2,2'dinitrobiphenyls, in which the C atoms that formerly carried the lithium atoms have become joined.



(35)

5.2. Dinitro and Trinitro Aromatic Compounds

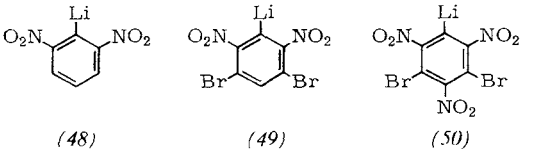
With 2,4-dinitrobromobenzene and picryl bromide, the addition described in Section 3 predominates to such an extent that the lithium compounds formed by halogen-metal exchange are detected as at most 23% of 2,4-dinitrobenzoic acid and 13% of trinitrobenzoic acid respectively. However, by utilizing the fact that the addition is strongly inhibited if the *m*-nitro group is twisted out of the plane of the ring by bulky neigh-



(45) 23%

(46) 77%

(47) 85%



(48) 68%

(49) 65%

(50) 85%

[119] *F. Reverdin*, Org. Syntheses 7, 28 (1928); *V. Gold* and *C. H. Rochester*, J. chem. Soc. (London) *1964*, 1692, 1697.

[120] *P. J. Hutchison* and *R. J. L. Martin*, Austral. J. Chem. *18*, 699 (1965).

[121] *V. Gold* and *C. H. Rochester*, J. chem. Soc. (London) *1964*, 1704, 1717, 1727.

[122] *R. L. Letsinger*, *O. B. Ramsey*, and *J. H. McCain*, J. Amer. chem. Soc. *87*, 2945 (1965).

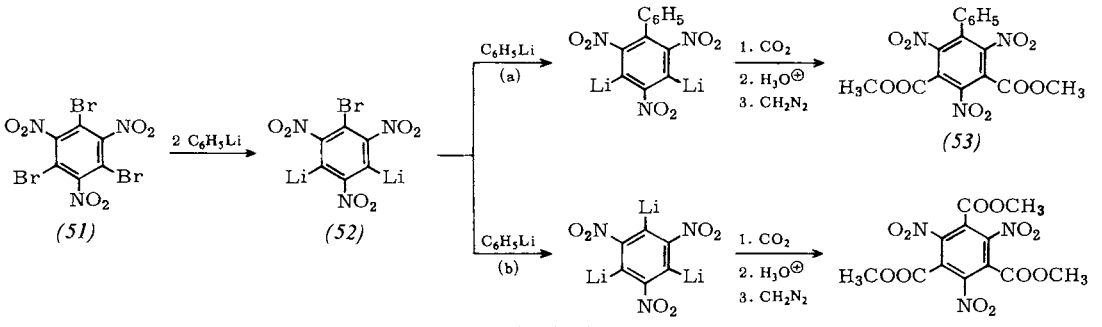
[123] For all the results from this section see [18]; cf. *G. Köbrich* and *P. Buck*, Angew. Chem. *78*, 1062 (1966); Angew. Chem. internat. Edit. *5*, 1044 (1966).

[124] *G. Wittig* and *U. Schöllkopf*, Tetrahedron *3*, 91 (1958).

[125] *B. F. Hofferth*, Iowa State J. Sci. *26*, 219 (1952); Chem. Abstr. *47*, 8672 (1953); *R. D. Topsom* and *J. Vaughan*, J. chem. Soc. (London) *1957*, 2842.

boring groups, one can again obtain dinitro and trinitro aryllithiums in good yields. This steric influence can be seen from the results of the halogen-metal exchange in compounds *(45)* to *(50)*. (The yield of carboxylic acid is given under the compound.)

sym-Trilithiotrinitrobenzene *(54)* can be prepared from *(51)* with an excess of phenyllithium. *(53)* is formed at the same time by a coupling reaction.



(51) *(52)* *(53)* *(54)*

It is surprising to find that the bromine atom in *(52)* [or one of the bromine atoms in *(50)*] can be released both anionically (a) and cationically (b) under the same conditions on reaction with the same base.

6. Electron Donor-Acceptor Complexes

Aromatic nitro compounds, particularly 2,4,6-trinitro compounds, are excellent acceptor molecules for electron-acceptor complexes. Many complexes of this type are known with 1,3,5-trinitrobenzene and picric acid [126]; these include the picrates used for the identification of tertiary amines or unsaturated hydrocarbons. They have been extensively investigated by ESR [40] and NMR spectroscopy [79,127], gas chromatography [128], and other methods [126].

Owing to their low basicity aromatic amines often form only electron donor-acceptor complexes with 2,4,6-trinitro aromatic compounds, whereas aliphatic amines can give Meisenheimer compounds and possibly higher adducts. This is clear from UV spectroscopic studies. When aromatic amines [129,130] are added to solutions of aromatic trinitro compounds, a relatively uncharacteristic band immediately appears in the near UV or visible region, whereas with aliphatic amines [130,131], several bands appear in the visible region at a measurable rate.

Electron donor-acceptor complexes are preferentially formed with weak bases having suitable π bonds (aromatic amines, aromatic compounds with other electron-donating substituents, olefins, *etc.*). Hard bases (aliphatic amines OR^-, OH^-, *etc.*) generally give σ complexes, such as Meisenheimer compounds.

Electron donor-acceptor complexes can, however, also be prepared from aliphatic amines by the use of apolar solvents such as cyclohexane, though Meisenheimer compounds are also formed when the concentrations are increased [132].

I am grateful to Prof. Dr. G. Köbrich for reading the manuscript and for his interest in this work.

Received: March 18, 1968 [A 682]
German version: Angew. Chem. *81*, 136 (1969)

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Errata

In the article "The Chemistry of Hypervalent Molecules" by *J. I. Musher*, Volume 1, January 1969, the following corrections should be made:

On page 64, left-hand column, line 5 "The first of these is linear, like I^-..." should read "The first of these is linear, like I_3^-...". On page 64, right-hand column, 12th line from bottom. "other halogen-F bonds" should read "other X-F bonds".

On page 65, left-hand column, line 13. "$\varepsilon_1 < \varepsilon_2$" should read "$\varepsilon_{(5)} < \varepsilon_{(6)}$".

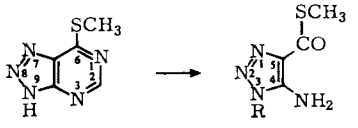
On page 65, left-hand column, lines 21 and 22 "$\varepsilon_{(5)} < \varepsilon_{(6)}$" should read "$\varepsilon_{(6)} < \varepsilon_{(5)}$".

The Hydrolysis of 6-Methylthio-8-azapurines to Thiol Esters of 1,2,3-Triazolecarboxylic Acids

By *A. Albert* [*]

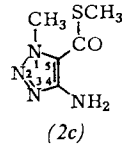
When boiled for 15 minutes with 1 M hydrochloric acid, 6-methylthio-8-azapurine *(1)* gives an almost quantitative yield of 4-amino-5-(methylthio)carbonyl-1,2,3-triazole *(2a)*, m.p. 201 °C, which could be isolated by filtration.

The 7-, 8-, and 9-methyl derivatives of *(1)* [1] gave *(2d)*, *(2c)*, and *(2b)*, melting at 132, 108, and 215 °C, respectively. They are all sparingly soluble in boiling water, but recrystallize well from a little methanol. They are stable to acid.

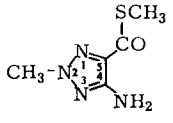


(1)

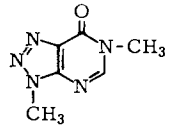
(2a), R = H
(2b), R = CH_3



(2c)



(2d)



(3)

A prominent peak occurs, in the ultraviolet spectrum of each compound, between 287 and 312 nm (log ε about 4.0, in methanol). The infrared spectrum (solid state) shows two very strong peaks at about 1640 (C=O stretching) and 900 cm^{-1} (=C–S stretching). The ^{1}H-NMR spectrum (in [D_6]-DMSO/D_2O) shows two peaks at τ = 6.2 (N–CH_3) and 7.7 (S–CH_3) (TMS internal standard).

Until now, thiol esters have been almost unknown in heterocyclic chemistry, but many examples are known in the benzene series with very strong infrared absorption in these two regions [2]. That the new triazoles are not the isomeric thione esters is shown by the stability of *(2a)*–*(2d)*, and by the absence of infrared absorption between 1000 and 1200 cm^{-1} [3].

With aqueous ammonia (stirred at 20 °C and then refluxed), *(2a)*–*(2d)* give almost quantitative yields of the carboxamides, identical with authentic specimens [1b–1d] (much methanethiol is liberated). Aqueous methylamine similarly gives *N*-methylamides, *e.g.* those compounds derived from *(2b)* and *(2d)* (m.p. 105 and 235 °C, respectively). Such *N*-methylamides have not previously been made. 4-Amino-3-methyl-1,2,3-triazole-5-carboxymethylamide [from *(2b)*], when heated with formamide at 225 °C, gives 1,9-dimethyl-6-oxodihydro-8-azapurine *(3)*, m.p. 207 °C, λ_{max} = 257 nm (log ε = 3.92 in H_2O [4]), quite free from 9-methyl-6-oxo-dihydro-8-azapurine, and which was isolated by filtration.

Reductive desulfurization of the thiol esters affords 4-amino-1,2,3-triazole-5-carbaldehyde and 4-amino-5-aminomethyl-1,2,3-triazole (and nuclear methylated derivatives of these) [5].

Received: November 5, 1968 [Z 900 IE]
German version: Angew. Chem. *81*, 115 (1969)

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[1] For preparation of the four starting materials, see a) *R. Weiss, R. K. Robins*, and *C. W. Noell*, J. org. Chemistry *25*,765 (1960); b) *A. Albert* and *K. Tratt*, J. chem. Soc. (London) *C 1968*, 344; c) *A. Albert, ibid.* 2076; d) *A. Albert, ibid. 1969*, 152.

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[4] Cf. [1c]: 254 nm (log ε = 3.98) for 6-hydroxy-9-methyl-8-azapurine.

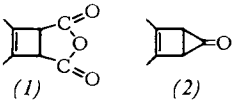
[5] *E. Mosettig*, Org. Reactions *8*, 229 (1954).

Formation of 1,2-Dimethylcyclobutadiene on Photolysis of Dimethylcyclobutenedicarboxylic Anhydride [1] [**]

By *G. Maier* and *U. Mende* [*]

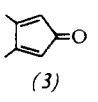
Irradiation of tetramethylcyclobutenedicarboxylic anhydride leads to products [permethylated derivatives of *(6)*, *(7)*, *(15)*, and *(16)*] whose formation can be readily interpreted on the assumption of tetramethylcyclobutadiene as an intermediate stage. The products found, however, do not suffice to prove this hypothesis [1].

On irradiation of the anhydride *(1)* (Hanovia 450-W Hg high-pressure lamp; Vycor filter; ether; 18 °C; 2 h) and subsequent chromatography on silica gel we obtained a mixture of the three isomeric tetramethylcyclooctatetraenes *(7)*, *(10)*,



(1)

(2)



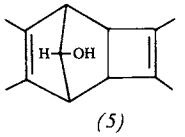
(3)



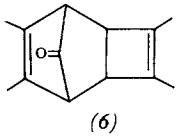
(4a)



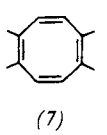
(4b)



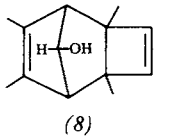
(5)



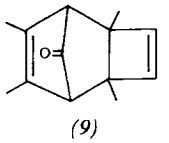
(6)



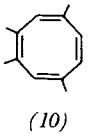
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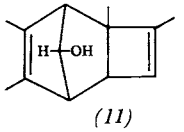
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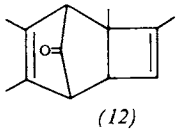
(9)



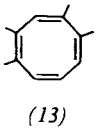
(10)



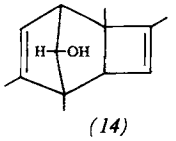
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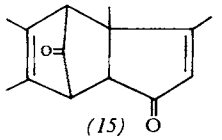
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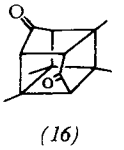
(13)



(14)



(15) O



(16)

and *(13)*[2] (total yield 8.8%), *o*-xylene (0.6%), durene (1.0%), pseudocumene (3.0%), an inseparable mixture of ketones (11.5%), the dimer *(15)* of dimethylcyclopentadienone *(3)* (8.1%), and the cage diketone *(16)* (6.0%). The decisive intermediates seem to be the ketones, for the isolated mixed ketones gave the same hydrocarbons on renewed irradiation [though less *(10)* was formed] as did *(1)*.

The aromatic compounds were identified by gas chromatography and NMR spectroscopy. From the mixture of cyclooctatetraenes, only *(13)* could be separated cleanly; according to analysis of the NMR spectrum, the mixture contained the proportions *(7)*:*(10)*:*(13)* = about 5:2:10. In order to analyze the mixed ketones better, they were reduced by $LiAlH_4$; the alcohols formed could be separated by column chromatography; each ketone gave only one alcohol, stereospecifically. The alcohols *(5)* and *(11)*, and thus the ketones *(6)* and *(12)*, occurred in the ratio 1:2.

Cpd.	M.p. (°C)	NMR [a]
(5)	137–139	6.04 (1) T, 7.12 (2) M, 7.75 (2) M, 8.18 (1) br. S, 8.42 (6) S, 8.53 (6) S
(11)	88–89	4.55 (1) Q, 5.92 (1) T, 7.25 (1) M, 7.75 (1) M, 8.10 (2) M, 8.40 (3) br. S, 8.46 (3) S, 8.49 (3) D, 8.57 (3) S
(14)	40–41.5	[b] 4.55 (2) M, 6.40 (1) M, 7.66 (1) M, 8.08 (1) M, 8.43 (3) D, 8.52 (1) S, 8.56 (3) D, 8.63 (3) S, 8.94 (3) S
(15)	142–144 [c]	3.99 (1) Q, 6.94 (1),double D, 7.36 (1) D, 7.58 (1) D, 7.95 (3) D, 8.32 (6) S, 8.65 (3) S
(16)	148–150 [d]	7.69 (2) S, 7.86 (2) S, 8.79 (6) S, 8.89 (6) S

[a] τ values, no. of protons, type of splitting; solvent $CDCl_3$; TMS as internal standard. [b] In CCl_4. [c] IR (CCl_4): C=O bands at 1705 and 1785 cm^{-1}. [d] IR (CCl_4): band at 1755 cm^{-1}.

The alcohol *(8)* was not found, but instead a small amount of the isomeric *(14)*. [The structure was derived from the NMR spectrum.]

For the following reason, the products isolated prove that cyclobutadiene is actually formed on photolysis of anhydrides of type *(1)*: photolytic removal of CO_2 to yield *(2)*, ring opening of the latter to yield *(3)*, and addition to *(3)* of the dimethylcyclobutadiene arising from *(2)* on elimination of CO should give the ketones *(6)*, *(9)*, and *(12)*. Insofar as cyclobutadiene is a rectangular singlet molecule with localized double bonds[3] and undergoes rapid valence isomerization, the three ketones must arise in the proportion 1:1:2 – provided that steric factors do not lead to selectivity. In all the other plausible ways [dimerization of *(2)* or *(3)*, or reaction of *(2)* with *(3)* and subsequent removal of CO], only the ketones *(6)* and *(9)* or compounds of totally different structure would be formed. The relative amounts of the tetramethylcyclooctatetraenes isolated, and of the aromatic compounds and alcohols, indicate that dimethylcyclobutadiene reacts in the two forms *(4a)* and *(4b)*, the doubly methylated double bond in *(4a)* being, however, less amenable to addition than the unsubstituted double bond[***].

Received: November 18, 1968 [Z 907 IE]
German version: Angew. Chem. *81*, 114 (1969)

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

[1] Part 6 of Small Rings. – Part 5: *G. Maier* and *U. Mende*, Angew. Chem. *80*, 532 (1968); Angew. Chem. internat. Edit. *7* 537 (1968).

[2] *R. Criegee*, *W. Eberius*, and *H.-A. Brune*, Chem. Ber. *101*, 94 (1968).

[3] *M. J. S. Dewar* and *G. J. Gleicher*, J. Amer. chem. Soc. *87*, 3255 (1965).

[***] *Note added in proof* (January 8, 1969): On irradiation of tetramethylcyclobutenedicarboxylic anhydride [1] in an organic glass (ethanol, isopentane, ether) at –196 °C, a deep yellow color appears which disappears immediately when the matrix melts. The adduct of tetramethylcyclobutadiene to tetramethylcyclopentadienone and the dimer of tetramethylcyclopentadienone [permethylated analogs of *(6)* and *(15)*] were isolated as the sole products. These compounds could not have been present during photolysis, since otherwise – as shown by control experiments – their photoproducts [*e.g.* octamethylcyclooctatetraene or the permethylated cage diketone *(16)*] would also have been detectable.

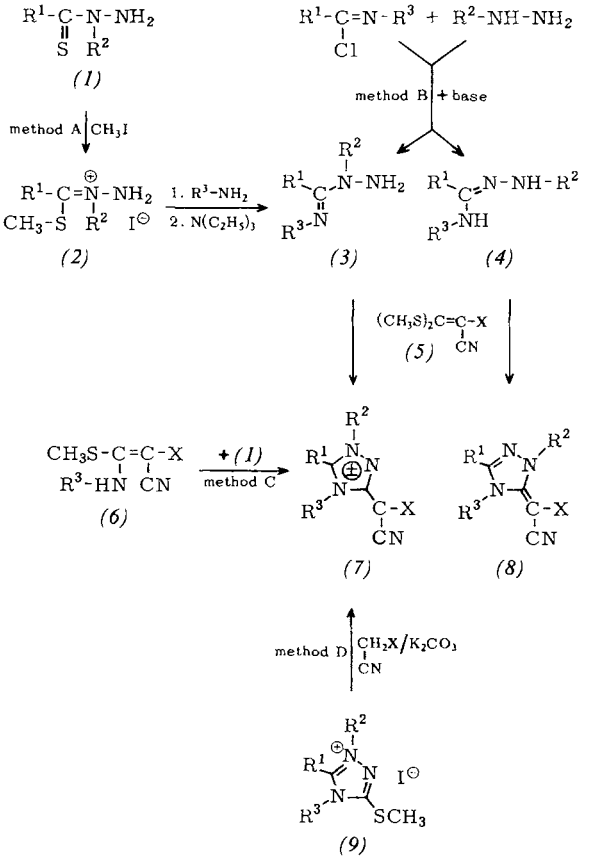
These results show that tetramethylcyclobutadiene and tetramethylcyclopentadienone can exist as monomers when frozen into a glass at the temperature of liquid nitrogen.

Mesoionic 3-Methylene-1,2,4-triazoles[**]

By *R. Grashey* and *Margit Baumann*[*]

Numerous mesoionic systems[1] contain heteroelements bound exocyclically. We now report mesoionic 1,2,4-triazole derivatives *(7)* with carbon as the exocyclic atom; we obtained these from N^2,N^3-disubstituted amidrazones and 3,3-bis(methylthio)acrylonitrile derivatives *(5)*[2,3].

The classical synthesis of amidrazones of type *(3)* (method **B**)[4,5] from imidoyl chlorides and monosubstituted hydrazines gives mainly N^1,N^3-disubstituted amidrazones *(4)* when arylhydrazines are used, and the products *(3)* and *(4)* must be separated before the treatment with *(5)*. However, if methylhydrazine in acetonitrile solution is used, then formation of *(3)* (R^2 = CH_3) is dominant, so that isolation of the amidrazones can be omitted and the mixture of *(7)* with a little *(8)* arising in the subsequent reaction with *(5)* can be readily separated by crystallization.



Cpd.	R^1	R^2	R^3	X	Method	Yield (%)	M.p. (°C)
(7a)	CH_3	CH_3	C_6H_5	CN	D	21	334–335
(7b)	CH_3	C_6H_5	C_6H_5	CN	D	41	304–305
(7c)	C_6H_5	CH_3	CH_3	CN	C	34	307–308
(7d)	C_6H_5	CH_3	C_6H_5	CN	A [a]	57	254–256
					B [a]	63	
					D	32	
(7e)	C_6H_5	CH_3	C_6H_5	CO_2CH_3	A [a]	79	296–297
					B [a]	52	
(7f)	C_6H_5	CH_3	p-$CH_3C_6H_4$	CN	A [a]	59	252–253
(7g)	C_6H_5	CH_3	p-$CH_3C_6H_4$	CO_2CH_3	A [a]	61	238–239
(7h)	C_6H_5	CH_3	p-$CH_3OC_6H_4$	CO_2CH_3	A	83	238–239
(7i)	C_6H_5	C_6H_5	CH_3	CN	C	38	299–301
(7j)	C_6H_5	C_6H_5	C_6H_5	CN	B	99	335–336
(7k)	C_6H_5	C_6H_5	C_6H_5	CO_2CH_3	B	97	279–280
(7l)	C_6H_5	C_6H_5	p-$CH_3OC_6H_4$	CO_2CH_3	A	87	275–276
(7m)	C_6H_5	C_6H_5	p-ClC_6H_4	CN	A	90	328–329

[a] Working *in situ*.

The action of primary amines on methylthiohydrazonium iodides *(2)* gives exclusively N^2,N^3-disubstituted amidrazones *(3)* (method A). In this case also the amidrazones are often prepared only *in situ*.

Lower yields are obtained on treatment of thiohydrazides *(1)* with 3-amino-3-(methylthio)acrylonitrile derivatives *(6)* [2,6] (method C), a reaction which in boiling dimethylformamide or acetonitrile containing potassium carbonate leads directly to the triazole derivatives *(7)*. A further possibility (method D) is offered by the action of malonic acid derivatives and potassium carbonate on methylthio-1,2,4-triazolium salts *(9)*, which are obtained from the mesoionic 1,2,4-triazolethiones [1,5] and methyl iodide in acetonitrile at 80 °C.

The colorless to greenish-yellow triazoles *(7)* are characterized by ease of crystallization and great stability. Analytical and spectral data (no heterocumulene band at 2000–2070 cm^{-1}), as well as molecular-weight determinations accord with the proposed structures. The nitrile or ester groups of *(7)* and *(8)* absorb between 2146 and 2193 and between 1653 and 1667 cm^{-1}, respectively, thus showing the expected bathochromic shift.

Preparation of (7e) by method (A):

Compound *(2)* [R^1 = C_6H_5, R^2 = CH_3] (1.232 g) is heated with aniline (3 ml) on a steam bath for 30 min. The crude amidrazonium salt, which crystallizes when the reaction mixture is digested with ether, is taken up in acetonitrile (10 ml) and heated with *(5)* [X = CO_2CH_3] (0.813 g) and triethylamine (1 ml) for 10 h under reflux. After concentration under vacuum, addition of methanol results in precipitation of *(7e)* (1.05 g); colorless needles having m.p. 296 to 297 °C (from acetonitrile).

Received: November 30, 1968 [Z 908 IE]
German version: Angew. Chem. *81*, 115 (1969)

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

[1] For reviews, see *W. Baker* and *W. D. Ollis*, Quart. Reviews *11*, 15 (1957); *L. B. Kier* and *E. B. Roche*, J. pharmac. Sci. *56*, 149 (1967).

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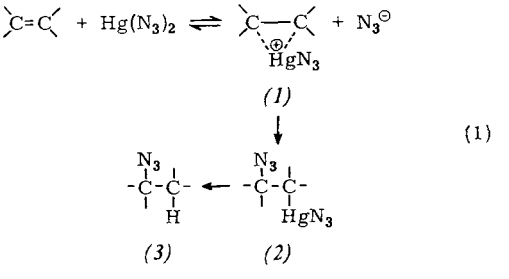
A New Synthesis of Alkyl Azides [**]

By *C. H. Heathcock* [*]

Alkenes react with mercury(II) salts in aqueous solution to yield β-hydroxyalkylmercurials [1], which may be reduced *in situ* by sodium borohydride to yield alcohols [2]. We have found that an adaptation of this procedure allows the convenient synthesis of alkyl azides from certain alkenes.

General procedure:

To a solution of 0.3 moles of sodium azide and 0.1 mole of mercuric acetate in 200 ml of 50% aqueous tetrahydrofuran [3] is added 0.1 mole of alkene. After stirring at 50 to 90 °C for an appropriate period (16–70 h), the two-phase mixture is diluted with 100 ml of 15% aqueous potassium hydroxide and treated with a solution of 2 g sodium borohydride in 100 ml of 15% potassium hydroxide solution. The alkyl azide is isolated by ether extraction followed by distillation at reduced pressure.



(1)

The method works well for the synthesis of secondary or tertiary alkyl azides from terminal alkenes or strained cyclic alkenes (norbornene) but fails in the case of normal internal

Table 1. Synthesis of alkyl azides from alkenes.

Alkene	Product	Time (h)	Temp. (°C)	Yield (%)
1-heptene	2-heptyl azide	17	50	88
1-octene	2-octyl azide	24	30	55
3,3-dimethyl-1-butene	3,3-dimethyl-2-butyl azide	43	80	61
2-methyl-1-heptene	2-methyl-2-heptyl azide	40	90	50
methylenecyclohexane	1-methylcyclohexyl azide	68	90	60
norbornene	*exo*-2-norbornyl azide	16	50	75
cyclohexene	cyclohexyl azide	68	90	4
methylcyclohexene	—	40	90	< 1
styrene	—	40	90	< 1

alkenes, either disubstituted or trisubstituted. It is of interest that such unreactive alkenes do not undergo hydroxymercuration either.

The observed order of reactivity closely parallels the known order of alkene-silver(I) stability constants[4], and suggests a mechanism (eq. 1) involving a rapid prior equilibrium, giving an ion *(1)*, which reacts with azide ion in a slow step to yield *(2)*. The remarkable efficiency with which azide competes with water in the reaction argues strongly for the existence of the ionic intermediate *(1)*, since $k_{N_3^-}/k_{H_2O}$ is known to increase greatly with increasing delocalization of a cation[5].

Received: November 28, 1968 [Z 909 IE]
German version: Angew. Chem. *81*, 148 (1969)

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[3] Caution: Solid mercuric azide is sensitive to light and shock. The salt is insoluble in water, but readily dissolves in 50% aqueous tetrahydrofuran. We have found that such solutions may be handled without danger.

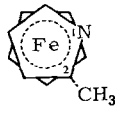
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Optically Active 2-Methylazaferrocene[**]

By *K. Bauer, H. Falk*, and *K. Schlögl*[*]

Unsymmetrically disubstituted metallocenes belong to the point group C_1; they are therefore chiral and can be obtained in optically active forms[1]. This symmetry condition is also valid for homoannularly monosubstituted azaferrocenes, which therefore should be resolvable into optical antipodes. This could now be verified for 2-methylazaferrocene *(1)*.



(−)-(2*R*)-*(1)*

Racemic *(1)* was obtained in 45% yield as an oil from the potassium salt of 2-methylpyrrole and $C_5H_5Fe(CO)_2I$ in dioxane[2]. Elemental analysis, NMR spectrum [$CDCl_3$, methyl protons at δ = 2.32, ring protons at 5.34 (1H), 4.50 (2H), and 4.22 (5H)], and mass spectrum[3] [*m/e* = 201 $(C_{10}H_{11}FeN)^+$, 186 $(M-CH_3)^+$, 135 $(C_5H_5FeN)^+$, 121 $(C_5H_5Fe)^+$, and 80 $(C_5H_6N)^+$] prove the structure *(1)*.

Reaction of *(1)* with an equimolar amount of (−)-6,6′-dinitrodiphenic acid in ethanol afforded an amorphous precipitate; addition of petroleum ether to the mother liquor yielded a crystalline, rather unstable salt, which was recrystallized twice from acetone. This salt afforded levorotatory *(1)*: $[\alpha]_D^{20}$ = −62° (*c* = 0.04, cyclohexane)[4], m.p. 42–52 °C. (+)-*(1)*, $[\alpha]_D^{20}$ = +33°, was obtained from the mother liquor of the salt crystallization.

The ORD and CD curves, and the UV spectrum of (−)-*(1)* are reproduced in Fig. 1. In 0.1 N hydrochloric acid or on addition of $BF_3{\cdot}O(C_2H_5)_2$ the $\Delta\varepsilon$-values are increased, whereas the sign of rotation remains unchanged and the Cotton effects are shifted only slightly: *(1)* in ether, −0.15 (515 nm) and +0.15 (445 nm); *(1)* in 0.1 N HCl, −0.19 (496 nm) and +0.20 (421 nm); *(1)* · BF_3 in ether, −0.31 (500 nm) and +0.32 (435 nm) (cf. Fig. 1).

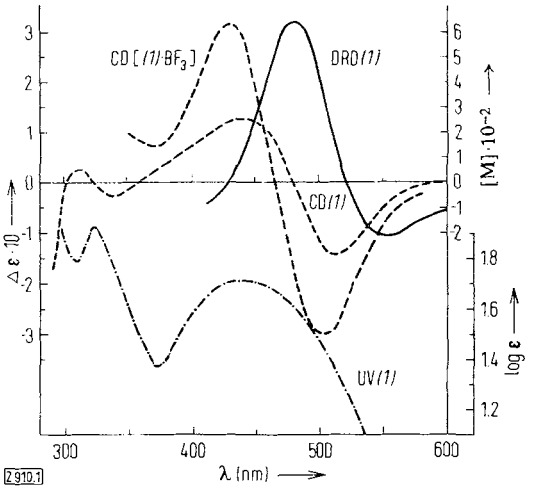


Fig. 1. ORD and CD curves and UV spectrum of *(1)* in cyclohexane, CD curve of *(1)* · BF_3 in ether.

The ORD curve of *(1)* is very similar to that of α-ethynyl- and α-cyanomethylferrocene, compounds *(2)* and *(3)*[5], respectively, in which no conformational contributions (of substituents) to the optical activity are possible either (cf.[1]).

This analogy, together with the fact that salt formation (protonation or addition of BF_3) increases the activity of the "metallocene absorption band" in the region of 430 nm, may be considered as evidence that the ring nitrogen dominates over the methyl group with regard to the perturbance of the metallocene chromophore[6], as does C≡CH or C≡N in *(2)* and *(3)*, respectively.

Therefore, the assumptions seems to be justified that (−)-*(1)*, (−)-*(2)*, and (−)-*(3)* with positive Cotton effects around 430 nm have identical chiralities, and that (−)-*(1)* consequently [by analogy with (−)-*(2)*, (−)-*(3)*, and (+)-methylferrocene-α-carboxylic acid][5] has the absolute configuration (2*R*)[1].

Received: December 9, 1968 [Z 910 IE]
German version: Angew. Chem. *81*, 150 (1969)

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[**] This work was supported by the "Österr. Fonds zur Förderung der wissenschaftlichen Forschung".

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[3] We are indebted to Dr. *G. Schaden*, Darmstadt, for recording, and Dr. *H. Egger*, Wien, for the interpretation of the mass spectrum. For the mass spectrum of azaferrocene cf.: *F. Seel* and *V. Sperber*, J. organometallic Chem. *14*, 405 (1968).

[4] The optical purity of *(1)* is unknown. A tentative estimate (30–40%) seems feasible on comparing the $\Delta\varepsilon$-values (around 430 nm, "metallocene absorption band") of *(1)* with those of compounds such as *(2)*, *(3)*, or methylferrocene-α-carboxylic acid, which are similar with regard to the origin of their optical activity.

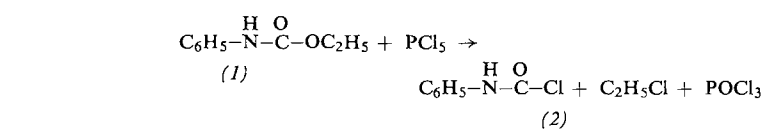
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[6] The $\Delta\varepsilon$-values of *(1)* and its salts are almost directly proportional to the molecular refractivities of $N_{arom.}$, NH^+, and N · BF_3; the dipole moment of azaferrocene in cyclohexane is 2.06 ± 0.05 D.

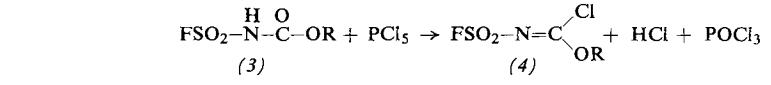
Action of Phosphorus Pentachloride on *N*-(Halogenosulfonyl)urethanes[1]

By *H. W. Roesky*[*]

Lengfeld and *Stieglitz*[2] obtained phenylcarbamoyl chloride *(2)* by the action of PCl_5 on *N*-phenylurethane *(1)*, but *Werner*[3] was able to isolate only phenyl isocyanate after this reaction. If, however, the phenyl group is replaced by a



more electronegative one, *e.g.*, fluorosulfonyl, then ester chlorides *(4)* of *N*-(fluorosulfonyl)carbonimidic acid are formed.

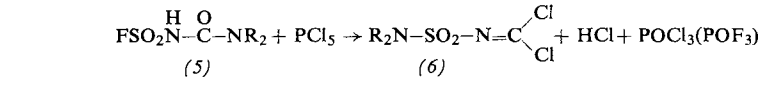


(4a), R = CH_3
(4b), R = C_2H_5
(4c), R = n-C_3H_7

	(4a)	*(4b)*	*(4c)*	*(4d)*
B.p. (°C/torr)	31–32/0.02	37–38/0.03	57–59/0.01	63–66/0.01
d_4^{20}	1.5829	1.4607	1.3932	1.5066
n_D^{20}	1.4349	1.4340	1.4368	1.4910
Yield (%)	57	53	59	63
Mol. wt. (cryoscop. in C_6H_6)	179.5	197	211	207
ν(C=N) (cm^{-1})	1610	1610	1610	1590
δ ^{19}F (ppm)	−51.8	−52.0	−52.3	–
δ ^1H (ppm)	−4.24	−1.52 (CH_3) −4.65 (CH_2)	−1.10 (CH_3) −1.87 (CH_2) −2.74 (CH_2O)	−1.66 (CH_3) −4.80 (CH_2) J_{H-H} = 7 Hz

At room temperature the compounds *(4)* (see Table) are colorless liquids with an aromatic odor and can be distilled at reduced pressure without decomposition.

If the alkoxy group in *(3)* is replaced by a dialkylamino group, then the analogous reactions with PCl_5 are accompanied by a rearrangement that leads to the known[4] dialkylaminosulfonyl isocyanide dichlorides *(6)*, together with POF_3.



Dimethylaminosulfonyl isocyanide dichloride: b.p. 162 to 163 °C/0.01 torr, ν(N=C) = 1600 cm^{-1}. Diethylaminosulfonyl isocyanide dichloride: m.p. 55–57 °C, ν(N=C) = 1580 cm^{-1}.

Only compound $ClSO_2-N=C(Cl)OC_2H_5$ *(4d)* could be isolated after treatment of the corresponding chlorine derivatives of *(3)* with PCl_5. The products with R = CH_3 or n-C_3H_7 cannot be distilled without decomposition at oil-pump vacuum.

Experimental:

1 mole of an alcohol is added dropwise with ice-cooling and stirring to a solution of 1 mole of fluorosulfonyl isocyanate (FSO_2NCO) in 300 ml of CCl_4[5]. 1 mole of PCl_5 is then added (or 1 mole of PCl_3 and chlorine is passed into the mixture), and the mixture is heated slowly and finally refluxed for about 6 h. CCl_4 and $POCl_3$ are then collected in a cold trap (acetone/dry ice) at water-pump vacuum, and the residue is distilled at oil-pump vacuum through a 30-cm packed column.

For *(4d)* the amount of solvent used was 200 ml and the mixture was refluxed for 3.5 h.

All the compounds were characterized by elemental analyses.

Received: July 8, 1968; revised: October 9, 1968 [Z 911 IE]
German version: Angew. Chem. *81*, 119 (1969)

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Addition Compound or Oxonium Salt? The Crystal Structures of Two Acid Hydrates

By *D. Mootz, J. Goldmann*, and *H. Wunderlich*[*]

Crystalline "hydrates" of strong acids (*e.g.* of $HClO_4$, HCl, HNO_3, *etc.*) contain H_3O ions and are therefore to be regarded as oxonium salts, $H_3O^+A^-$. In contrast, the compounds of weak acids (*e.g.* of carboxylic acids) with water are true acid hydrates, HA · H_2O. The methods available for distinguishing between these possibilities include crystal structure analysis, as well as IR and NMR spectroscopy; the first technique makes possible a simultaneous study of the stereochemistry of hydrogen bonds in such compounds, which is often of interest.

We have been able to show by crystal structure analyses of 2-phosphoric acid-1-water *(1)* and 1,2-ethanedisulfonic acid dihydrate *(2)* that *(1)* is a true acid hydrate and *(2)* is a dioxonium salt. This had already been established for the latter compound by *Blaschette* and *Bürger*[1], who used an IR spectroscopic technique.

As stated by *Smith, Brown*, and *Lehr*[2], the addition compound *(1)* crystallizes monoclinically in the space group $P2_1/c$ with four formula units in the unit cell; it is isomorphous with the corresponding arsenic compound[3]. The structure was determined from 832 independent reflections (molybdenum radiation, Weissenberg and precession photographs), and refined in the usual way (R = 0.084). The hydrogen atoms could not be located without making prior assumptions. Nevertheless, the question whether an oxonium salt or an acid hydrate is present can be answered unambiguously on the basis of the P–O bond lengths observed: In each of the two independent PO_4 tetrahedrons there are observed one particularly short bond length and three longer ones (Fig. 1[5], standard deviation 0.005 to 0.007 Å), as in the crystal structure of anhydrous phosphoric acid[4]. This finding sup-

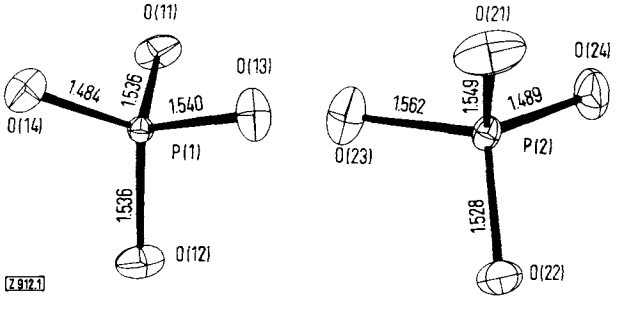


Fig. 1. The two independent PO_4 tetrahedrons in the crystal structure of 2 H_3PO_4 · H_2O *(1)*. The bond lengths are given in Å.

ports the structure $2\,H_3PO_4 \cdot H_2O$. In the case of an oxonium salt $H_3O^+H_2PO_4^- \cdot H_3PO_4$, however, two short and two long bonds should be observed in the anionic PO_4 tetrahedron.

Similar arguments applied to the structure of *(2)*, which has been determined much more accurately, indicate the presence of oxonium ions. Compound *(2)* crystallizes monoclinically in the space group $P2_1/c$ with two centrosymmetric formula units in the unit cell. With 746 independent photographic data (Cu radiation) an *R* factor of 0.059 was obtained.

The three S–O bonds are of equal length (Fig. 2, standard deviation 0.003 Å), thus clearly indicating the transfer of the acidic proton to the water molecule since the difference in length between an S–O and an S–OH bond is very large; in the case of oxonium hydrogen sulfate, $H_3O^+HSO_4$, it is 0.11 Å [6]. The difference Fourier synthesis of *(2)* was not so unambiguous regarding the hydrogen atoms of the oxonium ion.

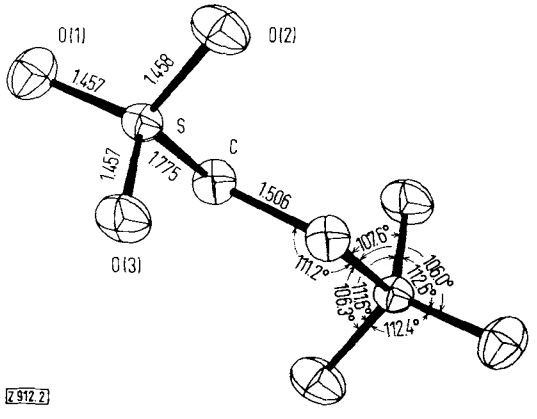


Fig. 2. The anion in the crystal structure of $2\,H_3O^+[O_3SCH_2CH_2SO_3]^{2-}$ *(2)*. The bond lengths are given in Å.

Relatively short hydrogen bonds occur in both crystal structures. Compound *(1)* shows four bridges of the type P–OH···O=P having O···O distances between 2.510 and 2.550 Å, and two of the type P–OH···OH_2 of 2.620 and 2.638 Å. Those bridges having the water molecule as proton donor are longer and cannot be assigned unequivocally without knowledge of the positions of the protons (five O···O distances between 2.897 and 3.013 Å). In *(2)* the oxonium ion is coordinated pyramidally and acts as proton donor for three short hydrogen bonds to independent oxygen atoms in different anions. The O···O distances lie between 2.549 and 2.578 Å.

Received: October 10, 1968 [Z 912 IE]
German version: Angew. Chem. *81*, 116 (1969)

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Calculation of the "Optical Electronegativity" of Transition Metal Ions from NQR Coupling Constants

By *P. Machmer* [*]

The "optical electronegativity" $\chi_{opt}(M)$ of the central ions of octahedral complexes has previously been determined from the wave number *E* of the first intense charge transfer band. With the aid of equation (1) [1]

$$E = 3 \times 10^4\ cm^{-1}\ [\chi_{opt}(L) - \chi_{opt}(M)] \qquad (1)$$

the relevant UV spectroscopic data afforded the values of $\chi_{opt}(M)$ listed in Table 1. [$\chi_{opt}(L)$ denotes the "optical electronegativity" of the ligands L].

In conjunction with the examination of the nuclear quadrupole resonance (NQR) spectra [2–5] of inorganic compounds, it can be shown that characteristic electronegativity values can also be derived from the NQR coupling constants of solids. The effectiveness of this technique, which is independent of solvent effects, will now be demonstrated for octahedral chloro complexes of a number of transition metal ions. The electronegativity values $\chi(M^{n+})$ of the central ions (Table 1) were calculated according to equation (2)

$$\chi(M^{n+}) = 0.38 \times \sqrt{\left(\frac{e^2Qq_{mole}}{h}\right)_{^{35}Cl}} \qquad (2)$$

from ^{35}Cl–NQR coupling constants (values of e^2Qq_{mole}/h for the ^{35}Cl ligands were taken from the literature [6–12]; the dimensions of the proportionality factor 0.38 are $MHz^{-1/2}$.

Table 1. Electronegativities calculated from NQR coupling constants of transition metal ions in chloro complexes compared with the optical values.

M^{n+}	$\chi(M^{n+})$	$\chi_{opt}(M)$ [13–15]	Complex	e^2Qq_{mole}/h for the ^{35}Cl ligands [6–12] (MHz)
W^{4+}	1.71	1.67 [13]	K_2WCl_6	20.44
Re^{4+}	2.00	2.0	K_2ReCl_6	27.78
Os^{4+}	2.20	2.2	K_2OsCl_6	33.68
Ir^{4+}	2.44	2.4 [14]	K_2IrCl_6	41.46
Pt^{4+}	2.73	2.7	K_2PtCl_6	51.64
				51.82
				52.04
Pd^{4+}	2.76	2.7	K_2PdCl_6	53.10
Pt^{2+}	2.27	2.3	K_2PtCl_4	35.85

The relationship between the electronegativity $\chi(M^{n+})$ of the central ion and the NQR coupling constants of the ^{79}Br ligands can also be formulated quantitatively for the analogous bromo complexes (proportionality factor $0.134\ MHz^{-1/2}$).

$$\chi(M^{n+}) = 0.134 \times \sqrt{\left(\frac{e^2Qq_{mole}}{h}\right)_{^{79}Br}} \qquad (3)$$

Table 2. NQR coupling constants of the halogen ligands ^{35}Cl and ^{79}Br calculated from equations *(2)* and *(3)*.

Complex	$\chi_{opt}(M)$ [15]	$(e^2Qq_{mole}/h)^{35}Cl$ or ^{79}Br (MHz)
$KPtCl_3C_2H_4$	2.3	36.6
K_3IrCl_6	2.25	35
K_2RuCl_6	2.4	40
K_3RhCl_6	2.3	36.6
K_3MoCl_6	1.7	20
K_2WBr_6	1.71 [a]	167.6
K_2OsBr_6	2.2	268
K_2IrBr_6	2.4	319

[a] From Table 1.

If χ_{opt} (M) is known with sufficient accuracy, it is also possible to estimate the NQR coupling constants e^2Qq_{mole}/h on the basis of equations (2) and (3). Values thus obtained for the NQR coupling constants of complexes whose NQR spectra have not yet been recorded are given in Table 2 (estimated error ± 5%). The validity range of the considerations sketched out in this communication remains to be defined.

Received: August 26, 1968 [Z 914 IE]
German version: Angew. Chem. *81*, 117 (1969)

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ESR Measurements under Pressure: Effect of Pressure on Chemical Equilibria involving Solvated Electrons

By *K. W. Böddeker, G. Lang,* and *U. Schindewolf*[*]

The physical properties of solvated electrons in liquid ammonia are highly pressure dependent[1]. As will be shown in this communication by considering various equilibria involving solvated electrons, the chemical properties of electrons dissolved in ammonia or in methylamine-ammonia mixtures (amine system) also are strongly affected by pressure.

The experiments were carried out ESR-spectrometrically since the solvated electrons, and in many instances the products of their reactions as well, exhibit characteristic ESR signals permitting a quantitative detection. We have investigated the reversible formation of solvated electrons by the reaction of amide ions with hydrogen[2,3]

$$e^- + NH_3 \rightleftharpoons {}^1/_2 H_2 + NH_2^- \quad (1)$$

and equilibria between solvated electrons and arene radical anions, *e.g.*

$$e^- + C_6H_6 \rightleftharpoons C_6H_6^- \quad (2)$$

The experimental arrangement is shown in Fig. 1a. The sample cell, a length of quartz capillary extending through the temperature-controlled cavity of the ESR spectrometer, is connected to the pressure generator and the storage autoclaves *via* steel capillaries by means of the pressure coupling shown in Fig. 1b[4]. The pressure generator with manometer is filled with pentane as pressure-transmitting fluid and can be closed to the remaining apparatus at valve 1. The storage autoclaves contain in glass vessels (i) the solution to be investigated (this autoclave can be cooled to −80 °C) and (ii) pure solvent used to clean the apparatus. The quartz capillaries (i. d., 1 mm; o. d., 5 mm) withstand pressures of up to 500 atm.

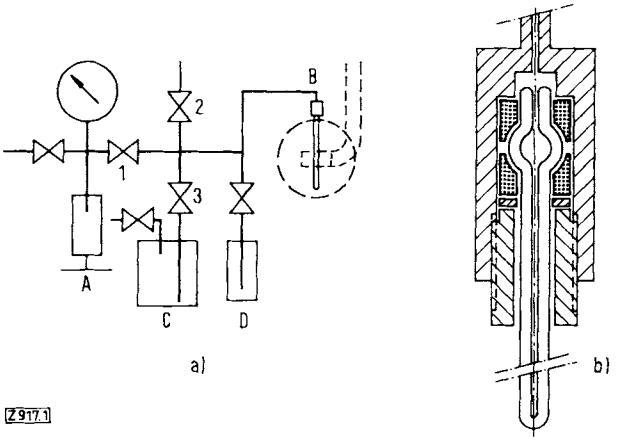


Fig. 1. a) Experimental arrangement for ESR measurements under pressure. A: pressure generator with manometer; B: sample cell with pressure coupling; C, D: storage autoclaves for solution and pure solvent; 1–3: valves; magnet and microwave guide of the ESR spectrometer are indicated by dotted lines.

b) Pressure coupling with Teflon packings connecting the quartz capillary.

To study the equilibrium (1), a 1 M solution of potassium amide in ammonia was saturated, at room temperature, with 100 atm of hydrogen in the storage autoclave and was transferred into the sample cell under this pressure. The intensity of the ESR signal of the solvated electrons, which is proportional to their equilibrium concentration ($< 10^{-4}$ M[3]), decreases by a factor of 2.3 as the pressure is raised by 300 atm (Fig. 2).

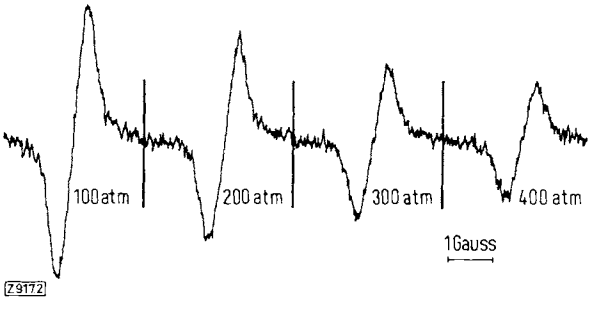


Fig. 2. ESR signal of the solvated electrons in a hydrogen-saturated (100 atm) solution of potassium amide (1 M) in ammonia at varying pressures at room temperature.

For the investigation of equilibrium (2) a solution of potassium (10^{-2} M) and benzene (10^{-1} M) in methylamine-ammonia (2:1) was prepared at −78 °C in the storage autoclave and was forced into the pre-cooled sample cell by inert gas under pressure (*e.g.*, nitrogen, 30 atm). The ESR spectrum of this system shows both the single-line signal of the solvated electrons and the spectrum of the benzene radical anions consisting of 7 lines of binomial intensity distribution (Fig. 3)[5]. On raising the pressure by 300 atm at −120 °C the concentration of solvated electrons decreases by a factor of 2.6 while that of the benzene radical anions increases by a factor of 3.2. – A corresponding pressure dependence was observed with other simple aromatic radical anions.

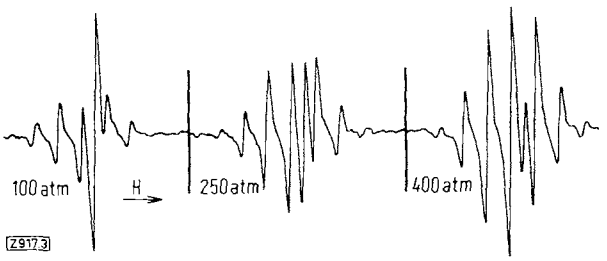


Fig. 3. Effect of pressure on the equilibrium (2) in methylamine-ammonia (2:1) at −120 °C. The electron signal appears superimposed on the ESR septet of the benzene radical anions.

According to the equation

$$d \ln K/dp = -\Delta V/RT \qquad (3)$$

the displacement of the equilibria (1) and (2), as determined from the spectra, results in a volume change associated with the reaction ΔV (= molar volume of the products minus molar volume of the reactants) of −63 and −71 ± 5 ml/mole, respectively, reflecting the large apparent volume of the electrons dissolved in the amine system.

For comparison, the equilibrium (2) was studied in tetrahydrofuran-dimethoxyethane (2:1; ether system), in which only the benzene radical anions give rise to an ESR spectrum. The intensity of the $C_6H_6^-$ spectrum, produced in the sample cell by reaction of a benzene-ether solution at the surface of a sodium wire, is independent of pressure in the region of 100 to 400 atm at −100 °C. This result indicates that the apparent volume of the diamagnetic electron species in the ether system is smaller than that of the electrons dissolved in the amine system.

Received: October 31, 1968 [Z 917 IE]
German version: Angew. Chem. *81*, 118 (1969)

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[5] The equilibrium is strongly temperature dependent; under the condidions used, the $C_6H_6^-$ spectrum becomes noticeable below about −100 °C.

Crystal Structure of 4-Thiouridine

By *W. Saenger* and *K. H. Scheit* [*]

After 4-thiouridine *(1)* had been discovered to be a constituent of tRNA of *E.coli* [1], *Lipsett* and *Doctor* [2] were able to show that tyrosine-specific tRNA from *E.coli* contains two 4-thiouridine units per molecule. Although the chemical and physical properties of *(1)* in oligo- and polynucleotides [3,4] have been investigated, the function of this nucleoside in *E.coli*-tRNA remains unclear. Since we had at our disposal analytically pure, crystalline *(1)* [5,6], we attempted to determine its structure with a view to contributing to the solution of this problem.

Compound *(1)* could be obtained in the form of yellow prismatic crystals by slow evaporation of its aqueous solution. Weissenberg photographs and diffractometer measurements showed the space group to be C2 and the dimensions of the unit cell to be a = 13.174, b = 7.492, c = 13.042 Å, β = 98.10 °. 1400 reflections were recorded with an automatic diffractometer and corrected for geometrical factors but not for absorption. The structure analysis was performed by the heavy atom technique. The usual Patterson and Fourier syntheses and five cycles of isotropic and anisotropic refinement resulted in an R factor of 0.10.

At this stage a number of structural peculiarities become clear (see Fig. 1):

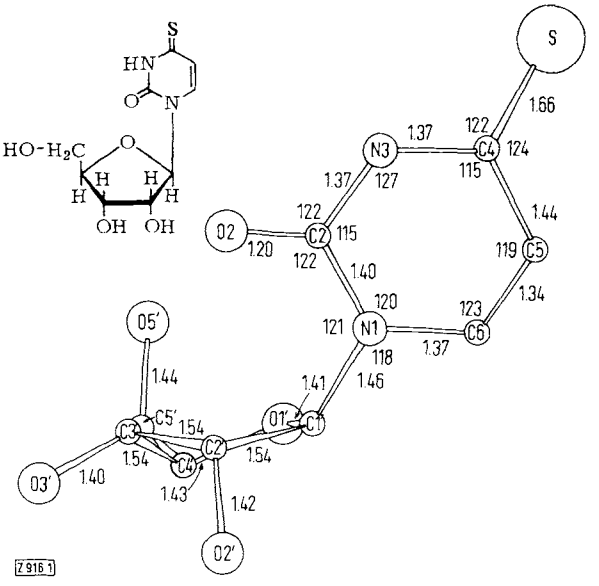


Fig. 1. Crystal structure of 4-thiouridine. Projection onto 100. Bond lengths (Å) and angles (°) not shown in the Figure are:

C4′–C5′ = 1.50	
C1′–C2′–C3′ = 103	N1–C1′–C2′ = 119
C2′–C3′–C4′ = 101	N1–C1′–O1′ = 109
C3′–C4′–O1′ = 103	C1′–C2′–O2′ = 105
C4′–O1′–C1′ = 110	O2′–C2′–C3′ = 110
O1′–C1′–C2′ = 107	C2′–C3′–O3′ = 115
C3′–C4′–C5′ = 119	O3′–C3′–C4′ = 114
C5′–C4′–O1′ = 110	C4′–C5′–O5′ = 113

a) Comparison of the nitrogen-containing rings in barium 5′-uridinephosphate [7] *(2)* and in *(1)* shows a similar arrangement of bond lengths and angles. The C-5–C-4 bond length in *(1)* is 0.03 Å greater than in *(2)*, whereas the N-3–C-4 and N-3–C-2 bond lengths are shorter by 0.025 Å, and the bond angle C-2–N-1–C-6 is reduced from 124 to 120 °.

The bond lengths C-2–O-2 and C-4–S are characteristic for keto structures [8,9]. The six-membered ring is largely planar; the ring atoms deviate from the "best" plane by no more than 0.04 Å but S and C-1 stand out from this plane by 0.48 and −0.23 Å respectively.

b) The ribose unit is puckered; the interatomic distances and bond angles agree well with those found by other authors [7,10]. C-3′ lies out of the "best" plane, which can be constructed through C-1′, C-2′, C-4′, and O-1′, by 0.59 Å, and is on the same side as C-5′; the ribose is therefore in the *endo* conformation.

c) The most surprising feature of the structure is the *syn* conformation of the nucleoside. The angle of twist about the glycosidic C-1′–N-1 bond (as defined by *Trueblood, Horn*, and *Luzzati* [10]) is +83 °. As far as we know, this conforma-

tion has not previously been observed for any pyrimidine nucleoside.

d) The molecules are arranged in the crystal such that hydrophobic and hydrophilic regions are oriented along the *a* axis. The nitrogen-containing rings are stacked parallel to one another, separated by about 3.3 Å, and form a hydrophobic channel along this axis. The ribose units occupy the interior of the unit cell and are bound to one another by water molecules (one and a half per asymmetric unit).

Further refinement of the structure is in progress.

Received: October 21, 1968 [Z 916 IE]
German version: Angew. Chem. *81*, 121 (1969)

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Hydridophosphinetris(trifluorophosphine)cobalt(I)

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Transition metal complexes containing PH_3 as a unidentate ligand have only recently become known [1,2]. Herein we report the compound $HCo(PF_3)_3PH_3$ *(1)*, which is the first example both of a hydrido-phosphine metal complex and of a phosphine-trifluorophosphine complex.

The new compound is a pale yellow sublimable solid (m.p. $\sim 25\,^{\circ}C$) which may be prepared by irradiating mixtures of $HCo(PF_3)_4$ [3] and PH_3 (molar ratio 1:2) for periods of up to one hour by means of a mercury discharge lamp, or for longer periods by exposure to sunlight. The compound was isolated from PF_3, PH_3, and unreacted $HCo(PF_3)_4$ by fractionation in a high vacuum system (10^{-6} torr), compound *(1)* being retained at $-46\,^{\circ}C$ whereas $HCo(PF_3)_4$ is condensed at $-64\,^{\circ}C$. Final purification was accomplished using a low-temperature distillation column (yield 20%).

The complex *(1)* was characterized by its mass spectrum, and by its infrared and nuclear magnetic resonance spectra. The mass spectrum shows a parent peak at *m/e* 358 and other major peaks corresponding to the fragment ions $HCo(PF_3)_2PH_3^+$, $HCo(PF_3)_2PH_2^+$, $HCo(PF_3)_2PH^+$, $HCo(PF_3)(PF_2)PH_3^+$, $HCo(PF_3)(PF_2)PH_2^+$, *etc.*

The gas phase infrared spectrum shows ν_{max} at 2369 (νP–H), 1967 (νCo–H), 1049 (δP–H), and 925, 885, and 851 cm^{-1} (P–F vibrations).

The ^1H–NMR spectrum (pure liquid, TMS as internal reference) shows a doublet of quartets at $\tau = 6.12$, (int. 3, PH_3) with $J_{P-H} = 352$ Hz and $J_{F_3P-H} = 17.6$ Hz, and a broad absorption at $\tau = 24.4$ (int. 1, CoH). This spectrum suggests that the hydrogen atom and the phosphine group are *trans* to one another, the three trifluorophosphine groups being in the equatorial positions of the trigonal bipyramid. The ^{19}F–NMR spectrum (liquid) consisted of two multiplets (separation 1117 Hz) centered at 9.8 ppm above CCl_3F.

The complex $HCo(PF_3)_3PH_3$ was also produced by treating $HCo(PF_3)_3CO$ with phosphine, showing that CO is displaced by PH_3 in preference to PF_3.

Received: October 14, 1968 [Z 918 IE]
German version: Angew. Chem. *81*, 120 (1969)

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Tris(trimethylsilyl)indium

By *H. Bürger* and *U. Goetze* [*]

In contrast to the large number of compounds in which silicon is bonded to elements of Groups IV to VII, only a few silyl derivatives of the electron-deficient elements of Groups I to III are known [1]. In most cases their formation could be deduced only from subsequent reaction products [2]. The first examples of relatively stable, fully silylated derivatives of a Group III element are the thallium compounds $(R_3Si)_3Tl$ ($R = CH_3$ [3], C_2H_5 [1]).

By means of the reaction

$$InCl_3 + 3\,(CH_3)_3SiCl + 6\,Li \xrightarrow{THF,\ -30\,^{\circ}C} [(CH_3)_3Si]_3In + 6\,LiCl$$

which is analogous to those used for the synthesis of $[(CH_3)_3Si]_4Ge$ and $[(CH_3)_3Si]_4Sn$ [4], we succeeded in preparing and isolating tris(trimethylsilyl)indium *(1)*. A yield of 40% is obtainable only by adherence to the procedure given since a higher reaction temperature and slow stirring for prolonged reaction times favor reduction of $InCl_3$ according to

$$InCl_3 + 3\,Li \rightarrow 3\,LiCl + In$$

and simultaneously inactivate the lithium metal.

On sublimation, pure *(1)* is deposited in the form of greenish-yellow crystals, which decompose under vacuum above 50 °C in the dark and above about 0 °C on exposure to daylight. The decomposition products are indium and hexamethyldisilane; the presence of CH_3In groups could not be established. In solution or in contact with its decomposition products, compound *(1)* even decomposes below room temperature.

Compound *(1)* is extremely reactive toward O_2; it is spontaneously inflammable in air and explodes at room temperature in a current of oxygen. Consequently, in order to ensure controllable combustion during CH analysis, we had to use a stream of Ar containing an increasing proportion of O_2. Owing to the sensitivity of the substance, which exceeds that of $[(CH_3)_3Si]_2Hg$, the values obtained from the C, H, and In analyses showed a scattering of up to ± 10%.

Even after extreme care had been exercised in the preparation of the sample, the IR spectrum invariably contained bands due to oxidation products (initially the strong bands due to an indium silanolate at 455 (νInO) and 895 cm^{-1} (νSiO) and subsequently those due to $[(CH_3)_3Si]_2O$ at 330 and 1060 cm^{-1}). It can be deduced from the way in which the spectra change with time that *(1)* exhibits medium absorption at 311 cm^{-1}, which can be assigned to $\nu_{as}Si_3In$, alongside those bands arising from internal $Si(CH_3)_3$ vibrations; the possibility that this band arises from decomposition products cannot be completely ruled out.

By a rapid recording technique we have, however, succeeded in obtaining an HeNe laser Raman spectrum[5], which shows no lines due to impurities and whose interpretation, together with the analytical data and the chemical properties, lends support to the structure assumed for *(1)*. The following lines were observed below 700 cm^{-1}: 111 m ($\delta_{as}Si_3In$), 157 vs (ρSiC_3), ≈ 165 sh (δ_sSiC_3), 224 w ($\delta_{as}SiC_3$), 307 s (ν_sSi_3In), 623 s (ν_sSiC_3), and 682 m ($\nu_{as}SiC_3$). Assuming a planar Si_3In system, we have carried out a normal coordinate analysis for the $(C_3Si)_3In$ unit (C_{3h} symmetry) in A′ and taken the inner potential constants of the SiC_3 group from other trimethylsilyl compounds[6].

The following set of normalized symmetry force constants simulate the Raman frequencies observed for ν_sSiC_3 (ν_1), δ_sSiC_3 (ν_2), and ν_sSi_3In (ν_3) to within ± 0.4 cm^{-1}: F_{11} 2.93, F_{22} 0.15, F_{33} 1.6, F_{12} 0.05, F_{13} 0.15, and F_{23} −0.15 mdyn/Å. If *f*(SiIn/Si′In) is limited to a value between those for $[(CH_3)_3Si]_2Hg$ (∢ Si_2Hg 180°; 0.25) and $[(CH_3)_3Si]_4Sn$ (∢ Si_2Sn 109°28′; 0.16), *i.e.* to 0.2 ± 0.05 mdyn/Å, a value of 1.2 ± 0.1 mdyn/Å is calculated for *f*(SiIn). Working on the same assumption $\nu_{as}Si_3In$ is calculated to be 305 ± 20 cm^{-1}; if the band observed at 311 cm^{-1} is real, *f*(SiIn) is 1.25 and (SiIn/Si′In) is 0.17 mdyn/Å. Therefore, *f*(SiIn) is smaller (in spite of the fact that the bonding electrons in In have the highest s character) than the SiEl stretching force constants in compounds analogous to *(1)* containing elements of the 5th period: $[(CH_3)_3Si]_4Sn$ (1.66), $[(CH_3)_3Si]_3Sb$ (1.53), $[(CH_3)_3Si]_2Te$ (1.64), and $(CH_3)_3SiI$ (1.80 mdyn/Å)[6]. This is in accord with the lability of the Si–In bond.

Procedure:

$InCl_3$ (0.05 mole), lithium turnings (0.3 g-atom), and $(CH_3)_3SiCl$ (0.3 mole) are allowed to react together in tetrahydrofuran (300 ml) at −30 °C under N_2 and with rapid stirring for 2–4 h. The solution is filtered while still cold and the tetrahydrofuran is removed under vacuum in the dark at −10–0 °C; the orange-brown residue is extracted with cold ether (100 ml) at −20 °C (under these conditions the orange-red ethereal solution can be kept for several days) and the ether is then sucked off at −30 °C in the dark. Compound *(1)* remains behind in *ca.* 40% yield as a crystalline, orange-red residue that can be sublimed portionwise at 10^{-4} torr and a bath temperature of 40 °C onto a cold-finger (+10 °C). The decomposition product $(CH_3)_3SiSi(CH_3)_3$ must be drawn off continuously.

Received: November 4, 1968 [Z 919 IE]
German version: Angew. Chem. *81*, 122 (1969)

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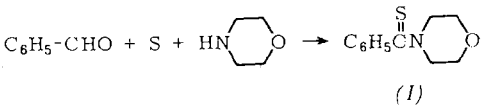
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A New Preparation of Thioformamides and Dithiocarbamates

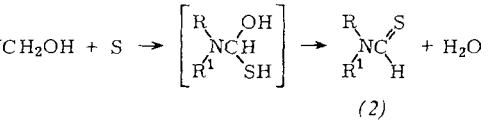
By *Ludwig Maier* [*]

Under the conditions of the Willgerodt-Kindler reaction[1,2], aromatic aldehydes react with sulfur and secondary amines to give good yields of thiocarbamides such as *(1)*. The corresponding reactions of aliphatic aldehydes appear to have been hardly investigated so far. Thus heptanal gave *n*-heptanamide in 46% yield on heating with $(NH_4)_2S_x$ and pyridine in a bomb tube[3], and morpholinium 4-morpholinedithiocarboxylate was obtained in 75% yield when morpholine was refluxed with paraformaldehyde and sulfur for 5 h[4]. Under the very mild conditions employed by *Asinger*[5], aliphatic aldehydes react reluctantly and in an unclear manner.

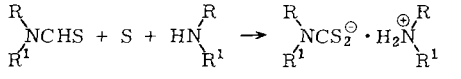


(1)

We have found that sulfur reacts readily with formaldehyde and amines, under the conditions used for the α-aminoalkylation of white phosphorus[6], to form thioformamides *(2)* and the amine salts of the corresponding dithiocarbamic acid *(3)*. If R, N, and R^1 are joined as a ring, compounds *(2)* and *(3)* can be regarded as *N*-thioformyl heterocyclic compounds or *N*-carbothialdehydes and amine salts of *N*-dithiocarboxylic acids, respectively.



(2)



(2) *(3)*

	R	R^1	*(2)* B.p. (°C/torr)	*(2)* Yield (%)	*(3)* M.p. (°C)	*(3)* Yield (%)
(a)	CH_3	CH_3	95–101/10	46	129–131	32
(b)	C_2H_5	C_2H_5	105–107/9	20	81–82	18
(c)	C_4H_9	C_4H_9	–	–	49–50	46
(d)	$-(CH_2)_4-$		100–110/1[a]	15	156–158	13
(e)	$-(CH_2)_5-$		87–89/0.07	25	168–171	18
(f)	$-CH_2CH_2OCH_2CH_2-$		[b]	59	sublimes	11
(g)	CH_3	H	125–128/12	16	–	–
(h)	C_2H_5	H	75–80/0.5	27	–	–

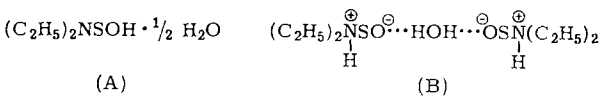
[a] M.p. 32–33 °C; [b] M.p. 68–70 °C.

The yields of the individual products depend on the molar ratios of the reactants and on the solvent. The highest yields of thioformamide *(2)* are obtained at a molar ratio of sulfur/dialkylaminomethanol = 3:1, and with water/alcohol (1:2 v/v) as solvent (80 °C, 4–11 h). The yield of dithiocarbamate increases steadily with increasing amounts of sulfur.

Under the above conditions morpholinomethanol does not react with sulfur; however, on addition of catalytic amounts of pyridine excellent yields of *N*-thioformylmorpholine *(2f)* are obtained.

On reaction of diethylaminomethanol with sulfur a further white crystalline product having the composition $C_4H_{12}NSO_{1.5}$ and m.p. 132–136 °C (decomp.) is formed in 6 to 9% yield along with diethylthioformamide *(2b)* and diethylammonium diethyldithiocarbamate *(3b)*. The pH of an aqueous solution (0.038 M) of this product is 6.1. On heating with hydrochloric acid SO_2 is evolved and elemental sulfur is precipitated. An aqueous solution of silver nitrate is reduced by the compound. The ^1H-NMR spectrum (in D_2O) of the compound contains signals for CH_3 at = δ 1.70 (T, J_{HH} = 7 Hz), $CH_3\underline{CH_2}$ at δ = 3.51 (Q, J_{HH} = 7 Hz), and a singlet at δ = 5.28 (1H): in $(CH_3)_2SO$ the signals for CH_3 appear at δ = 1.21, that for $CH_3\underline{CH_2}$ at δ = 2.91, and a very broad signal is observed between δ = 5.83 and 7.0 (1H). The mass spectrum contains peaks corresponding to the decomposition products

$(C_2H_5)_2NH$, sulfur (S_1 to S_8), SO_2, SO, and H_2O. These properties would be expected for a substance having structure A or B. The IR spectrum shows a sharp band at 2440



(A) (B)

cm^{-1} corresponding to $-\overset{\oplus}{N}HR_2$, thus suggesting the betaine structure B. B is therefore the first stable derivative of an *N*-sulfoxylic acid.

N-Thioformylpyrrolidine (2d) and pyrrolidinium N-pyrrolidinedithiocarboxylate (3d):

To a 37% aqueous solution of formaldehyde (15 g, 0.5 mole) are added first pyrrolidine (35.5 g, 0.5 mole), with ice cooling, and then sulfur (48 g, 1,5 mole), water (35 ml), and ethanol (100 ml); the mixture is subsequently refluxed for 4 h. The excess of sulfur is filtered off and, after removal of ethanol, the filtrate is extracted with ether. Distillation of the ether extract affords *(2d)* (9 g, 15%), b.p. 100–110 °C/1 torr, m.p. 32–33 °C (b.p. 157–160 °C/16 torr, m.p. 31.5–32.5 °C, according to ref. [7]).

Concentration of the aqueous phase yields *(3d)* (7 g, 13%), m.p. 156–158 °C, together with 20 g of a black greasy substance.

Received: December 3, 1968 [Z 920 IE]
German version: Angew. Chem. *81*, 154 (1969)

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Tungsten(IV) Oxide Bromide, $WOBr_2$

By *J. Tillack* and *Renate Kaiser* [*]

In connection with investigations on the reactions occurring in halogen incandescent lamps we were able to synthesize $WOBr_3$ [1]; we have now also succeeded in preparing the hitherto unknown compound $WOBr_2$.

Tungsten, tungsten trioxide, and bromine (molar ratio 2:1:3) were transferred to an evacuated sealed tube (length 180 mm, diameter 25 mm) and placed in a temperature gradient of of 450/*ca.* 40 °C in such a way that the W/WO_3 was in the hotter half and the bromine in the cooler half of the slightly inclined tube. After about 30 min almost all of the bromine had reacted with part of the other components to give higher tungsten bromides and oxide bromides, so that further reaction could be carried out in a temperature gradient of 580/450 °C without danger of explosion.

$$2\,W + WO_3 + 3\,Br_2 \rightleftharpoons 3\,WOBr_2 \qquad (1)$$

The $WOBr_2$, which is formed in the hot zone, was deposited by a chemical transport process [2] – probably in accord with equation (2) – in the cooler half of the tube (450 °C) in the form of well-crystalline, grayish black lustrous needles.

$$WOBr_2 + WOBr_4, g \rightleftharpoons 2\,WOBr_3, g \qquad (2)$$

A slight excess of bromine (3–5 mg more bromine per ml of tube volume than required stoichiometrically) prevents dissociation of the $WOBr_2$ deposited. With a stoichiometric charge of 20 mg-atoms of tungsten, 10 mmoles of WO_3, and 30 mmoles of bromine the above procedure afforded 10.2 g of $WOBr_2$ (yield *ca.* 95%; regarding analytical procedures, see refs. [1, 3]).

Owing to the reversibility of the reaction, $WOBr_2$ may also be prepared from tungsten and oxygen or WO_2, and bromine.

In a temperature gradient of 550/470 °C the mixture described repeatedly gave large amounts of a dull, blue-black substance at 470 °C, which has the approximate composition $W_2O_3Br_3$ and which clearly differed in its chemical behavior and X-ray diffraction pattern from $WOBr_2$; this substance has not yet been investigated further.

When dry $WOBr_2$ is heated in a test tube yellowish brown fumes of WO_2Br_2 with a little bromine are evolved and WO_3 is left behind as residue. No reaction is observed between $WOBr_2$ and water or dilute acids (HCl, H_2SO_4, CH_3COOH) at room temperature; when heated to boiling with water, conc. hydrochloric acid, or dilute acetic acid nothing more than a slight blue coloration is noted, whereas conc. sulfuric acid and conc. nitric acid decompose $WOBr_2$.

The compound is attacked neither by cold nor by hot aqueous ammonia. However, treatment with 2 M NaOH yields a voluminous, blackish brown precipitate that was not examined further. In both cases, subsequent addition of approximately 3% H_2O_2 gives clear yellow solutions.

At room temperature $WOBr_2$ decolorizes a $KMnO_4$ solution that has been acidified with sulfuric acid. Organic solvents, *e.g.* ethanol, acetone, toluene, dichlorobenzene, and trichloroethylene, do not have any effect on the compound.

Regarding the X-ray characterization of $WOBr_2$, we report the following *d* values and the estimated intensities (in parentheses) of the first reflections up to $\vartheta = 38°$:

7.31 (3); 6.55 (8); 3.63 (10); 2.68 (8); 2.36 (4); 2.22 (1); 2.19 (1); 2.08 (2); 2.00 (7); 1.89 (5); 1.71 (1); 1.68 (2); 1.64 (1); 1.55 (5); 1.43 (1); 1.26 (2).

The density was determined pycnometrically in toluene at 25.0 ± 0.1 °C as 6.13 g/cm³.

Received: November 28, 1968 [Z 927 IE]
German version: Angew. Chem. *81*, 149 (1969)

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Trisubstituted Formamidines

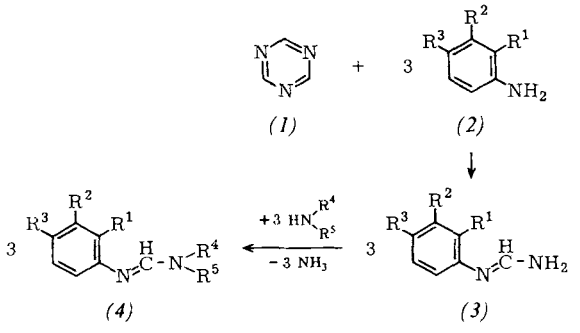
By *M. F. G. Stevens* and *A. Kreutzberger* [*]

The aminomethinylation reaction that takes place on nucleophilic attack of *s*-triazine *(1)* on amines *(2)* [1] can be utilized in a new synthesis of aminoquinazolines [2]. The ease of this additive cyclization decreases as the basic strength of the amino group in *(2)* decreases, so that 2-amino-5-nitrobenzonitrile does not react with *(1)* under the conditions used, even in pyridine. By contrast, reaction occurs with violent evolution of ammonia when the starting materials are heated in piperidine; however, the reaction course deviates from that

of aminoquinazoline formation. The base peak at *m/e* 84 and the fragment ions observed in the mass spectrum of the end product at *m/e* 69, 56, 41, 30, and 28 are analogous to the fragments formed by formimidoylpiperidine groups[3]. On the basis of this fragmentation pattern and the molecular ion observed at *m/e* 258, and in accord with other spectroscopic and chemical data, the reaction product was identified as 1-[*N*-(2-cyano-4-nitrophenyl)formimidoyl]piperidine *(4a)*.

This reaction proves to be very amenable to variation and represents a general method for the preparation of N^2-aryl-N^1,N^1-dialkylformamidines *(4)*, in which R^4 and R^5 can also be parts of a heterocyclic ring.

Attack of *(1)* on CH-acids, such as 4-nitrophenylacetonitrile[3] and α-picoline *N*-oxide[4], in the presence of secondary amines is a reaction comparable to the formation of *(4)*. The class of trisubstituted formamidines contains representatives having ovicidal[5], herbicidal[6], antiviral, and antibacterial[7] activity.



(1) *(2)* *(3)* *(4)*

Cpd.	R^1	R^2	R^3	R^4	R^5	Yield (%)	M.p. (°C)
(4a)	C≡N	H	NO_2	$-(CH_2)_5-$		90	136–137 [a]
(4b)	H	H	C≡N	$-(CH_2)_5-$		88	53–54 [b]
(4c)	NO_2	H	NO_2	$-(CH_2)_5-$		79	108–110 [a]
(4d)	NO_2	H	H	$-(CH_2)_5-$		84	62–63 [b]
(4e)	H	NO_2	H	$-(CH_2)_5-$		80	57–58 [b]
(4f)	H	H	NO_2	$-(CH_2)_5-$		75	79–80 [b]
(4g)	H	H	OH	$-(CH_2)_5-$		70	176–178 [c]
(4h)	H	H	Cl	$-(CH_2)_5-$		90 (oil)	193–194 [d]
(4i)	H	H	H	$-(CH_2)_5-$		95 (oil)	182–183 [e]
(4j)	H	H	NO_2	$-(CH_2)_2-O-(CH_2)_2-$		85	112–113 [b]
(4k)	H	H	NO_2	C_2H_5	C_2H_5	75	61–62 [b]

[a] Recrystallized from benzene/light petroleum; [b] from ether/light petroleum; [c] from ethanol; [d] from ethanol, m.p. of the picrate; [e] from ethanol/ether, m.p. of the tosylate.

4-[N-(4-Nitrophenyl)formimidoyl]morpholine (4j)

Rapid evolution of ammonia occurs when a mixture of *s*-triazine *(1)* (1.6 g, 0.02 mole) and 4-nitroaniline *(2j)* (5.5 g, 0.04 mole) in morpholine (13.1 g, 0.15 mole) is heated to boiling. After 2 hours' heating and subsequent cooling, compound *(4j)* (8 g, 85%) is isolated by vacuum concentration; m.p. and mixed m.p.[6] 112–113 °C, after recrystallization from ether/light petroleum.

Received: December 18, 1968 [Z 921 IE]
German version: Angew. Chem. *81*, 154 (1969)

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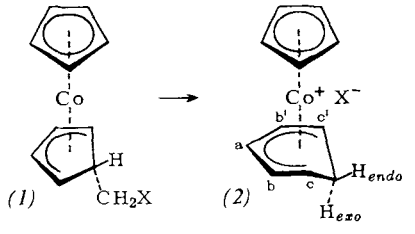
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Solvolytic Ring Expansion in a Transition Metal π-Complex[1]

By *G. E. Herberich* and *J. Schwarzer*[*]

Alkyl halides and esters that carry a ferrocenyl group or a similar complex substituent in the α-position undergo solvolysis as readily as triphenylmethyl halides and esters[2,3]. The intermediate carbonium ion is stabilized by the neighboring group effect of the complex substituent, the nonbonding d electrons of the central atom or ion seemingly



(1) *(2)*

(1a): X = Br *(2a)*: X = Br
(1b): X = I *(2b)*: X = I

playing a key role in this stabilization[3]. Ligand rearrangements have not hitherto been observed during solvolyses of this kind.

We now wish to report on a novel type of an exceptionally rapid solvolysis. The 5-*exo*-halogenomethyl derivatives *(1)*[4] of cyclopentadienecyclopentadienylcobalt, which are stable in hexane solution, rearrange irreversibly in polar media to give cyclohexadienylcyclopentadienylcobalt salts *(2)*.

This is the first example of a solvolytic ring expansion in a ligand of a transition metal π-complex.

The solvolysis of *(1a)* can readily be followed by spectrophotometric techniques: the reaction is first order with respect to *(1a)*; a rate constant of $k_1 = 1.1 \times 10^{-4}$ sec^{-1} was found at 30 °C in ethanol/*n*-hexane (95:5). By contrast, compound *(1b)* rearranges in the solid state at 0 °C almost quantitatively to *(2b)* within two days.

The salts of the cyclohexadienylcyclopentadienylcobalt cation *(2)*, which has now been obtained for the first time, are red, air-stable substances that are somewhat sensitive to light; the composition of the iodide and of the hexafluorophosphate were established by elemental analysis. The constitution of the cation is evidenced by the ^{1}H-NMR (see Table 1) and by the IR spectrum. The ^{1}H-NMR spectrum

Table 1. ^{1}H-NMR spectrum *(2a)* in D_2O (60 MHz; 20 °C).

Signal	Rel. Int.	τ [a]	Multiplicity	Coupling constants (Hz)
H_a	1/4:2/4:1/4	2.83	3 [b]	J_{ab} = 5,5
H_d	5	4.53	1	
H_b, H_b'	1/2:2/2:1/2	4.69	"3" ≙ 2 × 2	$J_{ab} \approx J_{bc} \approx 6$
H_c, H_c'	1/2:2/2:1/2	6.05	"3" ≙ 2 × 2 [b]	$J_{bc} \approx J_{endo,c} \approx 7$
H_{endo}	1 [c]	7.29	2 × 3	$J_{endo,exo} = 16$; $J_{endo,c} = 7$
H_{exo}	1 [c]	8.86	2 [b]	$J_{endo,exo} = 16$

[a] Measured with respect to TMS as external reference.

[b] Further splitting of the order of 1 Hz is observed.

[c] The relative intensities of the components deviate significantly from those of a first order spectrum.

contains signals having relative intensities 1:2:5:2:1:1; the cyclohexadienyl protons show a coupling very similar to that in tricarbonylcyclohexadienyliron tetrafluoroborate[5,6]. Since the methylene group in cyclohexadienyl ligands is directed outwards (by 50 ° in the case of tricarbonyl-1,2,3,4,5,6-*endo*-hexamethylcyclohexadienylrhenium[7]), H_{exo} is more strongly shielded by the π-electrons of the cyclohexadienyl ligands, whereas the shielding of H_{endo} is reduced. At the same time, the dihedral angles $\sphericalangle H_cCCH_{endo}$ and $\sphericalangle H_cCCH_{exo}$ are changed in such a way that $J_{endo,c} > 6$ Hz and $J_{exo,c} < 2$ Hz would be expected from the Karplus equation. According to both these arguments, the doublet at τ = 8.86 must be assigned to the *exo* proton and the multiplet at τ = 7.29 to the *endo* proton. In addition to the absorption of the cyclopentadienyl ring, the IR spectrum shows various bands (in cm^{-1}: 1446 m, 1405 s, 1324 w, 1296 s, 1138 m, 1047 s, 993 s, 947 m, 901 w, 870 m, 809 m), which are all observed in other cyclohexadienyl complexes too.

In the two-phase system ether/water, compound *(2)* can be converted at 20 °C into cyclohexadienecyclopentadienylcobalt[8] (yield 90%).

Received: November 28, 1968 [Z 925 IE]
German version: Angew. Chem. *81*, 153 (1969)

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$Ni_5(C_5H_5)_4S_4$, a Pentanuclear Metal Complex Containing a Square-Planar Nickel(0) Atom[**]

By *H. Vahrenkamp* and *L. F. Dahl*[*]

In continuation of our attempts to prepare $Ni_3(C_5H_5)_3S$[1], an electronic equivalent of $Co_3(CO)_9S$[2], we instead isolated $Ni_5(C_5H_5)_4S_4$ *(1)* from the decomposition of $Ni_3(C_5H_5)_3S_2$ *(2)* in ether solution. The equation

$$2\ Ni_3(C_5H_5)_3S_2 \rightarrow Ni(C_5H_5)_2 + Ni_5(C_5H_5)_4S_4$$
(2) *(1)*

indicates the probable stoichiometry of this reaction and makes it understandable why the main products from the reaction of $Ni_2(C_5H_5)_2(CO)_2$ *(3)* with elemental sulfur are nickel sulfides and $Ni(C_5H_5)_2$, since analogous formal abstraction of $Ni(C_5H_5)_2$ from *(1)* would finally lead to an $[Ni_3S_4]_x$ species. Compound *(1)* was characterized by a single-crystal X-ray study, which also further substantiated the predicted drastic influence of valence electrons on the molecular configuration of *(2)*[1] and thereby provided additional support for the bonding principles recently proposed for transition metal cluster carbonyl systems[1,3].

Crystals of *(1)* are monoclinic with two formula species in a unit cell of symmetry $P2_1/c$ and dimensions a = 7.870 ± 0.005 Å, b = 12.704 ± 0.007 Å, c = 11.661 ± 0.007 Å, β = 99 °52′ ± 1′; ρ_{calcd} = 1.97 g cm^{-3} *versus* $\rho_{obsvd.}$ = 1.96 g cm^{-3} (flotation method). Three-dimensional intensity data consisting of 838 observed independent reflections and 274 unobserved or pseudo-unobserved reflections (*i.e.*, $I < 2\sigma(I)$) were collected with Mo Kα radiation on a four-angle automated diffractometer (General Electric). The structure and composition were elucidated by application of the symbolic addition method of phase determination[4]; full-matrix least-squares refinement with anisotropic temperature factors for the nickel atoms and isotropic ones for the sulfur and carbon atoms resulted in identical unweighted R_1 and weighted R_2 discrepancy values of 6.7%.

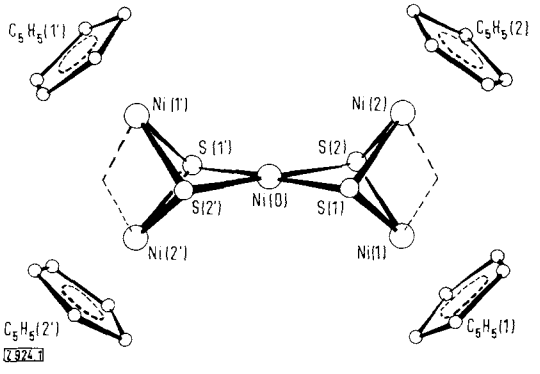


Fig. 1. Molecular configuration of $[Ni_2(C_5H_5)_2S_2]_2Ni$.

Crystalline *(1)* consists of discrete molecules (Figure 1). Each of the two molecules in the unit cell is constrained by the space group symmetry to possess crystallographic C_i-$\bar{1}$ symmetry with the central nickel atom of each molecule lying on a center of inversion. With the assumption of cylindrical symmetry for each cyclopentadienyl ligand, the entire molecule has approximately D_{2h}-2/m 2/m 2/m symmetry. The five nickel and four sulfur atoms form two distorted Ni_3S_2 trigonal bipyramids which are connected to each other by corner sharing of the one common equatorial nickel atom such as to give this unique central nickel atom a square-planar coordination with the four axially-positioned sulfur atoms. In accord with the resulting formula of $[Ni_2(C_5H_5)_2S_2]_2Ni$ and a pseudo-D_{2h} geometry, the prominent molecular dimensions are: (1) a bonding Ni(1)–Ni(2) distance of 2.495 ± 0.003 Å compared to two equivalent nonbonding Ni(0)–Ni(1) and Ni(0)–Ni(2) distances of the same value, 2.979 ± 0.002 Å; (2) six crystallographically independent Ni–S distances all equal within 0.01 Å to the average value of 2.18 Å; (3) equivalent nickel-to-(cyclopentadienyl carbon) distances of 2.14 Å (av.) and cyclopentadienyl C–C bond lengths of 1.43 Å (av.); (4) two equivalent Ni(1)-S-Ni(2) angles of 69.9 ° and 70.0 ° (indiv. esd, 0.1 °) *vs.* four equivalent Ni(1)–S–Ni(0) and Ni(2)–S–Ni(0) angles of range 86.0 to

86.3° (indiv. esd, 0.1°); (5) S(1)–Ni(0)–S(2) and S(1)–Ni(0)–S(2′) angles in the Ni(0)–S_4 plane of 82.1(1) and 97.9(1) degrees, respectively.

Considerable similarity exists between the $[Ni_2(C_5H_5)_2S_2]Ni_{1/2}$ fragment comprising one-half the molecule of *(1)* and its chemical precursor *(2)* with respect to their overall configurations and their virtually identical Ni–S and Ni–C bond lengths. The salient structural difference is that the regular trigonal bipyramidal Ni_3S_2 cluster system in *(2)* has three equivalent long Ni–Ni distances of 2.801(5) Å in contrast to the markedly distorted trigonal bipyramidal $[Ni_2S_2]Ni_{1/2}$ fragment containing one much shorter bonding and two significantly longer nonbonding Ni–Ni distances. Since the central Ni(0) atom no longer is effectively bonded directly to the other four chemically equivalent nickel atoms, the molecule *(1)* instead of being treated as an interconnected Ni_5-cluster system may simply be regarded as being composed of two $Ni_2(C_5H_5)_2S_2$ units linked together only by the Ni(0) atom. It then becomes obvious that the two identical units (in which each sulfur atom by its donation of one electron to each nickel atom has two resulting unshared electron pairs) are of the $M_2(C_5H_5)_2X_2$ type structure represented in molecular form by the electronically equivalent and structurally analogous complex *(3)* [5] and $Co_2(C_5H_5)_2\{P(C_6H_5)_2\}_2$ *(4)* [6].

The structure of the $Ni_2(C_5H_5)_2S_2$ unit with its nonplanar Ni_2S_2 bridging system closely resembles that of *(4)* [6]. The fact that a rational basis for a distinct Co–Co σ-bond of considerable bond strength was provided [6] for the phosphorus-bridged CoC_5H_5 dimer in order to account for its molecular geometry with sharply acute bridging angles and with a Co–Co bonding distance of 2.56 Å is in complete accord with the assignment of the Ni–Ni interaction in the $Ni_2(C_5H_5)_2S_2$ unit as an electron-pair bond in order for each nickel to attain a closed-shell electronic configuration. The somewhat longer Ni(1)–Ni(2) distance of 2.495(3) Å compared to the Ni–Ni σ-bonding distance of 2.36 Å observed in *(3)* [5] and of 2.33 Å found in $Ni_2(C_5H_5)_2(C_6H_5C_2C_6H_5)$ [5] is expected in that it has been shown [7] that the electron-pair metal-metal bonding distances in ligand-bridged complexes primarily depend on both the size and effective electronegativity of the bridging atoms. Through a σ-bond interaction involving the use of one of the two unshared electron pairs on each of the four sulfur atoms of the two $Ni_2(C_5H_5)_2S_2$ units, the central Ni(0) atom also attains a closed-shell electronic configuration without any direct interaction with the other four nickel atoms. To our knowledge the square-planar coordination is unprecedented for a tetracoordinated "zerovalent" nickel atom which normally forms tetrahedral-like complexes (*e.g.*, $Ni(CO)_4$ [8] and 1,5-cyclooctadieneduroquinonenickel [9]).

The changes in the Ni–Ni distances of the Ni_3S_2 system that occur on going from *(2)* to *(1)* can be nicely rationalized from the same qualitative MO considerations utilized to formulate the nickel-nickel bonding in *(2)* [1]. In this latter complex the "effective" Ni–Ni bonding among the three nickel atoms is due to only one strongly bonded electron in a nickel symmetry orbital delocalized over the entire trinickel cluster system. Experimental support of this MO formulation of weak Ni–Ni bonding in *(2)* is given by the observed long Ni–Ni distances. The formal replacement of the one cyclopentadienyl ring with two sulfur atoms not only removes the orbital degeneracy of the metal atoms in the Ni_3S_2 system but more importantly reduces the number of antibonding electrons by one. Hence, the *net* difference between the corresponding occupied bonding and antibonding levels (which are assumed to cancel one another's bonding) is *two* bonding electrons. The localization of this bonding electron pair between the two equivalent nickel atoms in each $[Ni_2S_2]Ni_{1/2}$ fragment accounts for the observed localized C_{2v} deformation from the regular trigonal bipyramidal Ni_3S_2 structure in *(2)* to give the one much shorter Ni–Ni distance of single bond value and the other two longer Ni–Ni nonbonding distances.

Procedure:

An ether solution of *(2)* [1] (prepared from 0.76 g of *(3)* and 0.10 g sulfur) was filtered and allowed to stand at room temperature under nitrogen. After one to three weeks, black crystalline *(1)* and some brown powder had precipitated on the walls of the flask. Yield 24 mg (2.7%), m.p. 135 °C (with vigorous decomposition upon rapid heating).

Received: November 19, 1968 [Z 924 IE]
German version: Angew. Chem. *81*, 152 (1968)

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[**] We are indebted to the National Science Foundation (GP 4919) for their financial support of this work and to the Deutsche Forschungsgemeinschaft for a traveling grant (for *H. V.*). The use of the CDC 1604 and 3600 computers at the University of Wisconsin Computing Center was made available through partial support of NSF and WARF through the University Research Committee.

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Preparation and Properties of $AuTe_2I$

By *A. Rabenau, H. Rau*, and *G. Rosenstein* [*]

Hydrothermal synthesis in halogen hydracids [1] is a most suitable method for the preparation of chalcogenide halides [2, 3]. Hitherto, chalcogenide halides with gold as constituent have been unknown. Reaction of gold and tellurium in hydriodic acid, however, leads to the formation of crystals of a compound, which on analysis has the composition $AuTe_2I$ *(1)*.

If an excess of gold is present in such a reaction well-developed shiny silvery single crystals of *(1)*, in the form of needles up to 1 cm and more in length, are formed: 10 g of a mixture of gold powder and tellurium (in the atomic ratio 1:1) is transferred to a quartz ampul of 10–11 ml capacity and 10 M hydriodic acid is added until the ampul is 65% full and frozen with liquid air. After sealing under vacuum, the ampul is transferred to an autoclave [4], heated to 450 °C, and then allowed to cool to 150 °C over a period of 10 days. The $AuTe_2I$ crystals which precipitate out can easily be separated from the gold crystals which are formed at the same time; only occasionally do both types of crystals associate (Fig. 1). When subjected to mechanical stress, the crystals of *(1)* easily shred longitudinally into fibers. The compound is obtained in a pure, polycrystalline form by tempering a mixture of gold powder, TeI, and tellurium (in the stoichiometric ratio 1:1:1) in a sealed ampul at 350 °C.

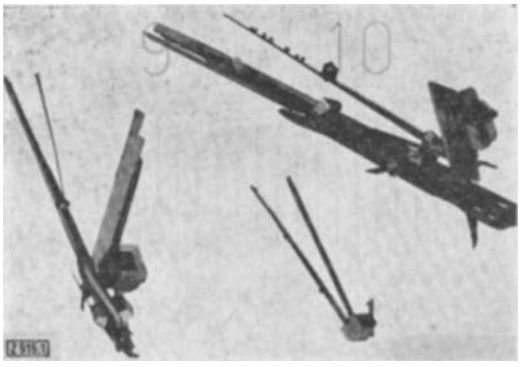


Fig. 1. Needles of $AuTe_2I$ associated with gold. (Figures in cm.)

According to DTA measurements, compound *(1)* is stable up to a temperature of 371 °C in the absence of air. The electrical resistance[5] of the crystals increases linearly with temperature – as in metallic conductors.

The compound is insoluble in dilute acids and alkalis; it decomposes in concentrated nitric and concentrated sulfuric acids.

From single-crystal photographs it can be concluded that $AuTe_2I$ crystallizes rhombically: $a = 4.735$, $b = 4.046$, $c = 12.55$ Å; $Z = 2$, $d_m = 8.00$, $d_x = 7.98$ g/cm³. Probable space groups $Pmc2_1$, Pma2, Pmma.

The indexing of a powder diagram is given in Table 1.

Table 1. Diffractogram of $AuTe_2I$.

d (Å)	I/I_1	hkl	d (Å)	I/I_1	hkl
6.28	100	002	2.094	15	006
4.74	1	100	2.025	4	020
3.78	3	102	1.946	7	115/212
3.41	1	012	1.916	5	106
3.14	60	004/103	1.861	7	016/120
3.08	5	110	1.729	1	116
2.989	6	111	1.701	2	024/123
2.763	4	112	1.602	1	124
2.617	7	104	1.568	7	206/008
2.480	22	014/113	1.552	2	117
2.215	1	202	1.492	4	108/222
2.196	2	114	1.466	12	018/216

Received: October 17, 1968 [Z 915 IE]
German version: Angew. Chem. *81*, 148 (1969)

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The Crystal Structure of Zirconium(IV) Chloride: A New AB_4-type Structure

By *B. Krebs*[*]

According to *Hansen*[1], $ZrCl_4$ *(1)* ought, by analogy with $TiCl_4$, to have an SnI_4-type (molecular) structure with tetrahedral coordination of the Zr atoms. This argument, however, cannot be correct since the physical properties[2] and the vibration spectrum investigated by *Weidlein*, *Müller*, and *Dehnicke*[3] exclude a molecular structure. We have therefore carried out a complete X-ray structural analysis on single crystals of $ZrCl_4$ (flat needle-like crystals obtained by slow sublimation at about 300 °C in a closed system). *(1)* crystallizes in the monoclinic space group P2/c (C_{2h}^4) with $a = 6.361 \pm 0.004$, $b = 7.407 \pm 0.004$, $c = 6.256 \pm 0.004$ Å, $\beta = 109.30 \pm 0.04°$, $V = 278.2$ Å³. $Z = 2$; $d_{x\text{-ray}} = 2.782$ g/cm³, $d_{pyc} = 2.80$ g/cm³. A total of 614 independent reflections were measured with an automatic Hilger-Watts four angle diffractometer ($\omega/2\theta$ scan, Zr filtered Mo–K_α radiation, scintillation counter). The structure was determined by interpretation of the three-dimensional Patterson synthesis. Least squares refinement with anisotropic temperature factors afforded an R_1 factor of 4.9%. The atomic parameters are: Zr: 0; 0.1641; 0.25; Cl(1): 0.2263; 0.1076; −0.0022; Cl(2): 0.2552; 0.6371; −0.0205.

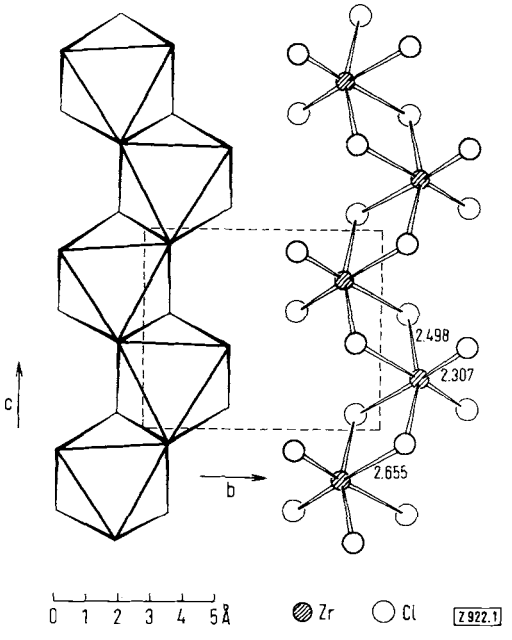


Fig. 1. Crystal structure of $ZrCl_4$. Projection of one chain on the *bc* plane.

(1) has a previously unknown AB_4-type structure (Fig. 1): $ZrCl_6$ octahedrons are coupled to each other by two edges to form a zig-zag chain; the common edges with neighboring octahedrons do not lie in a *trans*-position to one another as *e.g.* in NbI_4[4]. The chain structure gives rise to considerable macroscopic cleavability parallel to (100) and (010) of the needle shaped crystals. The $ZrCl_6$ octahedrons are very much distorted: two Zr–Cl bridge bonds having different lengths (2.498 and 2.655 Å; standard error ±0.003 Å) are present for each two terminal bond lengths (2.307 Å). The bridge bonds, which must be assumed to be 50% heteropolar in character, are significantly weaker than the terminal bonds according to their lower formal bond orders. The terminal bond lengths are comparable with those of the tetrahedral $ZrCl_4$ molecule in the gas phase (2.32 Å[5]). The shortest Zr–Zr distance of 3.962 Å between neighboring octahedrons excludes the participation of metal-metal bonding.

The atomic arrangement can be described as a relatively slightly distorted cubic close packing of Cl atoms with one quarter of the octahedral holes being occupied by Zr atoms. The twelve Cl neighbors of each Cl atom are situated at distances of 3.30 (bridge edges of octahedrons) to 3.93 Å.

The chain structure represents a transition from the more covalently bound molecular structures of $TiCl_4$ and Nb_2Cl_{10} to the corresponding more heteropolar compounds of Sc, Y, and the rare earths: The octahedron chains of *(1)* can be regarded as sections of the layers of the YCl_3 lattice ($AlCl_3$-type)[6], whilst the Nb_2Cl_{10} double octahedron[7] formally represents a section of the $ZrCl_4$ structure. Similar relationships exist between *(1)* and the BiI_3 and $CrCl_3$ layer structures. The metal-chlorine bond lengths in the series YCl_3,

$ZrCl_4$, Nb_2Cl_{10}, Mo_2Cl_{10}[8] exhibit a physically meaningful trend.

The tetrahedral form of the $ZrCl_4$ molecule in the gas phase is already latent in the distorted octahedrons of the crystal structure. Accordingly, the cleavage of the longest Zr–Cl bond with subsequent easy rehybridization at the Zr is assumed to be a plausible vaporization- and sublimation mechanism (cf.[9]). $ZrBr_4$ and $HfCl_4$, and probably $HfBr_4$, are isostructural with *(1)*.

Received: November 8, 1968 [Z 922 IE]
German version: Angew. Chem. *81*, 120 (1969)

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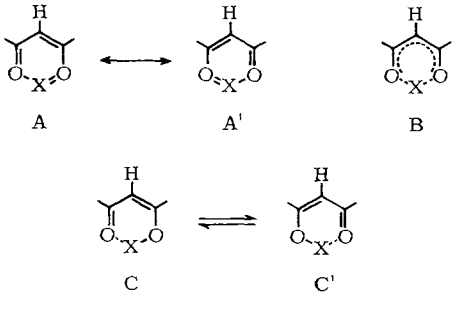
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Are β-Diketone-Metal Complexes Aromatic?[1]

By *M. Kuhr* and *H. Musso*[*]

The metal chelates of β-diketones have, for a long time, been considered to exhibit a benzenoid resonance A ↔ A[1] [2] and as a consequence to possess an aromatic or quasi-aromatic character[3]. Numerous attempts to deduce such a property, as in the case of benzene, from the shift of the NMR signal for the protons bound in the plane of the chelate ring have been differently interpreted[4–6].



A A' B

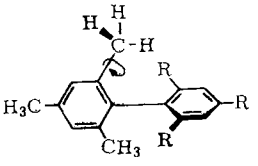
C C'

The vibration spectra of isotopically substituted 2,4-pentanedionato complexes (acetylacetonates) of various metals indicate that a complete bond delocalization is present in solution and in the crystalline state (A or B) but not in the enol form of 2,4-pentanedione (X = H), as in C ⇌ C'[1,7].

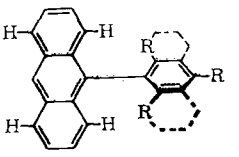
In order to determine unequivocally whether or not a cyclic conjugation of the six π electrons continues over the metal atom, we have examined derivatives of 2,4-pentanedione in which protons are situated not in the plane but over the chelate ring. A shift of the signal of such protons to higher magnetic field in the NMR spectrum is a sure indication of aromatic character[8].

From the chemical shift differences $\Delta\delta$ (cf. Table 1) of the *o*- and *p*-methyl groups in the ^{1}H-NMR spectra of phenylmesitylene *(1)* (0.30 ppm), bimesityl *(2)* (0.45 ppm), and 9-mesitylanthracene *(4)* (0.78 ppm) and of the 1,8- and 4,5-hydrogen atoms of 9-phenylanthracene *(3)* (~0.45 ppm), *(4)* (0.70 ppm), and 9,9'-bianthryl *(5)* (1.10 ppm) it can be concluded that a shift difference of *ca.* 0.5 ppm is to be expected if an aromatic ring is present beneath these protons. The observed differences in these models (0.30–1.10 ppm) depend, on the one hand, on the somewhat different average angles of twist of the two aromatic systems and, on the other, on the fact that the 1,8-anthryl protons in *(3)*, *(4)*, and *(5)* are fixed better over the other ring than are the protons of the rapidly rotating CH_3 groups in *(1)*, *(2)*, and *(4)*, in which only the mean value for the shift of favorable and unfavorable positions is indicated; finally, the electron density in the phenylmesityl- and central anthryl-ring is naturally different.

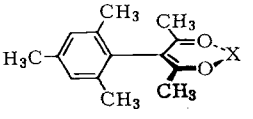
By way of comparison, the analogous shift differences in 3-mesityl- and 3-anthryl-2,4-pentanedione – *(6)*, X = H and *(7)*, X = H – are small. Since these differences in the metal complexes of *(6)* (X = K, Na, Li, Be, Al, Pd, Co) and *(7)* (X = K, Li, Be, Pd) of greatly varying stability do not increase significantly with respect to the hydrogen compounds (X = H) and the



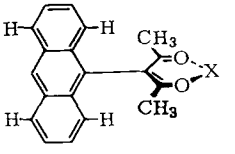
(1), R = H
(2), R = CH_3



(3), R = H
(4), R = CH_3
(5), Bianthryl



(6), X = H, K, Na, Li, Be, Al, Pd, Co



(7), X = H, K, Li, Be, Pd

Table 1. Chemical shifts of a few protons of the 2,4-pentanedione derivatives (δ in ppm) [a].

	Solvent	Mesityl-		Anthryl-		Δδ
		o-CH_3	*p*-CH_3	*H* 1,8 [b]	*H* 4,5 [b]	
Mesitylene	$CDCl_3$	2.25		—	—	0.00
(1)	$CDCl_3$	1.86	2.16	—	—	0.30
(2)	$CDCl_3$	1.88	2.33	—	—	0.45
(6), X = H	$CDCl_3$	2.09	2.29	—	—	0.20
	DMSO	2.06	2.25	—	—	0.19
X = K	DMSO	2.03	2.20	—	—	0.17
X = Na	DMSO	2.08	2.21	—	—	0.13
X = Li	DMSO	2.08	2.22	—	—	0.14
X = Be	$CDCl_3$	2.16	2.30	—	—	0.14
X = Al	$CDCl_3$	2.15	2.28	—	—	0.13
X = Co^{III}	$CDCl_3$	2.13	2.29	—	—	0.16
X = Pd	$CDCl_3$	2.07	2.29	—	—	0.22
Anthracene	$CDCl_3$	—	—	7.95		0.00
(3)	$CDCl_3$	—	—	~7.10	7.55	~0.45
(4)	$CDCl_3$	1.68	2.46			0.78
				7.32	8.02	0.70
(5)	$CDCl_3$	—	—	7.10	8.20	1.10
(7), X = H	$CDCl_3$	—	—	7.89	7.94	0.05
	DMSO	—	—	7.50	7.60	0.10
X = K	DMSO	—	—	7.41	7.48	0.07
X = Li	DMSO	—	—	8.03	8.16	0.13
X = Be	$CDCl_3$	—	—	7.99	8.11	0.12
X = Pd	$CDCl_3$	—	—	7.98	8.06	0.08

[a] Varian A 60, TMS as internal standard (±0.02 ppm).

[b] Centers of the A- and A- and D parts of the A_2B_2- and ABCD-multiplets.

free anions (X = K in DMSO), these chelate complexes do not possess magnetic anisotropy typical of aromatic compounds and consequently are not aromatic in character.

Daltrozzo came to the same conclusion *via* a different approach [9]. Use of the term "quasiaromatic" [3, 10] in connection with such systems is best avoided, since "non-aromatic" is not generally understood to be included under this heading.

It would appear attractive to study, in this way, the bonding character of further metal complexes and other five- and six-membered chelates and heterocycles (*e.g.* [11–13]), since the method used here is obviously less susceptible to polar and other effects than the position of the signals of protons in the plane of the ring [6].

According to their NMR spectra, compounds *(6)* and *(7)* (X = H) are present almost completely in the enolized form. These compounds were obtained from iodomesitylene and 9-bromoanthracene and from the chromium complex of 3-bromo-2,4-pentanedione respectively, by heating in the presence of copper powder (4 h, 240 °C) followed by acid hydrolysis: *(6)*, X = H, m.p. 83 °C, yield 40%; *(7)*, X = H, m.p. 182 °C, yield 7%. Although the Ullmann reaction is a well known classical method for the coupling of aromatic rings, it has been used here to provide evidence against the aromatic character of the metal complexes of *(6)* and *(7)*.

Received: November 14, 1968 [Z 923 IE]
German version: Angew. Chem. *81*, 150 (1969)

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CONFERENCE REPORTS

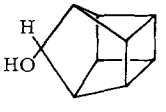
New Olefin Reactions

A Symposium was held at the University of Manchester Institute of Science and Technology, June 25 and 26, 1968, that dealt with some of the more important recent advances and trends in olefin reactions.

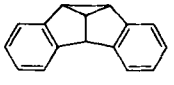
G. Wilke (Mülheim, Germany) reviewed the factors which influence the reactions of olefins with transition metals. Metal-olefin complexes are in general stabilized by the presence of basic ligands in the molecule, and by partial decoupling of the olefin π-orbitals, usually achieved by ring strain in the case of cyclic olefins, or in mono-olefin complexes by rotation of the olefin so that it is at an angle to the plane of the molecule. The point was also made that complexes of chelating diolefins are more stable than the analogous mono-olefin complexes.

Several factors influence the reactivity of the complexed olefin, for example, charge transfer can occur from metal to ligand or from ligand to metal, and evidence was presented that in the compound bis(bipyridyl)cyclooctadienenickel the cyclooctadiene exists as a dianion. Hydrogen transfer reactions are also known in metal-olefin complexes, for example, the compound bis(cyclooctadiene)cobalt hydride exists as an equilibrium mixture of a σ-enyl and π-allyl structure.

R. Pettit (Austin, Texas, USA) reviewed the chemistry of cyclobutadiene complexes of transition metals and demonstrated how these complexes may be used as a convenient source of cyclobutadiene in the synthesis of organic compounds. The synthesis was reported of several *para*-bonded benzene derivatives by oxidative cleavage of $(C_4H_4)Fe(CO)_3$ in the presence of acetylenes. The preparation of pentacyclo-[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]nonan-9-ol *(1)* from 5,5-diethoxycyclopentadiene and $(C_4H_4)Fe(CO)_3$ was also described.



(1)



(2)

Oxidative cleavage of (benzocyclabutadiene)iron tricarbonyl in the presence of Ag^+ gives 4b,8b,8c,8e-tetrahydrodibenzo-[*b*,*e*]cyclopropa[*g*,*h*]pentalene *(2)*, by a normally forbidden (Woodward-Hoffmann rules) disrotatory ring opening of the Diels-Alder adduct, which becomes allowed when the adduct is complexed to silver.

The lecture concluded with some observations on the structure of free cyclobutadiene. A study of some Diels-Alder reactions of cyclobutadiene with dimethylmaleate and fumarate tentatively suggests that cyclobutadiene reacts in the singlet state (as a rectangular diolefin).

J. K. Hamblin (Sunbury-on-Thames, England) reported the dimerization of propene to methylpentenes (mainly 4-methyl-1-pentene) at 150 °C and about 100 atm with sodium or potassium on pure graphite or potassium carbonate. This reaction can be carried out on a pilot-plant scale and under the best conditions a yield of 92% of 4-methyl-1-pentene has been achieved.

Allylic anions from propene or butenes will react with ethylene. In a typical reaction a 1:1 molar ratio of ethylene and propene gives a 92% yield of *n*-pentenes with small amounts of hexenes and heptenes. Similarly, reaction of ethylene with 1-butene gives 3-methyl-1-pentene and 2-hexene. The reactivity of the allylic anions towards ethylene decreases in the order $C_3H_5^- > n\text{-}C_4H_7^- > iso\text{-}C_4H_7^-$.

R. D. Cramer (Wilmington, Delaware, USA) dealt with olefin complexes of Rh^{I} and Rh^{III}. Ethylene can be dimerized to butenes (mainly 1-butene) in up to 95% conversion by $RhCl_3 \cdot 3\,H_2O$, $[(C_2H_4)_2RhCl]_2$, or $(acac)_2Rh(C_2H_4)_2$ in the presence of hydrogen chloride in ethanol. The mechanism of the reaction has been elucidated by a combination of kinetic and spectroscopic techniques and involves the insertion of a coordinated ethylene into the ethyl-rhodium bond in the complex $[C_2H_5Rh^{III}Cl_3(C_2H_4)S]^-$ (where S = solvent molecule) as the rate determining step. The codimerization of ethylene and butadiene to give 1,4- and 2,4-hexadiene, 3-ethyl-1,4-hexadiene, and 3-methyl-1,4-heptadiene was described. This reaction differs from the ethylene dimerization in that the reactive intermediates are π-allylrhodium complexes.

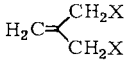
G. Wilkinson (London, England) reported that the compounds $HRh(CO)[P(C_6H_5)_3]_3$ and $HRhCl[P(C_6H_5)_3]_3$ are effective catalysts for the hydrogenation of terminal olefins at ambient temperature. The reaction with $HRh(CO)[P(C_6H_5)_3]_3$ has been shown to involve the coordinatively unsaturated Rh^{I} complex *trans*-$HRh(CO)[P(C_6H_5)_3]_2$, and the high specificity towards 1-alkenes and the lack of olefin isomerization in this reaction was explained by a combination of the influence of the phosphine ligand on the direction of addition of the metal hydride to the olefin, and the steric effect of the bulky *trans* phosphine ligands in preventing formation of the branched-chain alkyl derivative.

The rhodium complex $HRh(CO)[P(C_6H_5)_3]_3$ catalyzes the hydroformylation of olefins to aldehydes (normal:branched chain ratio *ca.* 20:1) in 95% yield at room temperature and 1 atm CO pressure. The efective catalyst in this reaction is thought to be $HRh(CO)_2[P(C_6H_5)_3]_2$ formed by the rapid equilibria:

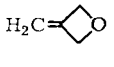
$$HRh(CO)[P(C_6H_5)_3]_3 \xrightarrow[+H_2]{\text{fast, } -CO} HRh(CO)_2[P(C_6H_5)_3]_2 \xrightarrow[+H_2]{\text{slow, } -CO} [P(C_6H_5)_3]_2CORh(CO)_2RhCO[P(C_6H_5)_3]_2$$

The iridium complex $HIr(CO)_2[P(C_6H_5)_3]_2$ has been prepared, and has been shown to exist as an equilibrium mixture of two unidentified species in solution. Neither this iridium compound nor the compound $HRhCl[P(C_6H_5)_3]_3$ are effective hydroformylation catalysts at room temperature.

F. Weiss (Lyon, France) reviewed the methods of synthesis and the chemistry of $\alpha\alpha'$-substituted isobutenes of type *(3)* (where X = halogen, OH, H, CO_2R, or CN) and the related compound 2-methyleneoxetane *(4)*.



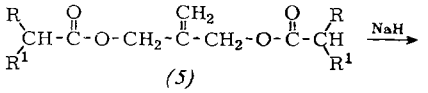
(3)



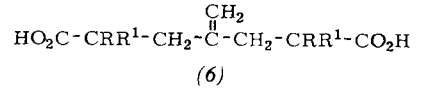
(4)

The epoxide of compound *(3)* (X = Cl) is reported to polymerize to a high molecular weight polyether of the 'PENTON' type with triethylaluminum.

The compounds of type *(3)* (X = halogen) behave normally in substitution reactions to give, in the main, disubstituted products, although monosubstitution can be achieved under controlled conditions. Substituted isobutene derivatives undergo some interesting molecular rearrangement reactions. Thus esters such as *(5)* rearrange with sodium hydride to pimelic acids *(6)*. These pimelic acid derivatives and the diols



(5)



(6)

resulting from their hydrogenation are potential intermediates for high temperature lubricants. $\alpha\alpha'$-Bis(aryloxy)isobutenes readily undergo Claisen condensation to give phenols.

E. J. Corey (Cambridge, Mass., USA) reported that $Ni(CO)_4$ catalyzes allylic dimerization at 50 °C in polar solvents, this reaction having been utilized in the synthesis of C_{12}, C_{14}, and C_{18} cyclic dienes from the compounds *(7)* (where n = 6, 8, or

$$BrCH_2\text{-}CH = CH(CH_2)_nCH = CH\text{-}CH_2Br \quad (7)$$

12 respectively); only poor yields of smaller ring compounds (C_8 or C_{10}) are obtained by this method. Allyl bromide is dimerized to 1,4-hexadiene at 0 °C in ether or dimethylformamide using $(\pi\text{-}C_3H_5NiBr)_2$, but as fast ligand exchange occurs this reaction cannot be extended to prepare mixed allyl dimers. Substituted methylallyl derivatives can be obtained in 70–90% yields from $(\pi\text{-}C_3H_5NiBr)_2$ and alkyl or aryl halides in dimethylformamide, and this reaction is a particularly effective means of introducing an allyl group into an organic molecule.

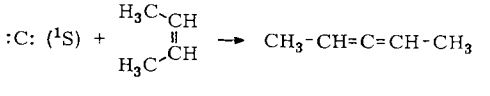
Selective cross coupling of alkyl groups can be achieved using copper salts of the type $R_2Cu^-Li^+$ (R = alkyl).

$$R\text{-halogen} + R^1_2Cu^-Li^+ \rightarrow R\text{-}R^1$$

This reaction gives high yields and is of general applicability for alkyl, allyl, benzyl, aryl, and vinyl halides and geminal dihalides.

P. S. Skell (University Park, Pennsylvania, USA) described the generation of C_1, C_2, C_3, and C_4 molecules by a carbon arc at low temperatures in high vacuum. These molecules have been caused to react with a variety of substrates when condensed on to neopentane on the surface of the reaction vessel at liquid nitrogen temperature.

The C_1 molecule exists in three forms, a ^1S (singlet state; :C:), a ^1D (singlet state: :C:), and a ^3p (triplet state; :$\dot{C}$) with stabilities increasing in the order $^1S < {}^1D < {}^3p$: The ^3p and ^1D species add stereospecifically to olefins and conjugated dienes to give dicyclopropane derivatives. The high energy ^1S species gives allene derivatives with olefins by an apparent insertion into the olefinic double bond.



Evidence was presented that two forms of the C_2 molecule exist, a singlet species (:C=C:) which reacts with hydrocarbons to give ethylene, and a triplet species (·C≡C·) which gives acetylene with the same substrate. The C_3 molecule can exist in three forms: two singlet species (:C=C=C:) and a triplet species (:C=C=$\dot{C}$). The latter has been shown to add stereospecifically to olefins, whereas one of the singlet species exhibits non-stereospecific addition to olefins and gives allene and propyne with hydrocarbon substrates. The other singlet species, generated by a hot carbon filament, gives allene exclusively with hydrocarbons.

A number of short papers read at the Symposium should also be mentioned. *D. H. Johnson* (Blackley, England) reported the oxychlorination of *n*-butenes at 350 °C with γ-alumina/cupric oxide/potassium chloride catalyst to give 1,4-dichlorobutadiene isomers.

A. J. Shuttleworth (Runcorn, England) described the pyrolysis of *trans*-1,2-dichloroethylene to give mixed isomers of trichlorobenzene, small amounts of dichlorobenzenes, and four isomers of trichlorobutadiene.

R. W. Humniel (Wantage, England) reported the isomerization of *cis*-2-butene to *trans*-2-butene upon γ-irradiation in the presence of 1% sulfur hexafluoride at 30 °C in an argon atmosphere.

O. Onsager (Oslo, Norway) reported the dimerization of propene to a mixture of *cis*-2-hexene, 2,3-dimethyl-1-butene, 2-methyl-1-pentene, and 4-methyl-1-pentene with a catalyst composed of tetramethylcyclobutadienenickel dichloride, ethylaluminum dichloride, and tri-*n*-butylphosphine.

C. F. Kohll (Amsterdam, Netherlands) described the synthesis of vinyl esters by the $PdCl_2$-catalyzed reaction of ethylene and sodium acetate in glacial acetic acid.

J. M. Locke (Southampton, England) described the hydrogenation of unsaturated polymers, *n*-dodecene, styrene, or diphenylacetylene using a catalyst prepared by the addition of bis(isopropylsalicylato)nickel to *n*-butyllithium in tetrahydrofuran or diglyme.

J. D. Littlehailes (Runcorn, England) reported the hydrodimerization of acrylonitrile to give an almost quantitative yield of adiponitrile with sodium amalgam and water in the presence of quaternary ammonium salts.

D. R. Taylor (Manchester, England) described the thermal cycloaddition of allene to fluoroolefins at 130 to 160 °C to give high yields of cyclobutane derivatives. Tetramethylallene (2,4-dimethyl-2,3-pentadiene) under similar conditions gives 1:1 adducts arising by a preliminary isomerization of the allene to 2,4-dimethyl-1,3-pentadiene. [VB 177 IE]

German version: Angew. Chem. *81*, 155 (1969)

The Specific Trypsin Inhibitor from Pig Pancreas

By *H. Tschesche*

The trypsin inhibitors of low molecular weight are plant or animal polypeptides with molecular weights of 6000–20000 (serum inhibitors: mol. wt. 75000). They may act either specifically or polyvalently and inhibit other endopeptidases as well as trypsin. The polyvalent inhibitors include, besides plant inhibitors (mol. wt. 20000), the callicrein inactivator from bovine organs which is identical with *Kunitz*'s trypsin inhibitor from bovine pancreas. Bovine pancreas contains, besides the intracellular *Kunitz* inhibitor, an inhibitor that is specific against trypsin – *Kazal*'s inhibitor – which is secreted in the fluid from the gland. Only the trypsin-specific inhibitor of the *Kazal* type is found in other species of mammals, *e.g.*, the pig [1].

The inhibitors inhibit proteases by complex formation, in that they mask the active center, usually in the ratio 1:1, as is found from the inhibition curve also for the inhibitor from pig pancreas. The reaction is competitive with this inhibitor. The dissociation constant can be estimated from the inhibition curve and is certainly less than 10^{-11} M. Whereas polyvalent inhibitors have permanent inhibition against trypsin, the specific trypsin inhibitors become inactive during the action; their inhibitory effect is only temporary [2].

This inactivation begins with selective hydrolysis of only one lysine bond in the native polypeptide chain of the inhibitor from pig pancreas (mol. wt. = 6000), which contains four lysine and two arginine units. This lysine unit lies between two disulfide bridges (loop) [3]. Its hydrolysis gives a modified inhibitor that is inactivated faster than the native molecule under physiological conditions. Its dissociation constant, which can be determined from the inhibition curve, is increased ($K_D = 10^{-9}$ M) and thus permits powerful interactions during tryptic inactivation.

The selective tryptic hydrolysis (modification) is responsible for the appearance of electrophoretically and chromatographically separable active inhibitors such as were isolated by *Kazal* and by *Fritz* and *Werle* from mammals of various kinds by way of water-insoluble trypsin resin.

The modification occurs at a lysine bond in the inhibitor from the pig and the dog, but at the arginine bond in the inhibitor from the ox. These bonds probably lie in the active center of the inhibitors [3,4]. Modification of this type is typical of all specific trypsin inhibitors of *Kazal* type; it occurs at the pH region of 2 to 10 with soluble trypsin and water-insoluble trypsin resin. The maximum of the tryptic modification occurs at pH 3.4 for the inhibitor (I) from pig pancreas. This is therefore a special substrate for trypsin (T), is bound to it as a complex owing to its high affinity for trypsin even in strongly acid solution, and, unlike other natural and synthetic substrates, is maximally hydrolyzed in this pH range because of the increasing dissociation of the complex [5]. From the selective hydrolysis, from experiments with insoluble trypsin resin, from the kinetics, and from the maximal modification at lower pH values it must be concluded that the inhibitor is being modified within the complex TI and not within a Michaelis-Menten complex TIT after further addition of excess trypsin.

Lecture at Dortmund on October 14, 1968
German version: Angew. Chem. *81*, 122 (1969) [VB 176]

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[1] *H. Fritz, F. Woitinas*, and *E. Werle*, Hoppe-Seylers Z. physiol. Chem. *345*, 168 (1966); *L. J. Greene, J. J. DiCarlo, A. J. Sussman, D. C. Bartelt*, and *D. E. Roark*, J. biol. Chemistry *243*, 1804 (1968).

[2] *M. Laskowski* and *F. C. Wu*, J. biol. Chemistry *204*, 797 (1953).

[3] *H. Tschesche*, Hoppe-Seylers Z. physiol. Chem. *348*, 1216, 1635 (1967).

[4] *K. Ozawa* and *M. Laskowski jr.*, J. biol. Chemistry *241*, 3955 (1966).

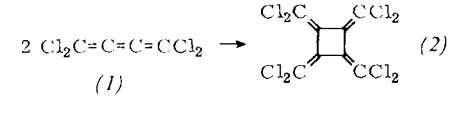
[5] *H. Tschesche* and *H. Klein*, Hoppe-Seylers Z. physiol. Chemistry, *349*, 1645 (1968).

Thermally Unstable Allenes and Related Compounds

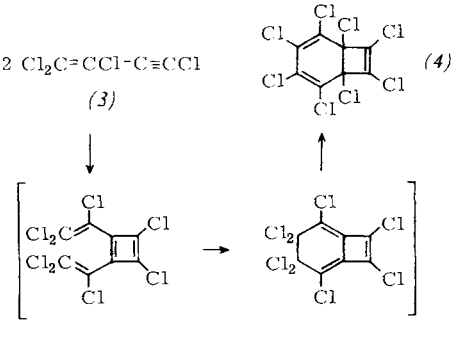
By *A. Roedig* [*]

The rate of thermal dimerization of allenes to 1,2-dimethylcyclobutane derivatives is greatly influenced by substituents. The accumulation of electron-acceptor groups destabilizes the allene system. Several dehydrohalogenations and fragmentations give rise to intermediates consisting of allenes that are thermally unstable, *i.e.*, can be preserved only below −60 °C and in some cases deflagrate in the undiluted state. They can be isolated by treating HCl-rich or HBr-rich precursors with $NaNH_2$ in liquid NH_3/propane or with a *tert*-butoxide of potassium or lithium in liquid propane or light petroleum at −75 °C.

On dimerization of trichloroallenes $Cl_2C{=}C{=}CClR$ (R = CN, $COOC_2H_5$, or C_6H_5) the electronically most active and the largest substituents appear in the exocyclic methylene groups. Kinetic measurements show that the rate of dimerization decreases in the order R = CN > $COOC_2H_5$ > Cl > C_6H_5 = Br > H. The activation entropy of dimerization of allenes is



(1) *(2)*



(3) *(4)*

strongly negative, but the activation enthalpy is relatively small (for R = Cl, $\Delta S = -45$ cal · mole^{-1} · grad^{-1}, $\Delta H = 11$ kcal mole^{-1}). A synchronous process is considered more likely than a two-stage radical mechanism.

Compared with perchloroallene, perchlorobutatriene *(1)* is remarkably stable thermally. It dimerizes only at 100 °C, giving perchloro[4]radialene *(2)*. Perchlorobutenyne *(3)*, on the other hand, dimerizes slowly even at 0 °C; the structure assigned earlier to the dimer[1] is untenable since it assumes *(1)* and *(2)* as unstable intermediates; meanwhile structure *(4)* has been proved for it by ozonolysis. The most probable course of the reaction is shown in the formula scheme.

The UV, IR, and NQR spectra, as well as the chemical behavior, indicate structure *(4)*. With nucleophilic reagents the compound gives either derivatives of perchlorobenzocyclobutene or some other aromatic compound, *e.g.*, with ammonia it gives perchlorobenzonitrile. Dechlorination gives dimers of perchlorobenzocyclobutene. Valence isomerization of *(4)* to perchlorocyclooctatetraene, whose structure is based on UV, IR, NQR, and Raman spectra, is effected by acid catalysis. Conversion into the benzocyclobutene system is more strongly favored thermally. $AlCl_3$ rearranges *(4)* and perchlorocyclooctatetraene to perchlorobenzocyclobutene. The structures of two further C_8Cl_8 isomers formed on thermal rearrangement of perchlorocyclooctatetraene are not firmly established.

Lectures at Würzburg (Germany) on December 6, 1968, and at Wayland, Mass. (USA) on May 6, 1968 [VB 182 IE]
German version: Angew. Chem. *81*, 157 (1969)

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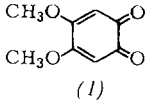
[1] *A. Roedig* and *R. Kohlhaupt*, Tetrahedron Letters *1964*, 1107.

SELECTED ABSTRACTS

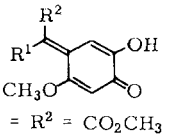
The existence of RuC, IrC, and PtB molecules has been demonstrated by *N. S. McIntyre, A. van der Auwera-Mahieu,* and *J. Drowart* using mass spectrometric methods. The metals were evaporated off graphite in Knudsen cells; boron carbide was added to the platinum. Evaluation of the intensity relationships of molecular ions and fragment ions (whose relation to one another was apparent from their identical appearance potentials) in the light of known thermochemical data afforded dissociation energies of 151.0 ± 3.0 kcal/mole for RuC, 148.4 ± 3.0 kcal/mole for IrC, and 113.3 ± 4.0 kcal/mole for PtB. / Trans. Faraday Soc. *64*, 3006 (1968) / –Hz.

[Rd 960 IE]

Alkoxy-*o*-benzoquinones, according to *H.-W. Wanzlick* and *U. Jahnke,* can be prepared by base-catalyzed addition of alcohols to *o*-quinones formed in solution. Dehydrogenation of pyrocatechol and 4-methylpyrocatechol in methanol and ethanol with PbO_2 in the presence of the alkoxide yields the alkoxy-*o*-quinones in 18 to about 60% yield. *(1)* can be



(1)



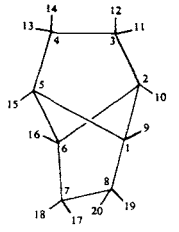
(2), $R^1 = R^2 = CO_2CH_3$
(3), $R^1 = C_6H_5$, $R^2 = CN$
(4), $R^1 = C_6H_5$, $R^2 = CO_2CH_3$

readily hydrolyzed to form 2,5-dihydroxy-*p*-quinone, which is converted into 2,5-dimethoxy-*p*-quinone by methanol and traces of mineral acid. The very reactive alkoxy-*o*-quinones form the quinonemethides *(2)*, *(3)*, and *(4)* on reaction with CH-acid compounds such as dimethyl malonate, benzyl cyanide, and methyl phenylacetate. / Chem. Ber. *101*, 3744 1968 / –Ma.

[Rd 947 IE]

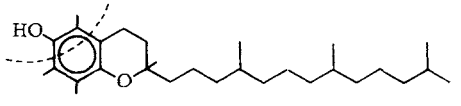
The structure of tricyclo[3.3.0.0^{2,6}]octane *(1)* prepared by mercury-sensitized photoisomerization of *cis,cis*-1,5-cyclooctadiene has been determined by *J. F. Chiang* and *S. H. Bauer* by diffraction of 70 keV electrons.

The symmetry of the molecule is D_{2d} [fourfold alternating axis (rotation + reflection) through the centers of C^3–C^4 and C^7–C^8; two twofold axes through the centers of C^1–C^2, C^5–C^6 and C^2–C^6, C^1–C^5; two planes of symmetry bisect the angles between the twofold axes]. The H^{11}–C^3–H^{12} angle is

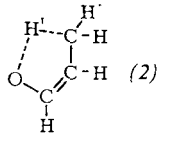


surprisingly small (105.8 ± 1.8 °). The dihedral angle in the cyclobutane ring (126.7 ± 0.3 °) is also unusually small (145 to 147 ° in cyclobutanes). On the basis of the average vibration amplitude of the C–C bonds (0.046 Å), the rigidity of the molecular skeleton is similar to that of cyclopropane. / Trans. Faraday Soc. *64*, 2247 (1968) / –Hz. [Rd 951 IE]

The energy content of the primary oxidation products of α-tocopherol (vitamin E) *(1)* has been determined by *R. Janoschek* by a wave-mechanical calculation. The oxidation of *(1)* occurs primarily in the area indicated, with the result that a 2-methylphenoxy radical and a 2-hydroxybenzyl radical come



(1)

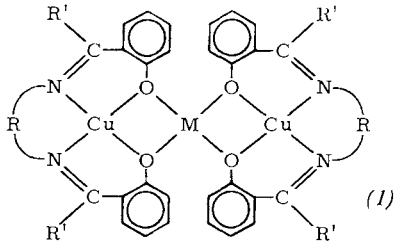


(2)

into consideration as tautomers of the primary product. To obtain a model for this, the energy of *(2)* was calculated as a function of the position of H′ · H′ thus moves on a potential surface having two minima, which correspond to the phenoxy and benzyl radicals. According to the calculation, the energy of the phenoxy radical lies 49.6 kcal/mole above that of the benzyl radical; the height of the potential barrier between the two forms of the radical (measured relative to the phenoxy form) is 54.6 kcal/mole. Assuming that H′ has to tunnel through the potential barrier during the transformation of the form of the radical, a mean life of 5.3 sec was calculated for the phenoxy radical. / Internat. J. Quantum Chem. *2*, 707 (1968) / –Hz.

[Rd 954 IE]

The magnetic properties of trinuclear complexes of quadridentate Schiff's bases were investigated by *S. J. Gruber, C. M. Harris,* and *E. Sinn.* The complexes *(1)* all contain the grouping CuMCu; the metal ions are linked to one another by oxygen bridges.



(1)

The observed magnetic moments are without exception smaller than expected and diminish rapidly with decreasing temperature between 400 and 80 °K. This phenomenon is interpreted as an antiferromagnetic resonance effect between M and Cu; the magnetic moments calculated on the basis of this resonance effect are in good agreement with the observed values. There is no evidence for any resonance effect between the terminal copper ions. / J. chem. Physics *49*, 2183 (1968) / –Hz.

[Rd 953 IE]

The surface species formed on adsorption of methanol and ethanol vapor on magnesium oxide have been characterized by *R. O. Kagel* and *R. G. Greenler* using IR spectroscopy. At room temperature a physically adsorbed layer is found whose structure corresponds to that of the liquid alcohols. Adsorbed alkoxide is found if this layer is desorbed by reducing the pressure and heating to about 160 °C. It can be assumed that the alcohol is dissociated by magnesium ions lying in the surface, an oxygen ion in the surface taking up the proton. If MgO is heated to 160 °C in the presence of methanol or ethanol vapor, formate and acetate are formed in the surface. On further heating, to 430 °C, alkyl carbonates are formed in the surface, which are probably produced from CO_2 (from decarboxylation of formate or acetate) and alkoxide; if there is no alkoxide in the surface, a layer of magnesium carbonate is found instead. / J. chem. Physics *49*, 1638 (1968) / –Hz.

[Rd 955 IE]

A simple method for the determination of the critical temperatures of volatile liquids has been developed by *H. W. Hoyer, A. V. Santoro,* and *E. J. Barrett.* Varying amounts of the substance to be investigated are placed in sealed ampuls and DTA cooling curves are recorded, in which separation of the sample into two phases is marked by a discontinuity. If the temperatures at which this discontinuity occurs are plotted against the overall density of the substance in the ampul, it is found that the temperature rises with increasing density to begin with and then remains constant, at the critical temperature, when the critical density has been exceeded. In this form, the method is restricted to substances whose critical pressure is not greater than about 45 atm. Comparison with values given in the literature for the critical temperatures of diethyl ether, acetone, cyclohexane, *n*-hexane, *n*-heptane, ethyl acetate, and benzene reveals deviations of up to 1.3 °C./ J. physic. Chem. *72*, 4312 (1968) / –Hz.

[Rd 956 IE]

The oxidation of hydrazine by molybdenum(VI) in the pH range of 1.2–3.2 has been investigated by *T. Huang* and *J. T. Spence* using spectrophotometric methods of analysis. During the reaction N_2 is evolved in stoichiometric quantities; no NH_3 can be detected. The reaction is of first order with respect to both reactants; the pH-dependence is complicated. Diimide has been indentified as an intermediate product both by mass spectroscopy and by interception with unsaturated organic acids. The reaction is thought to proceed as follows:

$$N_2H_5^+ + Mo^{VI} \rightarrow N_2H_2 + Mo^{IV} \quad (a)$$

$$H^+ + 2\,N_2H_2 \rightarrow N_2 + N_2H_5^+ \quad (b)$$

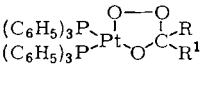
$$Mo^{IV} + Mo^{VI} \rightarrow 2\,Mo^{V} \quad (c)$$

$$2\,Mo^{V} \rightarrow Mo_2^{V} \quad (d)$$

Reaction (a) is the rate-determining process, (b)–(d) are fast. The reaction system investigated has some significance as a model for the biological fixation of nitrogen by enzymes containing molybdenum. / J. physic. Chem. *72*, 4198 (1968) / –Hz.

[Rd 957 IE]

The reaction of the bis(triphenylphosphine)oxygenplatinum(0) complex with carbonyl groups has been investigated by *R. Ugo, F. Conti, S. Cenini, R. Mason,* and *G. B. Robertson.* Both the recrystallization of $[(C_6H_5)_3P]_2PtO_2$ from acetone and its reaction with methyl ethyl ketone, acetaldehyde, or benzaldehyde give the new type of ketoperoxy chelates *(1)* to *(4)*. It is assumed that the bonding of the O_2 molecule in

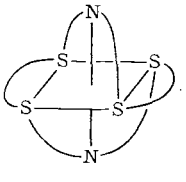


(1), R = R^1 = CH_3
(2), R = CH_3, R^1 = C_2H_5
(3), R = H, R^1 = CH_3
(4), R = H, R^1 = C_6H_5

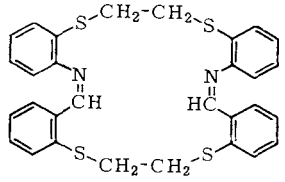
$[(C_6H_5)_3P]_2PtO_2$ resembles that of the excited $^3\Sigma_u$ state of the free O_2 molecule, *i.e.* a predominantly ionic structure $O^+–O^-$. The formation of *(1)* to *(4)* therefore has the characteristics of a conventional nucleophilic addition at the carbonyl group. The reactivity increases with increasing polarity of the carbonyl group. *(1)* is obtained as pale yellow monoclinic crystals with the lattice constants a = 9.83, b = 9.06, c = 37.90 Å, β = 95.6 °, Z = 4, belonging to the space group $P2_1/c$. The coordination of the platinum atoms is almost planar. The bond lengths have normal values; in particular, the O–O distance of 1.46 Å is characteristic of a peroxide group. / Chem. Commun. *1968*, 1498 / –Bl.

[Rd 961 IE]

A new sulfur-containing macrocyclic hexadentate ligand, 12,13,26,27-tetrahydrotetrabenzo [*e,i,o,s*]-[1,4,11,14,7,18]tetrathiadiazacycloeicosene, was synthesized by *L. F. Lindoy* and *D. H. Busch.* The complexes, which can only be octahedrally coordinated *(1)* because of the planarity of the S–N–S groups, were made by the reaction of a metal salt with 1,2-bis(2-aminophenylthio)ethane and 1,2-bis(2-formylphenylthio)-ethane, dissolved in stoichiometric quantities in the form of



(1)

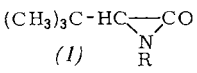


ms = *(2)*

the compounds (M ms)X_2 (M = Ni, X = ClO_4, I; M = Co, X = ClO_4). At room temperature the brown complexes (Ni ms)X_2 (X = ClO_4, I) have magnetic moments of 3.07 and 3.12 B.M., respectively. On heating (Ni ms) $(ClO_4)_2$ in DMF, the free macrocyclic compound *(2)* can be isolated in the form of yellow crystals. / Chem. Commun. *1968*, 1589 / –Ma.

[Rd 963 IE]

1-(1-Adamantyl)-3-*tert*-butylaziridinone *(1)*, a stable α-lactam, has been synthesized by *I. Lengyel* and *D. B. Uliss*; the synthesis was prompted by the fact that tertiary substituents have a pronounced stabilizing effect on α-lactams. 2-Bromo-3,3-dimethyl-*N*-adamantylbutyramide, which was obtained (m.p. 173–174 °C, 82% yield) from 2-bromo-3,3-dimethylbutyryl

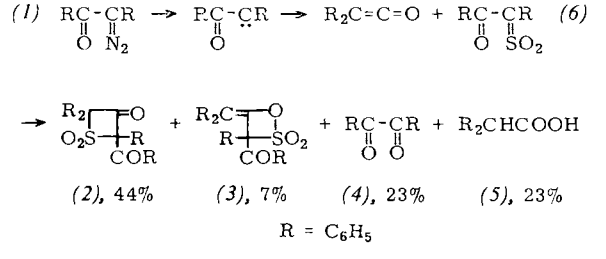


(1) R = Adamantyl

chloride and 1-adamantylamine in the presence of triethylamine in dichloromethane at 0 °C, could be cyclized with potassium *tert*-butoxide in ice-cold ethereal suspension to give *(1)*, m.p. 70 °C (λ_{max} = 254 nm [hexane], yield 65%). The compound is stable in water at room temperature; complete solvolysis is effected only after boiling for 48 hours in methanol. / Chem. Commun. *1968*, 1621 / –Ma.

[Rd 962 IE]

The formation of cycloadducts by the reaction of azibenzil *(1)* with SO_2 was observed by *T. Nagai*, *M. Tanaka*, and *N. Tokura*. The four-membered cyclic sulfones *(2)* and *(3)* were obtained, along with *(4)* and *(5)*, in boiling benzene. Diphenylketene is probably formed as an intermediate by the Wolff rearrangement, and this then undergoes cycloaddition



(1) → $R_2C{=}C{=}O$ + *(6)*

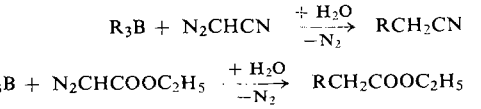
→ *(2)*, 44% + *(3)*, 7% + *(4)*, 23% + *(5)*, 23% + $R_2CHCOOH$

R = C_6H_5

with the ketosulfene *(6)*. Photochemical reaction of azibenzil with SO_2 in benzene at –5 to –20 °C (mercury high-pressure lamp) gave *(3)*, *(4)*, and *(5)* in 35, 44, and 13% yields respectively. / Tetrahedron Letters *1968*, 6293 / –Ma.

[Rd 964 IE]

Alkylation of diazoacetonitrile and ethyl diazoacetate with organoboranes, according to *J. Hooz* and *S. Linke*, is a new method of increasing the length of olefins by two carbon atoms with functional groups if organoboranes derived from olefins with terminal double bonds or cyclopentene are used:



$$R_3B + N_2CHCN \xrightarrow[-N_2]{+H_2O} RCH_2CN$$

$$R_3B + N_2CHCOOC_2H_5 \xrightarrow[-N_2]{+H_2O} RCH_2COOC_2H_5$$

The reactions with the nitrile proceed very fast even at 0 °C and give excellent yields (93–100%). The second reaction depends strongly on steric factors. For example: 1-hexene → octanenitrile, 100%; cyclopentene → cyclopentylacetonitrile, 99%; 1-octene → ethyl decanoate, 78%. / J. Amer. chem. Soc. *90*, 6891 (1968) / –Ma. [Rd 965 IE]

The dimerization products of α-methylstyrene in H_2SO_4 have been extensively investigated by *A. J. Švob* and *B. K. Černicki* by means of NMR spectrometry. Separation by gas chromatography (liquid phase SE 30) yielded six components: *cis*-2,4-diphenyl-4-methyl-2-pentene, 1,1,3-trimethyl-3-phenylindan, 2,4-diphenyl-4-methyl-1-pentene, *trans*-2,4-diphenyl-4-methyl-2-pentene, 1,3-diphenyl-3-methyl-2-butanone, and an oxidation product with $C_6H_5{-}C(CH_3)_2{-}$ and $-CH{=}C(\text{I})-CH_2-$groups. / Chimia *22*, 434 (1968) / –Ma.

[Rd 966 IE]

New catalysts for low-pressure carbonylation of methanol to give acetic acid have been developed by *F. E. Paulik* and *J. F. Roth*. A solution of an Rh compound such as $RhCl_3 \cdot 3\,H_2O$, $Rh_2O_3 \cdot 5\,H_2O$, $RhCl(CO)[P(C_6H_5)_3]_2$, $[Rh(CO)_2Cl]_2$ (5×10^{-3} M) and a halogen promoter such as hydriodic acid, CH_3I, $CaI_2 \cdot 3\,H_2O$, I_2 (0.05 M) in solvents such as benzene, water, acetic acid, methanol, and nitrobenzene catalyzes the carbonylation at 175 °C and 25 atm total pressure ($p_{CO} < 13$ atm). Appreciable carbonylation rates were observed even at CO pressures of 1 atm. There is preferential formation of acetic acid (> 99%). The active catalyst is a d^8-Rh^I complex. High rates of reaction can also be achieved at low pressure with similar homogeneous catalyst systems of Ir compounds in the presence of halogen promoters, particularly iodide. / Chem. Commun. *1968*, 1578 / –Ma. [Rd 967 IE]

BOOK REVIEWS

Handbuch der Lebensmittelchemie. (Handbook of Food Chemistry) Vol. 5, Part 2: Fruit, Vegetables, Potatoes, Mushrooms. Edited by *L. Acker*, *K.-G. Bergner*, *W. Diemair*, *W. Heimann*, *F. Kiermeier*, *J. Schormüller*, and *S. W. Souci*. Springer-Verlag, Berlin-Heidelberg-New York 1968. 1st. Edit., xxiv, 608 pp. 178 illustrations, bound. DM 174.60 / $ 43.65.

In modern food chemistry exclusive stress is no longer placed on chemical analysis; rather, the emphasis has shifted to individual factors involved in quality characteristics, to clarification of the nature and causes of changes, and to the determination of production and storage conditions influencing favorably the product quality. This theme finds its expression in the clearly arranged part of the new manual[1], both in the layout of the individual chapters, written by specialists, and in the way that newer methods of food preservation and processing (*e.g.* deep-freezing and freeze-drying) and new food sources (*e.g.* yeast and algae) are dealt with. The authors treat the subject fundamentally, without neglecting the technological aspects. Selected analytical methods are discussed in such detail that they can be applied directly. Literature references, in some cases up to 1965, are listed at the end of each contribution. 136 of the total of 178 illustrations appear in the contributions by *Czaja*. Copious numerical data are given in the tables. Printing errors are few, and the reviewer has not encountered any really serious mistakes. The very detailed subject index provides a key to the richness of the contents (an author index is dispensed with). The layout is excellent.

In the chapter "Fresh Fruit" (*H. Drews*, 75 pp.), under the "Fruit" section, there is a brief account of the fundamentals of fruit growing, the kinds of fruit, the classification of fruit into particular groups, fruit storage methods, the changes occurring during storage, and the chemical examination of fruit. There are also hints of evaluation in accordance with foodstuff legislation. The following are considered among durable fruit goods: Deep-frozen fruit (*J. Gutschmidt*, 17 pp.), canned and bottled fruit (*A. S. Kovacs*, 22 pp.), dried fruit (*K. Herrmann*, 12 pp.), and fruit in syrup (*K. Herrmann*, 4 pp.). Fruit products dealt with include preserves, jams, jellies, mousses, *etc.*, as well as semi-manufactured products (*K. Herrmann*, 45 pp.), fruit juices, unfermented wine, con-

centrates, and fruit-syrups (*K. Herrmann*, 63 pp.), fruit juice drinks, and other nonalcoholic drinks (*E. Benk*, 20 pp.). Finally there is a contribution on the microscopic examination of fruit and fruit products (*A. Th. Czanja*, 52 pp.).

The section "Vegetables" is similarly arranged. The chapter on fresh vegetables (51 pp.) is written by *P. Nehring*. Information on durable vegetable goods is given in the chapters: Deep-frozen vegetables (*J. Gutschmidt*, 33 pp.), canned and bottled vegetables (*P. Nehring*, 38 pp.), pickled vegetables (*F. Martens*, 18 pp.), and dried vegetables (*K. Herrmann*, 6 pp.), tomato juices and other tomato products, as well as other vegetable juices (*K. Herrmann*, 16 pp.). One chapter is devoted to potatoes and potato products (*H. Mohler* and *H. Sulser*, 34 pp.), and one to mushrooms and mushroom preserves (*W. Bötticher*, 31 pp.). A contribution on the microscopic examination of vegetables, salads, seasoning herbs, and edible mushrooms (*A. Th. Czaja*, 25 pp.) completes this field. The volume concludes with a chapter on the microbiological production of foodstuffs (*E. Reiff*, 14 pp.) in which yeast above all plays an important role.

The great amount of information to be found in this volume will ensure a wide readership. *J. Wolf* [NB 759 IE]

Standardmethoden der praktischen Chemie (Standard Methods of Practical Chemistry). Edited by *E. Poulsen-Nautrup*. Main group: Preparation Methods of Organic Chemistry. Friedr. Vieweg & Sohn, Braunschweig. Issue 1a: General Working Procedure. 1st Edit., 1963. viii, 54 pp., 46 illustrations, 19 tables; Issue 1b: General Working Procedure II. 1st Edit., 1966. viii, 54 pp., 49 illustrations, 18 tables; Issue 1c: General Working Procedure III, 1st Edit., 1966. viii, 50 pp., 28 illustrations, 19 tables; Issue 2: Basic Compounds I. 1st Edit., 1963. viii, 50 pp., 13 illustrations., 11 tables; Issue 3: Derivatives I, 1st Edit., 1964. viii, 50 pp.; Issue 4: Basic Compounds II. 1st Edit., 1964. viii, 60 pp., 15 illustration; Issue 11: Azo dyes. 1st Edit., 1964. viii, 44 pp., 13 illustrations 3 color tables. Each issue (in folder) DM 5.90.

"Preparative Methods", compiled by *E. Poulsen-Nautrup*, is part of "Standard Methods of Practical Chemistry". Each issue contains sets of detailed working instructions, printed on individual sheets of paper, that are suitable for use in schools. Issues 1a–1c relate to general techniques, including reaction vessels, gases, and work at elevated pressures. A thorough introduction is given to fundamental operations such as filtration, distillation, recrystallization, *etc.* Issues 2–4 each contain working instructions for ten preparations. Each sheet begins with an equation for the reaction in question, and continues with precise directions and with a discussion of the range of applications of the reaction. Hints are frequently given on testing the product purity or on preventing accidents during the preparation. Issue 3 is devoted to the preparation of derivatives, *e.g.* sodium alkoxides, and chlorides, and esters. Issue 11 covers azo dyes, describing the dyeing of wool and cotton as well as the preparation and chromatographic examination of the dyes.

The collection is highly recommended for all schools and technical colleges teaching chemistry. This series should also prove invaluable to those reading chemistry as a subsidiary subject at universities. *H. J. Bestmann* [NB 763 IE]

Dictionary of Science and Technology, English-German. By *A. F. Dorian*. Elsevier Publishing Company, Amsterdam-London-New York, 1967. 1st Edit., 1238 pp., bound, Dfl. 80.00.

Good technical dictionaries, even in such common languages as English and German, are such a rarity that it is no great exaggeration to say that they do not exist. It is thus scarely surprising that so many attempts are made to fill the void. The latest, published by Elsevier, contains more than 1200 pages, with some 50000 terms covering about 130 disciplines, predominantly in science and technology. Only two authors *A. F. Dorian* and *Liane Herzbruch*, appear to be responsible for this gigantic undertaking. The reviewer confesses that he was surprised by this, as also by the rather curious English foreward and its badly translated German counterpart.

It is of course unfair to judge such a vast work – its scope extends from Baking to Ecclesiastical History and from Biochemistry to Political Economics – on the basis of its treatment of Chemistry. At the same time it is not unreasonable to assume that the authors devoted the same degree of care to all the fields covered.

The selection of words is sensible and modern, though here and there somewhat haphazard. In many cases a brief English definition of the entry is given in addition to the translation, a very useful feature in view of the variety of subjects involved. Less pleasing is the (in the reviewer's opinion excessive) number of instances in which inaccurate or even totally incorrect renderings are given. These range from obsolete spelling (Karbonat, Oxyd) and nomenclature (Oxynaphthalin, Äthylmerkuriacetat), obvious printing errors (Magnesiumarseniat, Lutecium(!), arsine = Arsen), to downright nonsense (radius = Umkreis, ethylene = schweres Kohlenwasserstoffgas, shift = Austausch, chemical intermediate = Zwischenmittel, ethylbenzyl chloride = Benzochlorsäureäthylester !!, *etc.*).

An insert informs the user that the publishers intend to produce a German-English edition at the end of 1968, to be followed by supplementary volumes at intervals of 4 or 5 years, with an improved and revised edition of the main dictionary to appear every 8 years. The project is thus clearly an ambitious one; it seems most desirable, however, that the whole responsibility should not rest on the shoulders of just two authors, but that the help of other subject and language specialists be enlisted as a matter of urgency.

H. Grünewald [NB 769 IE]

Nobel Lectures, Physiology or Medicine 1901–1921. Sponsored by the Nobel Foundation, Elsevier Publishing Company, Amsterdam-London-New York, 1967. 1st Edit., xii, 562, bound, Dfl. 80.00.

The present volume in the "Nobel Lecture" series published by Elsevier comprises addresses given by the Medicine Prize Winners between 1901 and 1921. As usual, each lecture is preceded by the presentation speech at the prize-giving, and biographical details complete the picture.

The book is fascinating to read even if one is not a physician. Fundamental investigations are reported that belong so much to the undeniable, reliable fund of knowledge of our time that it is impossible to return to those years during which it was all discovered and formulated, often with endless toil, without inner participation. The volume begins with a lecture given by *Emil von Behring* on the serum therapy of diphtheria, which enabled this disease to be mastered. *Sir Ronald Ross* received the prize for his discovery of the etiology of malaria; this is followed by *Pavlov*'s extremely readable report about his famous experiments on the physiology of digestion. *Robert Koch*'s Nobel Lecture was entitled "The current state of the struggle against tuberculosis" and this enumeration of famous names and deeds could be continued. For the sake of topicality, special mention should be made of the lecture given by the Frenchman *Alexis Carrel*, who received his prize in 1912 for experiments on organ transplantation. The lecturer distinguishes between autoplastic transplants (within the same organism), which invariably succeed if the operation is carried out satisfactorily, and homoplastic transplants (between different living beings of the same species), which (at that time) always failed because even an organ transplanted correctly from the surgical point of view was rejected after a certain period. All this 60 years ago! It is interesting to note that in 1935 the same *Alexis Carrel* developed a machine for the sterile perfusion of isolated organs in collaboration with the famous flyer *Charles Lindbergh* who tackled the mechanical problems.

The 16 lectures forming the subject of this volume make fascinating reading which no one interested in history of modern natural science should forego.

H. Grünewald [NB 770 IE]

Carbonium Ions. An Introduction. By *D. Bethell* and *V. Gold.* Academic Press, London-New York 1967. 1st Edit., xii, 387 pp., numerous figures and tables, bound, $ 16.00 or 95 shillings.

Of the many reactive intermediates in organic chemistry, carbonium ions have attracted the closest attention during the last decade. The interest centers on the bridged carbonium ions and on stable solutions in 'superacids', in which even the methyl cation can be observed directly. Until recently there was no comprehensive treatment of the entire subject, and the present book attempts to fill this gap. Since an exhaustive treatment of the field would fill several volumes – as is evident from the 50 or so reviews and books cited – it was obviously necessary to reach some kind of a compromise. Its subtitle means that the book is addressed to students and chemical research workers active in other fields; it also means that it is a collection which can be used as a basis for introductory reading. We could thus expect at least a brief mention of all the fundamentals, while a too specialized discussion would be avoided. Finally, it should if possible offer a representative selection from the mass of available investigations. These aims have been only partially fulfilled.

After an introduction, the following subjects are considered: experimental methods in the investigation of carbonium ions (30 pp.), methods of preparation (13 pp.) and quantitative aspects of the formation of carbonium ions (51 pp.), factors which influence the stability (42 pp.), reactions of carbonium ions (60 pp.) and bridged carbonium ions (60 pp.); a few related species (acylium ions, singlet carbene, radical cations, and hetero-analogs) are mentioned briefly in the final chapter (21 pp.). The literature up to 1966 is taken into account (of the 1400 original citations, about 100 come from 1966 and 20 from 1967). The discussion is highly critical, which increases its value for the instructor or the practical chemical worker but it often appears not very didactic. An introduction should not, for example, devote nearly one quarter to 'non-classical' carbonium ions, the special position of which is debatable – the chapter is otherwise an excellent survey of all aspects of this special field – while the problem of the vinyl and aryl cations and the stereoelectronically directed course of the cyclopropyl → allyl cation rearrangement (*De Puy, Schöllkopf, Schleyer, Woodward, Hoffman*) on which intensive work has been carried out in the last few years has not even been mentioned.

The text is readable, though a little dry; the setting, printing, and production leave nothing to be desired, and only small misprints, of no significance to the understanding of the text, were found. The author index and the literature survey are excellently suited for a deeper penetration of the special subjects. The subject index is adequate. This first survey of the whole field is certain to be welcomed by many organic and physical chemists.

D. Seebach [NB 756 IE]

Organometallic Compounds. By *G. E. Coates, M. L. H. Green,* and *K. Wade.* Vol. II: The Transition Elements. By *M. L. Green.* Methuen and Co., Ltd., London 1968. 3rd. Edit., xiii, 376 pp., 86 figs., 31 tables, £ 5.0.0.

The number of publications dealing with organometallic compounds, especially those of the transition metals, has increased considerably in the last ten years. Although even in the second edition [1] the organometallic compounds of the transition elements were dealt with in about 100 pages and about 200 literature references, this work now appears as a separate volume with over 1300 references. The complex compounds are no longer arranged according to the group number of the transition element in the periodic table, but instead they are classified according to the type of the ligand. In this way, the alkyl group for example is indicated as a one-electron ligand, ethylene as a typical two-electron ligand, the π-allyl group as a three-electron ligand, and the π-cycloheptatrienyl group as a seven-electron ligand. Following this subdivision, the first seven chapters deal very clearly with a great number of characteristic complex compounds.

Another chapter is concerned with the reactions of the transition metal compounds with acetylene. A new addition is the last chapter, which deals with the catalytic reactions of transition metal compounds. In this, as the author remarks, only a few typical examples are outlined. Perhaps it is this chapter that might have been expanded, because of the increasing importance of this field in organometallic chemistry.

The book is recommended highly to advanced students of chemistry as an introduction to the organometallic chemistry of the transition metals and also to all others interested in this subject. The author is to be congratulated.

K. Jonas [NB 748 IE]

[1] Cf. Angew. Chem. *76*, 239 (1964).

The Names and Structures of Organic Compounds. By *O. Th. Benfey.* John Wiley and Sons, Inc., New York-London-Sydney, 1966. 1st Edit. xiv, 212 pp., board 23s.

Constructing the names of organic compounds according to the rules of systematic nomenclature is not to everyone's taste, nor has everyone the patience to plough through the IUPAC rules. *O. T. Benfey* has therefore written a pocket book for his students, in which the main rules and principles of nomenclature are very skilfully introduced in question and answer form. As the text progresses, the student is increasingly obliged to think for himself in order to find the right answer (which is always given). After 100 pages, the text leaves the subject of nomenclature, and a total of 66 pages are devoted to the calculation of formal charges, the writing of electronic formulas and resonance structures, and the calculation of the number of possible isomers for monosubstituted alkanes. The remainder of the book consists of revision questions (and answers) on the various chapters and a list of names of important compounds that are not mentioned in the main part.

First or second-semester chemistry students will find that this book presents, in an easily remembered manner, information that will be of use to them at a later stage. In any case, the book will certainly provide the teacher with many suggestions for dealing with the nomenclature of organic compounds.

H. Grünewald [NB 771 IE]

Plutonium Handbook – A Guide to the Technology. Edited by *O. J. Wick* with the cooperation of several associates. Preface by *G. T. Seaborg.* Gordon and Breach Science Publishers, New York-London-Paris 1967. 2 vols, x, 966 pp., numerous illustrations, diagrams, micrographs, and tables, Vol. 1. Cloth-bound. $ 26.00, Vol. 2 Cloth-bound $ 22.50. Professional Edition: Vol. 1. $ 15.50, Vol. 2 $ 13.25.

Although element 94, plutonium, has only been known for 28 years, today, along with uranium, it is the most important raw material for nuclear technology and one of the most significant primary sources of energy. Since plutonium literature has grown to an extent where it is now difficult to keep it under review, a comprehensive, critical survey has become necessary; the handbook described in this review fulfils this need very well. *O. J. Wick* has succeeded in getting some of the best-known plutonium technologists as authors of individual chapters.

The book is divided into seven sections: I. Physics, II. Metallurgy, III. Chemistry, IV. Chemical Reprocessing V. Production and Use, VI. Analysis and Inspection Procedures, and VII. Safety Precautions. It ends with a detailed author and subject index.

In section I. (*B. R. Leonhard jr.*), important nuclear data (half-lives, disintegration energies, resonance parameter,

reaction cross sections, *etc.*) are compiled into concise tables. (Unfortunately the standard work of *E. K. Hyde, G. T. Seaborg*, and *I. Perlman*: "Nuclear Properties of the Heavy Elements" has not been quoted.)

In section II, chapter 3 (*W. N. Miner* and *F. Schonfeld*) starts with a 20-page review of the physical properties of unalloyed plutonium. Regrettably, some of the results quoted are already superceded by more recent data. Chapter 4 (*H. R. Gardner*) deals with the mechanical properties of plutonium and its alloys (several tables and diagrams). The title of chapter 5: "Solid State Reactions" (*R. D. Nelson*) is somewhat misleading. It does not deal with solid state reactions in the sense of the chemist, but rather with the technologically very important single-phase changes between the allotropic modifications of plutonium. The chapter is illustrated with numerous instructive micrographs.

Chapter 6, on corrosion and oxidation (*J. T. Waber*), also provides information on corrosion protection. The references to the spontaneous ignition of unalloyed plutonium are important. Chapter 7, on the behavior of plutonium in alloys, is of interest to inorganic and physical chemists. It is divided into "Practical Aspects" (*C. C. Land*), "Phase Diagrams and Crystal Structure" (*F. H. Ellinger*), and "Alloying Theory" (*K. A. Gschneider jr.*). Sixty-five binary and ternary phases based on plutonium are described in detail; Table 7.12 contains structural data for about 80 intermetallic compounds, hydrides, chalcogenides and pnictides (binary compounds of a metal with a group V element).

Chapter 8, on refractory compounds of plutonium (*R. E. Scavdahl* and *T. D. Chikalla*), contains a wealth of information for anyone who wants to learn about, for example, reactor ceramics containing plutonium. Chapter 9, on metallography (*K. A. Johnson*), contains valuable information on the preparation of micrographs, with instructive original photographs. Chapter 10 is also important for the experimentalist ("Laboratory Techniques", *R. D. Nelson, C. C. Land*, and *F. H. Ellinger*). Unfortunately, the list of experimental techniques described is none too comprehensive. For example, references to the classical microtechniques are missing, and the number of illustrations could have been greater.

Chapter 11, ("Chemical Properties") in section III (*J. M. Cleveland*) appears superfluous, since the material could have been included in chapters 6 and 12. With its excellent survey of inorganic plutonium chemistry chapter 12 is well worth reading. Particular attention is called to the numerous clearly arranged tables containing thermodynamic and crystallographic data of individual compounds. Solutions of plutonium compounds, including those in molten salts, are described in chapter 13.

The treatment of chemical subjects is continued in volume 2, section IV (*J. M. Cleveland*). Chapter 14 ("Separation from Irradiated Uranium") does not contain detailed instructions for the separation of plutonium from irradiated uranium, but rather a comprehensive collection of separation procedures. Chapter 15 ("Plutonium Conversion Processes") is too short, with only 19 pages. For instance, no reference is given to the fully automatic plutonium reduction plant a Los Alamos (LA-1387). Chapter 16 ("Plutonium Recovery and Waste Disposal") to some extent parallels chapter 14, but is more detailed in text. Straightforward explanations of code expressions such as Redox, Purex, or Butex are lacking in chapters 14 to 16, and would have been desirable.

Fabrication and application of plutonium are treated in section V. Chapters 17 and 18 (*O. J. Wick*) describe the special metallurgical techniques developed for plutonium and its alloys; these are essentially influenced by the existence of 6 allotropic modifications of the metal, and its ready oxidation, which necessitates handling in an inert atmosphere and consequently, special furnace designs. Chapters 19 (*I. D. Thomas*) and 20 (*M. D. Freshley*) deal with the preparation and behavior of ceramic nuclear fuels based on plutonium. Attention is drawn to the many autoradiographs and micrographs.

Section VI again is of interest to the chemist. Although in chapter 21 ("Analysis", *R. J. Brouns*) a comprehensive survey of current analytical methods in plutonium technology is given, illustrations of special equipment are lacking, *e.g.* the spark chambers used for emission spectroscopy and low geometry counters for the absolute α determination. A reference in the bibliography to the compilation of Plutonium Emission Lines by *J. R. McNally* (ORNL-2154 Rev) would not have come amiss. Chapter 22 ("Inspection", *W. J. Bailey*) deals with nondestructive testing methods for fabricated pieces of plutonium or its alloys. The chapter contains numerous diagrams and photographs.

Section VII, describing safety aspects in working with the highly toxic and fissile plutonium, is considered to be of special importance, Chapters 23 (*R. C. Thompson*), 24 (*R. H. Wilson*), and 25 (*H. V. Larson*) deal with the biological effects of ingesting plutonium and with medical supervision of individuals working with plutonium. Chapter 26 (*L. G. Merker*) is devoted to the technical aspects of health protection. In spite of its very instructive illustrations, this chapter could have been more comprehensive. Although the bibliography contains a number of important reviews, reference is lacking to the numerous papers given at the Hot Laboratory Conferences.

Chapter 27 ("Nuclear Safety and Criticality", *E. D. Clayton* and *W. A. Rearden*) is of particular significance in working with larger (supercritical) masses of plutonium. There is unfortunately insufficient material on the insidiousness of the critical condition. Accounts are, however, given of critical data, and above all, practical directions are presented for protection against inadvertent critical excursions (numerous diagrams and illustrations). In chapter 28, *J. M. Nielsen* and *T. H. Beasley* describe the analytical methods used for the determination of plutonium in biological materials for the purpose of radiation survey and area monitoring.

To summarize, it may be said that the reader gets a very good general view of all parts of plutonium technology. The shortcomings mentioned are insignificant in comparison with the extent of material offered and they could easily be remedied in a second edition. The excellent presentation and the neat and clear printing make the price appear acceptable. Purchase of this book may be recommended to every chemical and metallurgical library.

F. Weigel [NB 761 IE]

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 4 50 75, Telex 461855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors**: *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 3
MARCH 1969
PAGES 157–226

The Composition and Conformation of Sugars in Solution

By S. J. Angyal[*]

The conformations of the aldoses in solution, and the compositions of the equilibrium mixtures formed from aldoses after dissolution in water, have been determined by NMR spectroscopy. Calculations based on non-bonded interactions and on the anomeric effect account for the observed conformations, and allow an approximate prediction of the α:β ratio of pyranoses in equilibrium and of the extent of anhydride formation from sugars in acid solution. In certain circumstances the furanose forms are more stable than the pyranose forms.

1. Introduction

Apart from their great biological importance, the carbohydrates are also of interest as model compounds for the study of chemical behavior and reactions, and particularly of stereochemistry. They are most suitable for this purpose because complete sets of diastereoisomers are readily available and the reactive carbonyl and hydroxyl groups allow the preparation of a great variety of derivatives. The determination by *Emil Fischer* of the configurations of all the pentoses and hexoses was a classical achievement in stereochemistry. The useful method of molecular rotation differences [1] was first established in the carbohydrate field [2]. Recognition of participation by neighboring groups, and of its steric requirements, also originated [3] in carbohydrate chemistry, as did knowledge of the steric requirements for epoxide formation by elimination [4].

Conformational analysis, in particular, is indebted to carbohydrate chemistry. The term "conformation", generally used in English, was introduced into organic chemistry by *Haworth* [5]. He considered the various possible conformations of sugar molecules and predicted "that these considerations open up a large field of inquiry into the conformation of groups as distinct from structure or configuration". The first suggestion of the importance of the conformations in the reactivity of acyclic compounds came in a paper by *Böeseken* and *Cohen* [6] on the reaction of the diastereoisomeric 2,3-butanediols with boric acid, a reagent particularly useful in carbohydrate chemistry. Studying the oxidation of aldoses by bromine, *Isbell* [7] recognized clearly, and probably for the first time, the effect of conformation on the rates of reactions; he attempted to classify sugar derivatives according to what we now call axial and equatorial substituents. The important observation that in NMR spectroscopy the coupling constants between protons on adjacent carbon atoms vary with the dihedral angle, was made on sugar acetates [8]; this observation led later to the Karplus equation [9].

On the other hand, the study of conformations is of major importance in carbohydrate chemistry. All of the monosaccharides belong to a few families of diastereomers; within these families, they differ only in their steric arrangement, and these differences can therefore be accounted for by conformational factors. If these factors could be exactly evaluated, the

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[1] *D. H. R. Barton* and *W. Klyne*, Chem. and Ind. *1948*, 755.

[2] *C. S. Hudson*, J. Amer. chem. Soc. *31*, 66 (1909).

[3] *H. S. Isbell*, Annu. Rev. Biochem. *9*, 65 (1940); *H. L. Frush* and *H. S. Isbell*, J. Res. nat. Bur. Standards *27*, 413 (1941).

[4] *H. Ohle* and *C. A. Schultz*, Ber. dtsch. chem. Ges. *71*, 2302 (1938); *A. Müller*, *M. Móricz*, and *G. Verner*, *ibid. 72*, 745 (1939).

[5] *W. N. Haworth*: The Constitution of Sugars. Edward Arnold and Co., London 1929, p. 90.

[6] *J. Böeseken* and *R. Cohen*, Recueil Trav. chim. Pays-Bas *47*, 839 (1928).

[7] *H. S. Isbell*, J. Res. nat. Bur. Standards *18*, 505 (1937); *20*, 97 (1938).

[8] *R. U. Lemieux*, *R. K. Kullnig*, *H. J. Bernstein*, and *W. G. Schneider*, J. Amer. chem. Soc. *79*, 1005 (1957).

[9] *M. Karplus*, J. chem. Phys. *30*, 11 (1959).

different chemical and physical properties of the various sugars could be predicted. Even without exact evaluation, semiquantitative application of conformational analysis can explain facts which, for many years, have been presented without any explanation: *e.g.*, why the equilibrium solution of lyxose [*] in water consists mostly of the α-pyranose, but that of xylose of the β-pyranose form; why the aqueous solution of altrose contains substantial proportions of furanose forms, whereas in the solution of glucose they are not detectable by our present methods; why idose is extensively converted in acid solution into an anhydride, whereas galactose is not.

It is the purpose of this paper to show how these facts are now readily explained by conformational analysis [10–13].

2. Conformations of Monosaccharides

2.1. Determination of Conformations

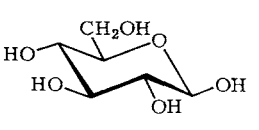
Conformational analysis of the sugars is based on the assumption that the geometry of the pyranoses is substantially the same as that of cyclohexane, and that of the furanoses the same as that of cyclopentane [10]: the substitution of two carbon-oxygen bonds for the slightly longer carbon-carbon bonds causes only a slight change in the molecular geometry. The pyranoid ring may, therefore, be in one of two chair forms or in the less stable flexible forms (skew and boat); the furanoid ring may be in one of the envelope or twist forms. In the solution of a sugar, these forms co-exist in equilibrium, but usually one conformation predominates. The physical properties, like the optical rotation, NMR spectra, *etc.*, of the sugar in solution will be determined by its predominant conformation; but chemical reactions may proceed through another conformation, though the activation energy of the reaction will then be increased by an amount equal to the difference between the free energies of the conformations.

The pyranoses will be considered first (Section 2.2) because most sugars exist and react mainly in this form, and because the conformations of the six-membered ring are clearly defined and readily recognized. The furanoses will be discussed in Section 2.5.

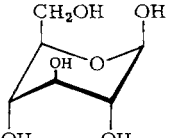
The conformations of pyranoses have been determined by several methods. The pioneering work of *Reeves* [14] was carried out by studying the formation of complexes from sugars in cuprammonium solution. X-ray crystallography, polarimetry, optical rotatory dispersion, and infrared spectroscopy have been used to determine the conformations of sugars, but the best source of information nowadays is NMR spectroscopy.

Reeves [14,15] determined the predominant conformations of many methyl glycosides by studying the complexes which some of them form with cuprammonium reagent. The extent of complex formation is shown by the decrease in electrical conductivity of the solution; the nature of the complex is often indicated by the change in optical rotation. By the study of suitable model compounds, *Reeves* found that complex formation requires the presence of two hydroxyl groups in close proximity: an equatorial and an axial, or two equatorial, hydroxyl groups on adjacent carbon atoms are suitable, and so are two *syn*-axial hydroxyl groups. Non-formation of a complex indicates that all hydroxyl groups are too far apart in the predominant conformation.

The method is open to the objection that a complex may be formed from a conformation other than the predominant one if the latter is incapable of reacting. Fortunately, this occurred in few of *Reeves'* examples, and most of his conformational assignments have been confirmed by later work. *Reeves* found the majority of D-sugars in what he called the C1 conformation and only methyl α- and β-D-arabinoside and methyl α-D-idoside were shown to be predominantly in the 1C conformation. [The conformations C1 and 1C are illustrated [*], for β-D-glucopyranose, by *(1)* and *(2)*.] All methyl glycosides were found to be in chair conformations, but a few (the altrosides and the lyxosides) appeared to contain substantial amounts of both chair forms in equilibrium.



(1)



(2)

The most definite and most accurate method for determining the conformations of a sugar is by complete X-ray crystal-structure analysis. It is not necessarily certain however that the conformation which occurs in the crystal is the one which predominates in solution, particularly since the conformation may vary with the solvent (Section 2.2.). X-ray crystallography yields valuable data on bond lengths, bond angles, and interatomic distances, and so far all of the pyranoid sugars which have been studied by X-ray analysis [16] have been

[*] Statements made for sugars without a D or L prefix apply equally to the D and L enantiomorphs.

[10] *E. L. Eliel, N. L. Allinger, S. J. Angyal,* and *G. A. Morrison*: Conformational Analysis. Interscience, New York 1965, pp. 351 to 432.

[11] *R. U. Lemieux* in *P. de Mayo*: Molecular Rearrangements, Interscience, New York 1963, pp. 713–769.

[12] *R. J. Ferrier* and *W. G. Overend,* Quart. Rev. (chem. Soc. London) *13*, 265 (1959).

[13] *B. Capon* and *W. G. Overend,* Advances Carbohydrate Chem. *15*, 11 (1960).

[14] *R. E. Reeves*, J. Amer. chem. Soc. *71*, 215 (1949); Advances Carbohydrate Chem. *6*, 107 (1951).

[15] *R. E. Reeves*, J. Amer. chem. Soc. *72*, 1499 (1950).

[*] In this paper, C1 and 1C always refer to D-sugars. In the L-series the assignments have to be reversed and therefore, unfortunately, the comparison of the conformations of D- and L-sugars is often somewhat confusing. As far as possible, D-sugars are used in this paper as examples; but when data are available for L-sugars only, these are given and, for clarity's sake, the conformations are designated as 1C(L) and C1(L). It must be kept in mind that the C1 form of the D-series and the 1C(L) form of the L-series are mirror images and therefore have the same (axial or equatorial) arrangement of each substituent.

[16] For a review, see *G. A. Jeffrey* and *R. D. Rosenstein*, Advances Carbohydrate Chem. *19*, 7 (1964).

found in the same chair conformations in their crystals as those which predominate in aqueous solution.

The advent of NMR spectroscopy was of utmost importance for the determination of the conformations of sugars. Although other spectroscopic methods [17], and methods based on optical rotatory power [18], have been used for this purpose, NMR is the first method which allows direct observation of conformationally significant data in aqueous solution, even when a mixture of several forms of a sugar is present. In such a case the NMR spectrum may, in favorable circumstances, be used to determine the composition of the mixture (Section 3.1) as well as the conformation of each component.

Two kinds of data provided by NMR spectra yield information on conformations: the coupling constants and the chemical shifts. The coupling constants for hydrogen atoms on adjacent carbon atoms vary with the dihedral angle according to the Karplus equation [9]:

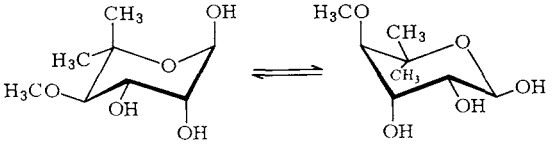
$$J = J_0 \cos^2 \Phi + K$$

where J is the coupling constant between two hydrogen atoms attached to neighboring carbon atoms at a dihedral angle of Φ, and J_0 and K are constants. Although it is now realized that this equation gives only approximate values [19,20], and that the coupling constants also depend on the nature and on the configuration of substituents, the magnitude of the coupling constant can often clearly distinguish between two possible conformations. For example, if two adjacent hydrogen atoms in a six-membered ring are *trans*, a large value of J (7–10 Hz) indicates a diaxial, a small value (2–4 Hz) a diequatorial arrangement of the hydrogen atoms.

The anomeric [*] protons of aldoses, being on a carbon atom attached to two oxygen atoms, appear at lower field than the other ring protons and are clearly distinguishable in the NMR spectra. The coupling constant of this proton alone will distinguish between the two possible chairs of the pyranose forms of those sugars in which the protons on C-1 and C-2 are *trans* to each other; these sugars are the α-forms of altrose, idose, mannose, talose, arabinose, and lyxose, and the β-forms of allose, galactose, glucose, gulose, ribose, and xylose. A coupling constant between 4 and 6 Hz, as found in α-D-lyxopyranose, α-D-altropyranose, and α-D-idopyranose, indicates that both chair conformations are present in substantial proportions in equilibrium.

The statement that a coupling constant intermediate between those expected for the two chair conformations indicates a conformational mixture, rather than a distorted chair or a skew form, probably needs to be supported. A good example is α-noviose (6-deoxy-5-*C*-methyl-4-*O*-methyl-α-L-lyxohexose). Methyl α-novioside in pyridine solution shows $J_{1,2}$ 1.9 Hz and several of its derivatives have $J_{3,4}$ between 9.3 and 10.0 Hz, approximately the values expected for the 1C(L) form *(3)* [21]. However, in aqueous solution methyl α-novioside has $J_{1,2}$ 2.3 and $J_{3,4}$ 8.8 Hz, and α-noviose has 3.9 and 7.7 Hz, respectively [22].

As the anomeric effect becomes smaller, larger contributions (see Section 2.4.) are made by the C1(L) form *(4)* for which the expected coupling constants are $J_{1,2}$ 7.4 and $J_{3,4}$ 3.3 Hz. A distortion of the 1C(L) form to reduce the axial-axial interactions would cause a decrease, not an increase, in $J_{1,2}$; and a skew conformation cannot be found which would show the observed coupling constants. α-D-Lyxopyranose shows similar behavior [23]. *Bhacca* and *Horton* [24] have recently shown that at −84 °C the NMR spectrum of tetraacetyl-β-D-ribopyranose in [D_6]acetone displays the signals of both chair conformers in the approximate proportion of 2:1. The spectrum at room temperature, with coupling constants intermediate between those of the two chair forms, is therefore a time-averaged spectrum of the two conformers in rapid interconversion.



(3) *(4)*

If the protons on C-1 and C-2 are *cis*, the coupling constant of the anomeric proton does not distinguish clearly between the two possible chair conformations, although the value for $J1$ (eq.), 2 (ax.) is usually 2.5 to 3.5, and for $J1$ (ax.), 2 (eq.) it is 1.0–1.5 Hz [20]. Often a decision can be made by determining the coupling constants of other hydrogen atoms either by direct inspection or by analysis of the spectrum. In this way, the conformations of most of the aldohexoses and aldopentoses have been determined; they are shown in Table 1.

The chemical shift of a proton is also characteristic of its environment, and may yield information about the conformation of the molecule. The rule [25] that an equatorial proton will appear at lower field than a chemically similar but axial proton appears to be generally valid, provided that the compounds compared are epimeric and are both in the same conformation [26]. For D-pyranoses in the C1 conformation, therefore, the anomeric proton of the α-anomer appears at lower field than that of the β-form. When the opposite is true, as it is for ribose, altrose, and idose, the α-forms are, at least partially, in the 1C conformation. The chemical shifts of ring protons in

[17] For reviews, see *W. B. Neely*, Advances Carbohydrate Chem. *12*, 13 (1957); *H. Spedding*, *ibid. 19*, 23 (1964).

[18] *D. H. Whiffen*, Chem. and Ind. *1956*, 964.

[19] *M. Karplus*, J. Amer. chem. Soc. *85*, 2870 (1963); *B. Coxon*, Tetrahedron *21*, 3481 (1965).

[20] *R. U. Lemieux* and *J. D. Stevens*, Canad. J. Chem. *44*, 249 (1966).

[*] Anomeric monosaccharides differ only in the irconfiguration at C-1.

[21] *B. T. Golding* and *R. W. Rickards*, Chem. and Ind. *1963*, 1081.

[22] *S. J. Angyal*, *V. A. Pickles*, and *R. Ahluwalia*, Carbohydrate Res. *1*, 365 (1966).

[23] *W. Mackie* and *A. S. Perlin*, Canad. J. Chem. *44*, 2039 (1966).

[24] *N. S. Bhacca* and *D. Horton*, J. Amer. chem. Soc. *89*, 5993 (1967).

[25] For a review, see *L. D. Hall*. Advances Carbohydrate Chem. *19*, 51 (1964).

[26] *R. U. Lemieux* and *J. D. Stevens*, Canad. J. Chem. *43*, 2059 (1965).

pyranoses are strongly dependent on the configurations of substituents in the ring. Axial protons, for example, are deshielded by neighboring and also by *syn*-axial hydroxyl groups. *Lemieux* and *Stevens* [20] have established simple empirical rules for predicting the chemical shifts of the ring protons in pyranoses. Comparison of the predicted values with the chemical shifts found experimentally can sometimes distinguish between two possible conformations.

In this discussion it has been assumed that only the two chair forms need to be considered for pyranoses. In no case has a monocyclic pyranose or one of its derivatives been found in other than a chair form. The chair form is known to be energetically more favorable than the flexible form. Nevertheless, the possibility cannot be excluded that some of the pyranose sugars may exist predominantly in a skew form. The NMR spectrum provides definite proof of a pyranose being in a chair form only if the coupling constants of several ring protons can be determined; this is the case with β-D-xylose, α-D-arabinose, β-D-ribose, and α- and β-D-allose. For the other sugars, available evidence does not definitely exclude the possibility of a skew form being present.

2.2. The Conformations of Pyranoses

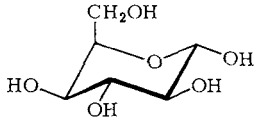
In aqueous solution, as the data in Table 1 show, the conformations of the aldohexopyranoses are governed mainly by the disposition of the bulkiest substituent, the hydroxymethyl group, which tends to assume an equatorial position. Hence, all of the β-anomers are predominantly in the C1 form, because the alternative 1C form involves a large interaction between the axial hydroxymethyl and the axial anomeric hydroxyl groups [see, *e.g. (2)*]. This interaction is absent from the 1C form of the α-anomers but most of these also prefer the C1 form; only α-D-idopyranose exists predominantly in the 1C form, and aqueous solutions of α-D-altropyranose and, probably, α-D-gulopyranose have substantial proportions of both chair forms in equilibrium.

In the absence of a hydroxymethyl group at C-5, the conformations of the aldopentopyranoses are governed by the dispositions of the hydroxyl groups. Thus, the D-arabinopyranoses favor the 1C form, α-D-lyxopyranose and α-D-ribopyranose are each conformational mixtures, and the other aldopentoses are predominantly in the C1 form.

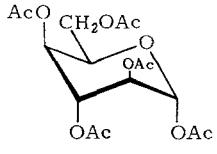
Not much is known about the conformations of the ketohexopyranoses. By analogy with the aldoses, one would expect that β-D-sorbopyranose and β-D-tagatopyranose would be mixtures of the two chair forms, and the other ketohexoses would have the conformation in which the hydroxymethyl group is equatorial, that is, β-D-fructopyranose and β-D-psicopyranose would be in the 1C, and all the α-anomers in the C1 form. Quite recently, *Jochims et al.* concluded [27] from their studies of long-range couplings of hydroxyl protons that α-D-sorbopyranose and α-D-tagatopyranose are in the C1 form in methyl sulfoxide solution and β-D-tagatopyranose is in the 1C form. In the crystalline state, α-L-sorbopyranose was found by X-ray analysis to be in the 1C (L) form [28].

All the preceding discussions refer to free sugars in aqueous solution. Conversion to glycosides, introduction of substituents, and change of solvent may alter the predominant conformation because they change the anomeric effect (Section 2.4); in most cases it becomes larger and therefore the conformational equilibrium of α-forms tends to shift towards the C1, that of β-forms towards the 1C, conformation. For example, α-D-idopyranose in aqueous solution is mainly, though not wholly, in the 1C form *(5)* [29]; methyl α-D-idopyranoside in aqueous solution is a mixture of approximately equal amounts of the C1 and 1C forms [30], and the NMR spectrum of penta-*O*-acetyl-α-D-idopyranose shows it to be in the C1 conformation *(6)* [31]. On the other hand, β-D-ribopyranose in aqueous solution is mainly, though not wholly, in the C1 form [32], β-D-ribopyranose in methyl sulfoxide [23] and methyl β-D-ribopyranoside in water [33] are mixtures of nearly equal amounts of the two chair forms, but tetra-*O*-acetyl-β-D-ribopyranose in acetone solution consists predominantly (2:1) of the 1C form [24].

The extreme examples are the triacetylpentopyranosyl halides in which that conformation predominates in which the halogen atom is axial, even if all the other substituents are also axial. For a further discussion, see Section 2.4 on the anomeric effect.



(5)



(6)

Ac = CH_3CO

2.3. Calculation of the Preferred Conformations from Interaction Energies

In order to understand, and even to predict, which conformation of a particular sugar is predominant and to what extent, one would need to know the relative free energy of each conformer. Data are at present not available for the exact calculation of these free energies [34]. However, even an approximate calculation serves as a useful guide and can be readily carried out by adding the values of all the non-bonded interactions occurring in each conformer, plus the value of the anomeric effect [32]. The calculations involve two assumptions: (a) that the free energies of conformational isomers are additive functions of energy terms associated with the presence of non-bonded interactions, that is, the occurrence of one interaction in a molecule does not affect the magnitude

[27] *J. C. Jochims, G. Taigel, A. Seeliger, P. Lutz,* and *H. E. Driesen,* Tetrahedron Letters *1967,* 4363.

[28] *S. H. Kim* and *R. D. Rosenstein,* Acta crystallogr. *22,* 648 (1967).

[29] *S. J. Angyal* and *V. A. Pickles,* Austral. J. Chem. *21,* in press (1969).

[30] *S. J. Angyal* and *V. A. Pickles,* unpublished result.

[31] *N. S. Bhacca, D. Horton,* and *H. Paulsen,* J. org. Chemistry *33,* 2484 (1968).

[32] *S. J. Angyal,* Austral. J. Chem. *21,* 2737 (1968).

[33] *R. J. Yu* and *C. T. Bishop,* Canad. J. Chem. *45,* 2195 (1967).

[34] The recent calculations by *P. R. Sundararajan* and *V. S. R. Rao* [Tetrahedron *24,* 289 (1968)] ignore polar interactions and employ parameters which produce results at variance with experimental data.

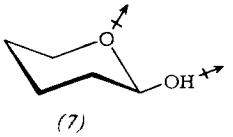
of another one; and (b) that the molecules are ideal chair forms, the shape not being affected by the interactions between substituents. Neither of these assumptions is strictly true and the results are therefore only approximate.

The interactions taken into account are not only those between axial groups but also *gauche* interactions between groups attached to contiguous carbon atoms. The values of interaction energies used in these calculations have been obtained, in aqueous solution, from the equilibria of cyclitols with their borate complexes [35] and from equilibria of sugars [22].

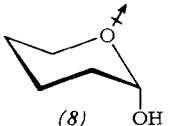
The following values were used in the calculations: interaction between an axial hydrogen atom and an axial oxygen atom, 0.45 kcal/mole; between an axial hydrogen atom and an axial methyl (or hydroxymethyl) group, 0.9; between two axial oxygen atoms, 1.5; between an axial oxygen atom and an axial methyl group, 2.5; between two vicinal oxygen atoms, unless they are both axial, 0.35; between a methyl (or hydroxymethyl) group and a vicinal oxygen atom, unless they are both axial, 0.45 kcal/mole. All other nonbonding interactions are believed to be negligible. These values were obtained in aqueous solutions at room temperature, and are only valid under these conditions.

2.4. The Anomeric Effect

Besides the interaction energies, another factor has to be taken into account in calculating the free energies of pyranoses. Most 1-substituted derivatives of α-D-glucopyranose (and many other sugars) are more stable than the corresponding β-D anomers, although the former have the bond to the substituent in the axial position, and the latter in the equatorial one. There appears to be an effect, first discussed by *Edward* [36] and named "anomeric effect" by *Lemieux* [11,37], which makes an equatorially attached group on the anomeric carbon atom less stable than it would be at other positions on the ring. An explanation of this effect was given [36] in terms of the repulsive interaction between the equatorial carbon-oxygen dipole and the dipole formed as the resultant of the two carbon-oxygen dipoles in the pyranose ring. These dipoles form a small angle when the substituent is equatorial, as in *(7)*, and a large one when it is axial, as in *(8)*. In accordance with this explanation, the anomeric effect varies inversely with the dielectric constant of the solvent, and is greatest when the effective charge density on the substituent atom attached directly to C-1 is high [38].



(7)



(8)

[35] *S. J. Angyal* and *D. J. McHugh*, Chem. and Ind. *1956*, 1147.

[36] *J. T. Edward*, Chem. and Ind. *1955*, 1102.

[37] *R. U. Lemieux* and *N. J. Chü*, 133rd Meeting Amer. chem. Soc., Abstracts of Papers *1958*, 31N.

[38] *B. Coxon*, Tetrahedron *22*, 2281 (1966).

The evaluation of the anomeric effect is the least satisfactory part of the calculations of the free energies of sugars, because the anomeric effect varies considerably not only with the nature of the solvent and of the anomeric group but is affected even by the presence and the configuration of substituents in other parts of the pyranose molecule. It is difficult, therefore, to obtain reliable figures for the values of the anomeric effect under different conditions. However, the anomeric effect of a hydroxyl group in aqueous solution is comparatively small and can be readily evaluated by considering the differences between the free energies of anomers [32].

The free energy of α-D-glucopyranose should be 0.9 kcal/mole higher than that of the β-D anomer, owing to the interaction of the anomeric hydroxyl group with two axially attached hydrogen atoms in the former. In fact, the equilibrium solution contains 36 % of α- and 64 % of β-D-glucose, corresponding to a free-energy difference of only 0.35 kcal/mole. The difference between the two values, 0.55 kcal/mole, is due to the anomeric effect. A similar calculation for the D-mannopyranoses gives a difference of 1.0 kcal/mole, for the 2-deoxyarabinohexoses, 0.85 kcal/mole. The magnitude of the anomeric effect, therefore, depends on the presence and on the configuration of the hydroxyl group on C-2. The presence or absence of a hydroxyl group on C-6 (and probably in other positions) also modifies the anomeric effect [37] but, in aqueous solution, this modification is small enough to be neglected. In these calculations, the anomeric effect was taken as 0.55 kcal/mole when the oxygen atom on C-2 is equatorially attached, and as 1.0 kcal/mole when it is axially attached.

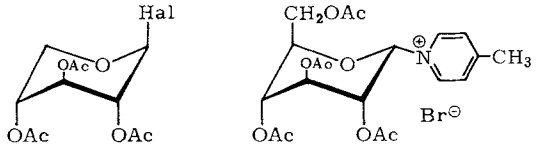
It is surprising that the anomeric effect increases with the extent of methylation of the hydroxyl groups. At equilibrium in aqueous solution D-mannose contains 67% of the α-pyranose form, 2-*O*-methyl-D-mannose 75%, 2,3-di-*O*-methyl-D-mannose 80%, and 2,3,4,6-tetra-*O*-methyl-D-mannose 86% [23]. Since the change in the non-bonding interactions of the anomeric hydroxyl group on moving it from the equatorial (β) to the axial (α) position is the same for each of these compounds, the increasing preponderance of the α-anomer must be caused by an increase in the anomeric effect. This is probably due to a decrease in the "effective dielectric constant" [39] of the molecule which, as well as the dielectric constant of the solvent, determines the magnitude of the dipole-dipole interaction. A similar increase of the α:β ratio has also been observed on methylation of other sugars [30].

The origin of the anomeric effect is not fully understood at present and its value can not yet be calculated. It is not even certain that the anomeric effect increases (by dipole repulsion) the free energy of the anomer which has an equatorial anomeric group; it is possible that it actually decreases (by dipole attraction) the free energy of the axial anomer. There are few reliable estimates of the anomeric effect; that of an amino group is less, that of an acetoxy group more, than the value for a hydroxyl group. In aqueous solution the anomeric effect of the methoxyl group is larger (by about 0.5 kcal/mole) than that of the hydroxyl group [30]. In solvents of low polarity the anomeric effect of halogen atom is so great (> 2 kcal/mole) that it often exceeds the sum of all the nonbonding steric interactions and decides the conformation of

[39] *F. H. Westheimer* and *J. G. Kirkwood*, J. chem. Physics *6*, 513 (1938).

the molecule. Thus all the triacetylpentopyranosyl halides adopt predominantly the conformation in which the halogen atom is axially oriented, even the tri-*O*-acetyl-β-D-xylopyranosyl halides *(9)* in which all the substituents are axial [40].

If a substituent is particularly bulky it will avoid the axial orientation. Thus α-D-mannopyranosyltheophylline in water, and its tetraacetate in chloroform, are in the 1C conformation, unusual for derivatives of mannose [41]. The effect of bulkiness is probably reinforced by the "reverse anomeric effect" of a positively charged substituent in *N*-(tetra-*O*-acetyl-α-D-glucopyranosyl)-4-methylpyridinium bromide which is in the 1C form *(10)* with all the other substituents axially attached [42].



(9) Ac = CH_3CO *(10)*

To calculate the free energy of a sugar in a particular chair conformation, all the interaction energies and the anomeric effect (if present) are totalled. The values listed in Table 1 for all the aldohexoses and aldopentoses were obtained in this way [32]. The conformation which has the lower free energy is, of course, the more stable one. When the free energies of the two chair forms differ by 0.6 kcal/mole or less, both conformations are listed since they would both be present in comparable amounts. It is seen that the calculations correctly predict the conformation of each aldose.

Table 1. Predominant conformations of D-aldopyranoses in aqueous solution.

Aldose	Conformation found by		Calculated interaction energies (kcal/mole)	
	NMR [20, 48, 49]	calculation [32]	C1	1C
α-D-Allose	C1	C1	3.9	5.35
β-D-Allose	C1	C1	2.95	6.05
α-D-Altrose	C1, 1C	C1, 1C	3.65	3.85
β-D-Altrose	C1	C1	3.35	5.35
α-D-Galactose	C1	C1	2.85	6.3
β-D-Galactose	C1	C1	2.5	7.75
α-D-Glucose	C1	C1	2.4	6.55
β-D-Glucose	C1	C1	2.05	8.0
α-D-Gulose		C1	4.0	4.75
β-D-Gulose	C1	C1	3.05	5.45
α-D-Idose	C1, 1C	C1, 1C	4.35	3.85
β-D-Idose		C1	4.05	5.35
α-D-Mannose	C1	C1	2.5	5.55
β-D-Mannose	C1	C1	2.95	7.65
α-D-Talose	C1	C1	3.55	5.9
β-D-Talose		C1	4.0	8.0
α-D-Arabinose	1C	1C	3.2	2.05
β-D-Arabinose		C1, 1C	2.9	2.4
α-D-Lyxose	C1, 1C	C1, 1C	2.05	2.6
β-D-Lyxose	C1	C1	2.5	3.55
α-D-Ribose	C1, 1C	C1, 1C	3.45	3.55
β-D-Ribose	C1, 1C	C1, 1C	2.5	3.1
α-D-Xylose	C1	C1	1.95	3.6
β-D-Xylose	C1	C1	1.6	3.9

[40] *D. Horton* and *W. N. Turner*, J. org. Chemistry *30*, 3387 (1965); *C. V. Holland, D. Horton*, and *J. S. Jewell, ibid. 32*, 1818 (1967); *L. D. Hall* and *J. F. Manville*, Carbohydrate Res. *4*, 512 (1967); *H. Paulsen, F. Garrido Espinosa, W. P. Trautwein*, and *K. Heyns*, Chem. Ber. *101*, 179 (1968).

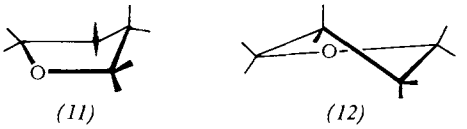
[41] *K. Onodera, S. Hirano, F. Masuda*, and *N. Kashimura*, J. org. Chemistry *31*, 2403 (1966).

[42] *R. U. Lemieux* and *A. R. Morgan*, Canad. J. Chem. *43*, 2205 (1965).

2.5. The Conformation of Furanoses

The conformations of the furanoses are more difficult to establish than those of the pyranoses. In contrast to the six-membered ring which has two principal conformations, often greatly differing in stability and separated by substantial energy barriers, the five-membered ring has numerous conformations, of similar free energies, separated by low barriers.

The furanose ring is not planar. To avoid extensive eclipsing, either one atom is out of the plane formed by the other four ["envelope" form, *(11)*] or two adjacent atoms are on opposite sides of the plane formed by the other three ["twist" form, *(12)*]. A small change, mainly in the position of one atom, converts an envelope form into one of two conformationally similar twist forms. The envelope and the twist forms are the free-energy minima in the cycle of conformational interconversions of cyclopentane; for a polysubstituted cyclopentane, or furanose, a conformation intermediate between an envelope and a twist form may be the most stable one.



(11) *(12)*

The conformation of the furanose ring has been determined by X-ray crystallography in many derivatives of D-ribofuranose [43]; there is considerable variation in the shape of the furanose ring from one compound to another. NMR has also been used to determine the conformations of furanoid sugars [44–45], and the spectra have been interpreted in terms of one predominant conformation; it is possible, however, that in many cases they represent time-averaged spectra of several conformations. It is best to regard the clearly defined envelope and twist conformations of a furanose in solution as an easy way to describe what in reality is an equilibrium of rapidly interconverting forms which do not differ greatly from each other.

Because eclipsing of a carbon atom and an oxygen atom requires less energy than that of two carbon atoms, the oxygen atom in the furanoid ring tends to occupy the least puckered part of the ring; hence, usually, either C-2 or C-3, or both, will be out of the plane. In most cases, the conformation is one intermediate between the ideal envelope and twist forms, and is governed by the disposition of the substituents. The section of the ring containing C-2 and C-3 resembles the half-chair form of pyranoses, and the substituents occupy quasi-axial and quasi-equatorial positions. The predominant conformation appears to be the one in which bulky substituents are staggered as much as possible, and assume quasi-equatorial positions on the most staggered carbon atoms. The substituents therefore tend to move into the plane of the furanose ring. On the other hand, the anomeric effect is operative in the furanoses too [45], and therefore the

[43] *M. Sundaralingam*, J. Amer. chem. Soc. *87*, 599 (1965).

[44] *R. U. Lemieux*, Canad. J. Chem. *39*, 116 (1961); *R. J. Abraham, L. D. Hall, L. Hough*, and *K. A. McLauchlan*, J. chem. Soc. (London) *1962*, 3699.

[45] *J. D. Stevens* and *H. G. Fletcher jr.*, J. org. Chemistry *33*, 1799 (1968).

oxygen atom on C-1 tends to take up a quasi-axial position, that is, tends to move out of the plane of the ring. Hence, *trans*-substituents at C-3 and C-4 usually form[45] a dihedral angle of less than 120°, those at C-1 and C-2, more than 120°; the constant of the coupling between *trans* hydrogen atoms on C-1 and C-2 is usually small, that between those on C-3 and C-4 usually large. On the basis of these tendencies it is often possible to predict the predominant conformation of a furanose, but a quantitative treatment, similar to that of the pyranoses, is not yet possible. The conformational behaviour of furanoses has been discussed in considerable detail by *Lemieux*[11], who made the simplifying assumption that they all have envelope conformations.

3. The Equilibrium Composition of Monosaccharides in Solution

3.1. Determination of the Composition

When a crystalline sugar – which is a single compound – is dissolved in a solvent, tautomerization occurs (of which mutarotation is the visible manifestation) and ultimately an equilibrium mixture of at least five compounds is formed: the α-pyranose, the β-pyranose, the α-furanose, the β-furanose, and the aldehydo form. Knowledge of the composition of this equilibrium mixture is the key to understanding the physical and chemical properties of sugars in solution; yet, until a few years ago, this composition had not been determined for any sugar. Only the study of the rate of the mutarotation provided some relevant information.

Mutarotation can be either "simple" or "complex"[46]. Sometimes the mutarotation may be described by the equation for a first-order reversible reaction, whether approached from the α- or from the β-pyranose ("simple" mutarotation). Then the equilibrium mixture consists predominantly of the two pyranose forms. Some sugars which show this behavior are glucose, mannose, and lyxose.

Other sugars, however, show "complex" mutarotation, consisting of an initial fast change, followed by a slow one, not necessarily in the same direction; more than two components are then involved in the equilibrium. The initial fast mutarotation is ascribed to a pyranose-furanose interconversion, and the slow one to the anomerization of pyranose forms. The occurrence of an initial fast mutarotation can be taken as an indication that substantial amounts of furanoses are present in equilibrium. Examples of such behavior are arabinose, ribose, galactose, and talose.

If the mutarotation is simple, and if both pyranose forms are available in the crystalline state and their rotations are therefore known, the proportions of the α- and β-pyranose forms can be calculated from the value of the equilibrium rotation. If the mutarotation is complex, it is still possible to calculate the contribution that the slow mutarotation (anomerization of the pyranoses) makes to the change in rotation. Provided, again, that both pyranose forms are known in the crystalline state, the extent of the slow mutarotation will give an approximate measure of the α- to β-pyranose ratio at equilibrium. The amount or proportion of the two furanose forms cannot be determined in this way, however, because the rotations of furanoses are not known.

The position of the equilibrium can also be studied by chemical reactions, of which the oxidation of aldoses by bromine has been most extensively studied[47]. The α- and β-pyranoses differ widely in their rates of reaction: the oxidation of the anomer which carries an equatorial anomeric hydroxyl group always occurs more rapidly. By studying the rate of the reaction it is possible to determine the proportion of the slowly reacting component in the equilibrium mixture; this is taken to be the pyranose with an axial anomeric hydroxyl group. The method yields useful data when only the two pyranoses are present in substantial amounts; the presence of furanoses, however, makes it unreliable since the rate of reaction of the furanoses is not known. In fact, until the advent of NMR, there was no method known capable of determining the amount of furanoses present in solution.

NMR spectroscopy has emerged as an excellent method for determining the composition of the equilibrium mixture of a sugar, particularly because it can be used in aqueous (D_2O) solution[20, 48, 49]. Whereas the signals of most of the other protons usually overlap, those of the anomeric protons of the different forms are often well separated from each other. A good example is the NMR spectrum (Fig. 1) of idose at equilibrium in aqueous solution[49]. Identification of the anomeric signals is, in most cases, easy: the pyranoses appear at higher field than the furanoses, and the β-pyranose at higher field than the α-pyranose if they both have the same conformation (Section 2.1). In the case of D-idose, the α-pyranose is predominantly in the 1C and the β-anomer in the C1 form but the signal of the α-pyranose is readily identified by its large coupling constant. Of the furanose forms, the *cis*-1,2 has a larger coupling constant than the *trans*-1,2 anomer (Section 2.5); in this particular case the signals of the furanose forms were also identified by their similarity to the signals given by the 5-*O*-methyl-D-glucofuranoses. (Gluco- and ido-furanoses have the same configuration of every carbon atom in the ring and differ only in the configuration of the extra-annular C-5 atom.) The composition of idose in aqueous solution is determined by integration of the anomeric signals. This case is a particularly interesting one because idose has never been crystallized and therefore none of the four tautomeric forms, the NMR signals of which have thus been identified, is known in the pure state.

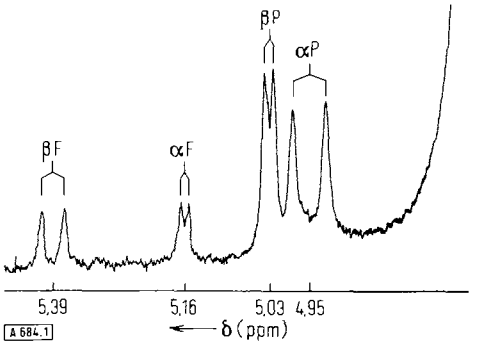


Fig. 1. The 100 MHz NMR spectrum of the anomeric protons of D-idose in D_2O solution at 60 °C. (αF, βF signify α- and β-furanose; αP, βP denote α- and β-pyranose.)

[46] *F. J. Bates et al.*: Polarimetry, Saccharimetry, and the Sugars. Nat. Bur. Standards (US) Circ. C440, Washington 1942, p. 439 ff.

[47] *H. S. Isbell*, J. Res. nat. Bur. Standards, A *66*, 233 (1962).

[48] *M. Rudrum* and *D. F. Shaw*, J. chem. Soc. (London) *1965*, 52.

[49] *S. J. Angyal* and *V. A. Pickles*, Austral. J. Chem. *21*, in press (1969).

Not every aldose gives such a clear-cut spectrum as idose in aqueous solution. Nevertheless, it has been possible to determine the composition of the aqueous equilibrium solution of every aldopentose and aldohexose, except that of gulose [49]. A good spectrum was, however, obtained from D-glycero-D-guloheptose which, probably, would have a composition similar to that of gulose. The results are shown in Table 2.

Table 2. Proportions of pyranose and furanose forms of aldoses at equilibrium in aqueous solution at 40 °C [20, 49].

Aldose	Pyranose		Furanose	
	α (%)	β (%)	α (%)	β (%)
D-Allose	18	70	5	7
D-Altrose	27	40	20	13
D-Glycero-D-guloheptose	10	88	2	
D-Idose [a]	31	37	16	16
D-Talose	40	29	20	11
D-Arabinose	63	34	*ca.* 3	
D-Ribose	20	56	6	18
3-Deoxy-D-ribohexose	26	46	6	22
2-Deoxy-D-arabinohexose	47.5	52.5	0	0

[a] At 60 °C.

Only those aldoses are listed that contain detectable amounts (more than 1–2 %) of furanose at equilibrium; the compositions of the other sugars are shown in Table 3.

Consideration should also be given to the presence in the equilibrium mixture of other forms of the sugars, such as the aldehydo form, septanose, *etc.* However, the NMR spectra show no peaks additional to those of the pyranoses and the furanoses. The aldehydo forms of the sugars are extensively hydrated in aqueous solution and show only a weak signal at very low field where the aldehydic protons usually appear [50–53]. The proton of the hydrated aldehyde group resonates at $\delta \approx 5.1$, amidst the anomeric protons of the sugars but has a coupling constant (5–7 Hz) that is rare for an anomeric proton. No such signal has been detected in the spectra of any of the aldoses but it is found in the NMR spectrum of 3,6-anhydro-D-allose, a compound which for steric reasons forms neither a pyranose nor a furanose ring [52].

The equilibrium solution of D-glucose contains only 0.0026 % of the aldehydo form, as determined by polarography [54]. Glucose, of course, has the lowest free energy of all the aldohexoses; but if one assumes that aldehydo-idose has the same free energy as aldehydo-glucose, then calculation, using the free-energy values in Table 1, indicates that the aqueous equilibrium solution of idose should contain 0.04 % of the aldehydo form. This is too little to be detected by NMR.

D-Idose was reported [55] to give a positive Schiff reaction for aldehydes, unlike the other aldoses (though we were unable to confirm this report). When the pyranose form of glucose is suppressed and the sugar is forced into the less stable furanose form, as is done by blocking O-5, the amount of the aldehyde form in equilibrium should be greatly increased. Indeed, 5-*O*-methyl-D-glucose does give a positive Schiff test [56], but the NMR spectrum shows only the peaks of the two furanose forms [52]. Similarly, 3,6-anhydro-D-glucose, the pyranose forms of which are strained, shows only the furanose signals. The aldehydo form of the sugars therefore occurs in a concentration too low to be detected by NMR.

Anet [51] has recently found that 2,3,4,5-tetra-*O*-methyl-D-glucose consists in aqueous solution of about equal amounts of the aldehydo form (partially hydrated) and a septanose form. The septanoses therefore have a stability similar to that of the aldehydo form and one would not expect to be able to detect them by NMR in the equilibrium mixtures of sugars.

3.2. The α:β Ratio of Pyranoses

The α:β ratio of the pyranose forms at equilibrium varies considerably from one aldose to another but conformational analysis can explain this variation. The free-energy values given in Table 1 provide the data for calculating a "theoretical" α:β ratio [32]. Each anomer is a mixture of two chair forms, and its free energy can be calculated by taking the weighted average of the two free-energy values, corrected for the entropy change on mixing [57]. The calculated free energies of each aldose are listed in Table 3. From these values the α:β proportions in equilibrium have been calculated and they are compared in Table 3 with the ratios found by NMR. It can be seen that the agreement between the calculated and the experimentally found data is satisfactory in view of all the approximations involved in the calculations. Therefore, the α:β ratios of the pyranose forms of the aldoses are now not only known but they are also understood.

Table 3. Conformational free energies and the proportions of the α-form in aqueous equilibrium solutions of D-aldopyranoses

Aldose	Free energy (kcal/mole)		α-Pyranose (%) [a]	
	α form	β form	calc. [32]	found by NMR [20, 48, 49]
Glucose	2.4	2.05	36	36
Mannose	2.5	2.95	68	67
Galactose	2.85	2.5	36	27
Talose	3.55	4.0	68	58
Allose	3.85	2.95	18	20
Altrose	3.35	3.35	50	44
Gulose	3.85	3.05	21	<22
Idose	3.65	4.0	64	46
Xylose	1.9	1.6	37	33
Lyxose	1.85	2.4	72	71
Arabinose	1.95	2.2	60	63
Ribose	3.1	2.3	20.5	26

[a] Percentage of the two pyranose forms, *not* of all forms of the sugar.

3.3. The Furanose:Pyranose Ratio

The amount of furanoses present in equilibrium varies considerably from sugar to sugar, and in many cases it is very small. Five-membered rings are generally less stable than six-membered ones but the very considerable amount (over 30 %) of furanoses present in the equilibrium mixture of some sugars (Table 2) shows that this is not the main reason for its low proportion in the others.

The furanose:pyranose ratio in equilibrium will depend on the difference between the free energies of the

[50] *E. F. L. J. Anet*, Carbohydrate Res. *3*, 251 (1966).

[51] *E. F. L. J. Anet*, Carbohydrate Res. *8*, 164 (1968).

[52] *S. J. Angyal* and *M. H. Randall*, unpublished work.

[53] *A. S. Perlin*, Canad. J. Chem. *44*, 1757 (1966).

[54] *J. M. Los, L. B. Simpson*, and *K. Wiesner*, J. Amer. chem. Soc. *78*, 1564 (1956).

[55] *L. von Vargha*, Chem. Ber. *87*, 1351 (1954).

[56] *L. von Vargha*, Ber. dtsch. chem. Ges. *69*, 2098 (1936).

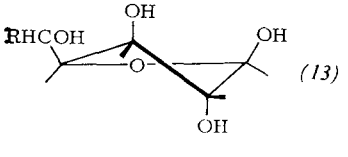
[57] Ref. [10], p. 24.

furanose and the pyranose forms. The free energies of the pyranoses have been calculated (Table 3); sugars of which the pyranose forms have low free energies, like glucose, mannose, xylose, have very little furanose in equilibrium. The relative free energies of the furanoses are not known but one can attempt to estimate them. The main interactions in five-membered rings are those between *cis* substituents on adjacent carbon atoms because these are never fully staggered. One would therefore expect furanoses with several *cis* pairs of substituents to be less stable than are those with *trans* substituents. It is particularly interesting to note that 3-deoxy-ribohexose ("3-deoxyglucose") has 28 % of furanose in equilibrium [49], whereas glucose itself has too little to be detected by NMR. It appears therefore that the interaction between O-3 and the side-chain on C-4, when these are *cis* to each other, is the most unfavorable one in the furanose ring. None of the sugars which has this interaction contains detectable amounts of furanose in its equilibrium mixture except idose, which has two rather unfavorable pyranose forms. Removal of an interaction between two *cis* oxygen atoms does not increase the stability of the furanose forms to the same extent: 2-deoxy-arabino-hexose ("2-deoxyglucose") does not show any furanose forms in its NMR spectrum.

Furanoses in which the substituents on C-2, C-3, and C-4 are all *cis* have a comparatively high free energy; accordingly, the NMR spectra of lyxose and mannose show no furanose and that of gulose shows very little. One would expect the all-*trans* furanoses of arabinose and galactose to be particularly stable, yet very little is found in the equilibrium mixtures. This may be due to *cis*-1,3 interactions, discussed in the following Section.

3.4. The α:β Ratio of Furanoses

One would expect that that anomer of the furanoses in which the hydroxyl groups on C-1 and C-2 are *trans* would always predominate at equilibrium over the *cis*-1,2 anomer. This is indeed what is found in most cases though the α:β ratio varies from sugar to sugar, indicating that other interactions also influence this ratio. However, in the equilibrium of idose and of 5-*O*-methyl-D-glucofuranose the two anomers are present in approximately equal amounts [52] at equilibrium. The comparative instability of the *trans* anomer is probably due to *cis*-1,3 interactions of the anomeric hydroxyl group with O-3 and C-5. The small coupling constant ($J_{1,2}$ = 0.7 Hz) of the *trans* anomer shows that O-1 and O-2 are both in quasi-axial orientation, and the conformation of the molecule is approximately as shown in *(13)*. Since O-3 is also quasi-axial, an interaction occurs between O-1 and O-3 which destabilizes the *trans*-1,2 anomer (β for glucofuranose, α for idofuranose). In "3-deoxy-D-glucofuranose" this interaction is not present and there is much more (3.7:1) of the β-furanose than of the α anomer.



(13)

Similar *cis*-1,3 interactions probably increase the free energy of the arabino- and galacto-furanoses. More quantitative data are required, however, for a better understanding of the non-bonding interactions in furanoses.

3.5. Equilibria in Solvents other than Water. The Effect of Substituents

The equilibrium compositions of the sugars in solution are affected by the temperature, by the nature of the solvent, and by the presence of substituents. If the solvent is less polar than water, the increased anomeric effect will, predictably, favor the α-pyranose over the β-pyranose form if the sugar is in the C1 conformation. However, other, unexpected changes in composition are also observed when the solvent or the substituents are altered.

There is now a considerable amount of information available on the composition of sugars in dimethyl sulfoxide solution, thanks to the work of *Perlin* [23, 58] who determined the compositions by comparing the NMR signals of the hydroxyl protons, rather than those of the ring protons. Aldoses with an axial hydroxyl group on C-2 (mannose, lyxose) contain a much higher proportion of the α-pyranose form in dimethyl sulfoxide than in water, whereas sugars with an equatorial hydroxyl group on C-2 (glucose, xylose) have approximately the same equilibrium composition in both solvents. An explanation of this observation is not apparent.

More striking is the increase in the proportion of the furanoses when changing from water as a solvent to pyridine [58a], dimethylformamide [58b], or dimethyl sulfoxide [23]. Arabinose, for example, contains 33 % furanose in the last named solvent, and only about 3 % in water. A great increase in the proportion of furanose also results from partial methylation; *e.g.* the equilibrium mixture of 2,3-di-*O*-methyl-D-arabinose contains 17 % furanose in aqueous solution and 65 % in dimethyl sulfoxide. As an extreme example of the effect of the solvent and methylation one can cite 2,3-di-*O*-methyl-D-altrose which changes to a considerable extent (*ca.* 80 %) into furanose forms on standing in dimethyl sulfoxide [23].

This surprising variation in the furanose:pyranose ratio is probably explained by differences in the extent of solvation. The hydroxyl group is solvated in water by forming hydrogen bonds through its oxygen and its hydrogen atom but the methoxyl group can form hydrogen bonds only through its oxygen atom. In dimethyl sulfoxide only the hydrogen atom of the

[58] *A. S. Perlin*, Canad. J. Chem. *44*, 539 (1966).

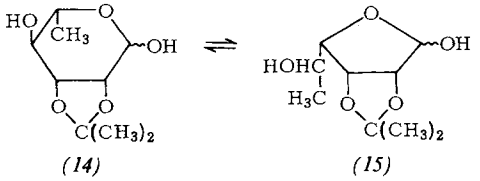
[58a] *R. Kuhn* and *H. Grassner*, Liebigs Ann. Chem. *610*, 122 (1957).

[58b] *C. C. Sweeley*, *R. Bentley*, *M. Makita*, and *W. W. Wells*, J. Amer. chem. Soc. *85*, 2497 (1963).

hydroxyl group will form hydrogen bonds and the methoxyl group will be weakly solvated by dipole association only [59]. The apparent bulk of the hydroxyl group in water will therefore be much larger than that of the methoxyl group in dimethyl sulfoxide. If the furanoses, with considerable eclipsing of their carbon atoms, are more destabilized by bulky substituents than are the pyranoses, the above results can be explained.

Accurate data are available for the equilibrium compositions of the methyl pentosides in methanol [60], and it is interesting to compare these with the equilibrium compositions of the corresponding sugars in water. Since the formation of glycosides and the change from water to methanol both enhance the anomeric effect, there is an increase in the proportion of the α-anomers of the pentoses (xylose, lyxose) which are in the C1 form, and of the β-anomer of arabinose which is in the 1C form. Since both anomers of ribose are conformational mixtures in aqueous solution, there is only a small change in the α:β ratio on converting them to methyl ribosides in methanol. Here, also, the 2-*O*-methyl and the 3-*O*-methyl, but particularly the 2,3-di-*O*-methyl glycosides have much more furanoside in equilibrium than have the unsubstituted glycosides. In particular, the equilibrium mixture of the methyl 2,3-di-*O*-methyl-D-arabinosides contains 75 % furanosides.

Fusion of a ring to the sugar can profoundly change the pyranose:furanose ratio by introducing strains into one or both of the forms. Thus 2,3-*O*-isopropylidene-L-rhamnose [*(14)* ⇌ *(15)*] consists in aqueous solution of about 65 % of the furanose form [61], and D-mannose 2,3-carbonate [62] and 3,6-anhydro-D-glucose [52] are completely in the furanose forms, whereas the parent sugars have no detectable amount of furanose in equilibrium. Fusion of a five- to a six-membered ring, whether 1,2 or 1,3, causes distortion of the latter, hence the pyranose forms of these sugar derivatives are strained; whereas the arrangement of two *cis*-1,2 fused five-membered rings, which occurs in the furanose forms, is free of steric strain [63] and is therefore favored.

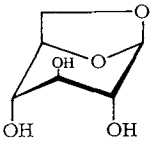


(14) *(15)*

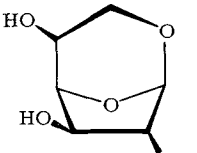
3.6. Equilibria in Acid Solution

When a sugar is heated in aqueous solution in the presence of a strong acid an equilibrium is set up which contains, in addition to the pyranoses and furanoses, other compounds as well. The most important amongst these are the anhydrides obtained by the formation of a glycosidic link with one of the sugar's own hydroxyl groups; these anhydrides are known as "glycosidic anhydrides" or "internal glycosides". The formation of the glycosidic anhydrides is very much slower than anomerization or pyranose-furanose interconversion. Subject to steric limitations, any of the hydroxyl groups of the sugar may take part in the formation of an anhydride; the amount of the anhydride at equilibrium will depend on the strain introduced by the formation of the anhydride ring.

The most stable internal anhydrides are the 1,6-anhydropyranoses, *e.g.*, 1,6-anhydro-β-D-glucopyranose *(16)*. The amount of this anhydride found at equilibrium varies within wide limits, from 0.2 % for glucose to 86 % for idose, according to the stability of the sugar and the steric interactions in the anhydride. In the glucose derivative *(16)*, for example, all the hydroxyl groups are axial and the interactions are severe [15]. Since the 1,6-anhydropyranoses have the conformation of the 1C form of the β-anomer, the difference between the free energy of that form and of the sugar in equilibrium provides an approximate measure of the relative stability of these anhydrides. Calculations based on the free-energy values in Table 1 provide the means for predicting approximately the proportion of the 1,6-anhydropyranoses at equilibrium [64].



(16)



(17)

Another type of glycosidic anhydride found in equilibrium are the 1,6-anhydrofuranoses, *e.g.*, 1,6-anhydro-β-D-glucofuranose *(17)*. This anhydride has the same ring system (dioxabicyclo[3.2.1]octane) as has the 1,6-anhydropyranose but there are more substituents in the five-membered (furanose) ring, and therefore more eclipsing. The proportion of these anhydrides at equilibrium is therefore much less than that of the 1,6-anhydropyranoses, and in many instances they have not yet been detected. Only in the case of D-talose are there about equal amounts (2.5 % each) of the two anhydrides in equilibrium [64].

There are indications of the presence of 1,4-anhydropyranoses (= 1,5-anhydrofuranoses) in the equilibrium mixtures of some sugars [65]. Aldoheptoses also give 1,7-anhydropyranoses and 1,7-anhydrofuranoses in addition to those already mentioned.

In acid solution of sugars there is, besides the formation of internal glycosides, also glycoside formation between sugar molecules, resulting in di- and oligo-saccharides. In dilute solution this reaction ("reversion") is negligible but in concentrated solutions of sugars it may be quite considerable. The equilibrium mixture is then extremely complex.

Received: March 16, 1968 [A 684 IE]
German version: Angew. Chem. *81*, 172 (1969)

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Catalase and Peroxidase Activity of Cu^{2+} Complexes

By H. Sigel[*]

The relation between the structure of Cu^{2+} complexes and their catalytic activity in the decomposition of H_2O_2 can be used as a "molecular probe", since it allows the deduction of the number of coordinated ligand groups in a Cu^{2+} complex from its catalytic activity. Since only coordinated ligand groups are oxidized by H_2O_2, further information about the coordination sphere of the metal ion can be obtained from the oxidation of certain parts of a ligand, which can be followed spectrophotometrically. The Cu^{2+} complexes of amides, polyamino acids, nucleotides, RNA, and native and denatured DNA have been investigated in this way. Kinetic studies provide an insight into the mechanisms of catalase and peroxidase reactions.

1. Introduction

The catalysis of the disproportionation of hydrogen peroxide by metal ions or their complexes in homogeneous systems has already been the subject of many investigations [1–3]. The best known catalyst for reaction (1) is catalase, an enzyme containing Fe^{III} porphyrin [4].

$$H_2O_2 + H_2O_2 \rightarrow O_2 + 2\,H_2O \qquad (1)$$

In the "catalase" disproportionation (1), one molecule of H_2O_2 is oxidized and another is reduced; if one of the two molecules is replaced by an H donor, *i.e.* by a substrate that can be oxidized by H_2O_2, reaction (2) occurs:

$$H_2O_2 + \text{substrate} \rightarrow \text{oxidized substrate} + H_2O \qquad (2)$$

This "peroxidase" reaction can also be catalyzed by metal ions or their complexes; the best-known catalyst for this reaction is peroxidase, another enzyme containing Fe^{III} porphyrin [4].

In view of the great biochemical importance of catalase and peroxidase, it is understandable that models (*i.e.* more or less catalytically active Fe^{III} complexes of various structures) for these two enzymes are constantly being sought – and found [5–8]; however, the activity of catalase is far superior to that of any of the known models [9].

All the existing results indicate that (*e.g.* of the elements of the first transition series) only those ions (possibly in the form of their complexes) whose 3d shells are not filled [2,9,10], *e.g.* Cr, Mn, Fe, Co, Ni, and Cu (cf. [11]), are catalytically active for reactions (1) and (2) in the homogeneous phase, whereas those with full d shells, such as Zn and Cd [10], are catalytically inactive. Among the complexes of the ions mentioned, those of Fe^{III} [5] and Cu^{II} [13] are particularly active. It is interesting to note that these ions also occur in many redox-active enzyme systems [14].

Whereas enzymes containing Fe have been extensively studied for some time [15], those containing Cu have only recently attracted much interest [12]. One of the main reasons for this is probably the fact that in many enzymes containing Fe the metal ion is bound in a porphyrin system, *i.e.* the ligand atoms are known and localized, and this facilitates the understanding of the course of catalysis. In the enzymes containing Cu (cf. *e.g.* [12]), such as tyrosinase, polyphenol oxidase, laccase, *etc.*, on the other hand, the ligand atoms are less obvious; in fact, the details of the coordination sphere of the metal ion are not known for any Cu enzyme or protein, so that one fundamental condition for the understanding of their action is lacking [16].

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[9] Cf. [3], pp. 2289, 2290.

[10] *H. B. Jonassen* and *H. Thielemann*, Z. anorg. allg. Chem. *320*, 274 (1963).

[11] The valency stages of Cu and their relative stability are discussed by *C. K. Jörgensen* in [12], p. 1. For Cu^{III}, cf. also *D. P. Graddon*: An Introduction to Coordination Chemistry, Pergamon Press, Oxford 1961, p. 34.

[12] *J. Peisach*, *P. Aisen*, and *W. E. Blumberg*: The Biochemistry of Copper. Academic Press, New York 1966.

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[14] Cf. *e.g.* in [12], pp. 9 and 131.

[15] *A. S. Brill* in *M. Florkin* and *E. H. Stotz*: Comprehensive Biochemistry. Elsevier Publishing Co., Amsterdam 1966, Vol. 14, p. 447; *H. Hermel* and *R. Havemann*, Biochim. biophysica Acta *128*, 283 (1966); cf. [42].

[16] Cf. *H. S. Mason*, in [12], p. 339.

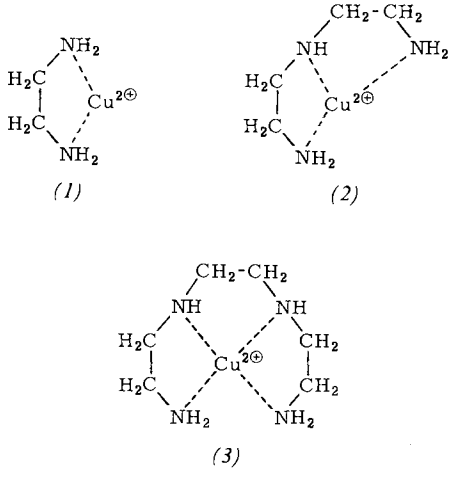
The principal possibilities for the coordination sites for metal ions in proteins are $-COO^-$, ArO^-, RS^-, $-NH_2$, $-CONH-$, and imidazole[17]. Consequently, Cu complexes containing at least some of these ligand groups have often been studied as models for Cu proteins or enzymes (cf. *e.g.* [17–21]).

In the present article we shall confine ourselves to a discussion of the catalase and peroxidase activity, in accordance with eq. (1) and (2), of Cu^{2+} complexes of various structures, some of which may also be regarded as models in the sense mentioned above. The attempt to characterize these catalytic processes in more detail led to a simple relation between structure and activity. This makes it possible to use the Cu^{2+} catalyzed decomposition of H_2O_2 as a "molecular probe", *i.e.* to draw conclusions regarding the structure of the Cu^{2+} complex in question from the nature and course of the catalysis.

2. Influence of the Number and Nature of the Coordinated Ligand Groups on the Catalysis

2.1. Influence of the Number of Coordinated Ligand Groups

It has repeatedly been found[22,23] that complexes of metal ions favor the decomposition of H_2O_2 only if they are not coordinately saturated, *i.e.* if they are still hydrated and so have coordination sites available for H_2O_2 or HOO^-; these sites will be described as "free". The relation between catalytic activity and free coordination sites was checked in the 1:1 complexes of the "homologous" series ethylenediamine *(1)*, bis(2-aminoethyl)amine (diethylenetriamine) *(2)*, and *N,N'*-bis(2-aminoethyl)-1,2-diaminoethane (triethylenetetramine) *(3)* with Cu^{2+}[24].



The initial rate constant k (pseudo-first order) of the decomposition of H_2O_2 was taken as a measure of the catalytic activity[23] (eq. (3)[25]):

$$k = (2.30/t) \cdot \log([H_2O_2]_0/[H_2O_2]_t)\ (\text{min}^{-1}) \qquad (3)$$

It was again found that the catalytic activity requires free coordination sites, *i.e.* it is connected with the possibility of formation of ternary Cu^{2+}-peroxo ligand complexes, which can be detected by the appearance of an absorption shoulder at about 360 nm[23,24]. As the number of free coordination sites on the Cu^{2+} decreases, k also decreases as a function of the pH value (= activity curve) (Fig. 1), *i.e.* the pH value at which the catalytic activity begins is higher; in the case of the 4-coordinate complex *(3)* it is practically zero. This relation and the occurrence of ternary Cu^{2+}-peroxo complexes indicate that the catalysis takes place within the coordination sphere.

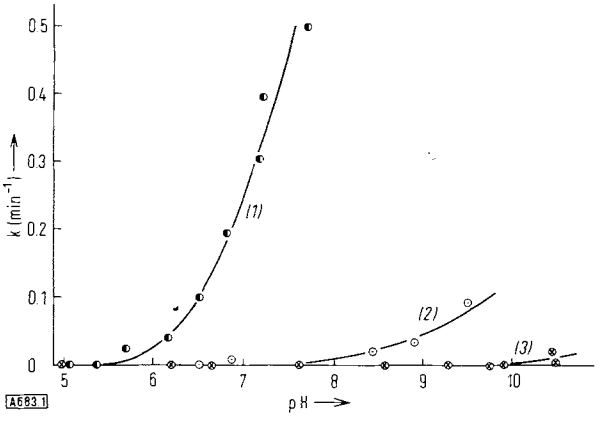


Fig. 1. Decrease in the catalytic activity of the Cu^{2+} chelates (4×10^{-4} M) with the number of free coordination sites on the metal ion, determined as the initial rate constant k (min^{-1}) of the decomposition of H_2O_2, which is pseudo-first order with respect to H_2O_2 (8×10^{-3} M), as a function of the pH value. *(1)* (◐) > *(2)* (⊙) > *(3)* (⊗).

In general, the catalysis of the decomposition of H_2O_2 begins in the neutral range with Cu^{2+} complexes having two free coordination sites, and in the weakly alkaline range with those having only one free site; Cu^{2+} complexes with no free coordination sites are catalytically

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[24] *H. Sigel* and *U. Müller*, Helv. chim. Acta *49*, 671 (1966).

[25] Measurements [24]: Before the addition of H_2O_2, the pH was adjusted with 2 N NaOH to a slightly higher value than was desired. After the addition of H_2O_2, the pH value was measured; to determine the decrease in the H_2O_2 concentration, samples were taken at fixed intervals, titanium reagent was added, and the extinction was measured at 410 nm ($\varepsilon = 737$ l mole^{-1} cm^{-1}); cf. also *A. C. Egerton, A. J. Everett, G. J. Minkoff, S. Rudrakanchana*, and *K. C. Salvoja*, Analytica Chim. Acta (Amsterdam) *10*, 422 (1954). Unless otherwise specified, the measurements were carried out at $T = 22$ °C and natural ionic strength.

inactive, these data being based on the assumption that Cu^{2+} has a coordination number of four under the reaction conditions [26, 32].

2.2. Influence of Ligand Groups Acting as H Donors

As we have shown, Cu^{2+} complexes having free coordination sites exhibit catalase activity; on the other hand, it is known that the Cu^{2+}/H_2O_2 system oxidizes pyrocatechol [18] and *o*-phenylenediamine [31], *i.e.* it exhibits peroxidase activity. We are thus faced with the question of the relation between the catalase and peroxidase activities of Cu^{2+} complexes.

Since the measured disappearance of H_2O_2 in such a system is due to consumption of H_2O_2 by both the catalase [eq. (1)] and the peroxidase [eq. (2)] activities, the catalytic activity (measured by the H_2O_2 consumption) is defined as the sum of the catalase and peroxidase activities.

Adenosine 5′-triphosphate (ATP), adenosine 5′-monophosphate N^1-oxide (AMP N^1-oxide) (cf. [34]), and native deoxyribonucleic acid (DNA) were chosen as the ligands for these investigations [33].

All three ligands have a well pronounced UV absorption band (ATP [35] and DNA [36] at 260 nm, and AMP N^1-oxide [37] at 272 nm), so that any degradation of the nucleic bases can be followed spectrophotometrically. The pseudo-first order initial rate constant k' with respect to the degradation of the bases [eq. (4)], measured by the resulting decreases in the extinction of the system, was taken as a measure of the peroxidase activity:

$$k' = (2.30\ t) \cdot \log(E_0/E_t)\ (\text{min}^{-1}) \qquad (4)$$

The "apparent" [38] initial rate constant k' as a function of the pH value (peroxidase activity curve) is shown in Figure 2 for all three complexes.

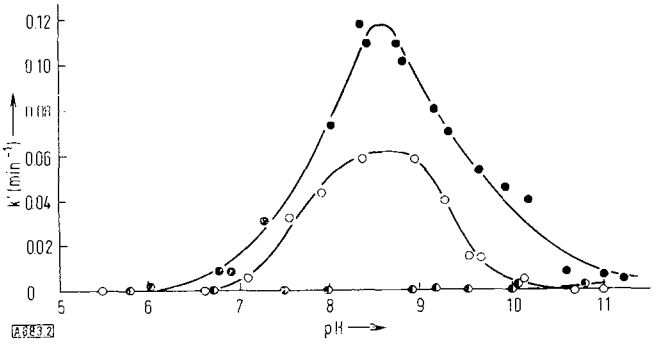


Fig. 2. Peroxidase activity ($[H_2O_2] = 8 \times 10^{-3}$ M), determined as the initial rate constant k' of the degradation of the nucleic bases, measured in 1 mm quartz cells as a pseudo-first order reaction with respect to the ligand concentration as a function of the pH value for the Cu^{2+} complexes (4×10^{-4} M) of ATP (●) and AMP N^1-oxide (○), as well as for the Cu^{2+}-DNA system (◐) ([DNA] = 0.04%; $[Cu^{2+}] = 4 \times 10^{-4}$ M, *i.e.* there are about 2.5 nucleotide units per Cu^{2+} [33]).

Comparison of the catalytic [33] activity (Fig. 1) with the peroxidase activity (Fig. 2) [39] reveals two points:

1. The peroxidase activity passes through a maximum at pH $\approx$ 8.5 (cf. [33]), whereas the catalytic activity increases "uniformly" in the pH range examined.

2. Though all three systems are catalytically active, only the bases of the two nucleotide complexes, but not those of the Cu^{2+}-DNA system, are degraded (cf. Fig. 2).

It can be concluded from these observations that:

1. The peroxidase degradation of nucleic bases is not brought about by free-radical secondary products of the catalase decomposition of H_2O_2, since the courses of the two reactions should otherwise be parallel. Moreover, free radicals, such as $HO^{\cdot}$, would probably also penetrate into the helix and reach the nucleic bases in the Cu^{2+}-DNA system (cf. Sections 4.2–4.4).

2. The degradation evidently takes place in the coordination sphere of the metal ion, and a condition for its occurrence is therefore that the nucleic bases should be complexed, as is the case in the Cu^{2+}-ATP [35] and AMP N^1-oxide [37] complexes, but not in the Cu^{2+}-DNA system.

3. Since both the catalase and the peroxidase reactions evidently proceed within the coordination sphere, it must be assumed that external factors determine the direction in which the common "intermediate" complex reacts [40] (cf. also [33]).

The above observations on the influence of the number and nature of the coordinated ligand groups on the catalytic and peroxidase behavior of Cu^{2+} complexes indicate the possibility of using this "structure-specific" behavior of Cu^{2+} complexes of unknown structure as a source of information about the coordi-

[26] Other examples of inactive tetracoordinated Cu^{2+} complexes are those with cyclam (= 1,4,8,11-tetraazacyclotetradecane) [27], hexamethylcyclam [28], and ethylenediaminetetraacetic acid [29]. Very recent studies [27] on the Cu^{2+}-phthalocyaninetetrasulfonic acid complex (a pure sample prepared in accordance with [30]) showed that this system, in contrast to earlier findings [24], is also catalytically inactive. – The assumption of the coordination number four for the Cu^{2+} in aqueous solution has also proved to be meaningful in other cases: *D. D. Perrin, I. G. Sayce*, and *V. S. Sharma*, J. chem. Soc. (London), A *1967*, 1755.

[27] *H. Erlenmeyer, P. Waldmeier*, and *H. Sigel*, Helv. chim. Acta *51*, 1795 (1968).

[28] *Th. Kaden* and *H. Sigel*, Helv. chim. Acta *51*, 947 (1968).

[29] *L. Erdey* and *I. Buzás*, Acta chim. Acad. Sci. hung. *6*, 77 (1955).

[30] *J. H. Weber* and *D. H. Busch*, Inorg. Chem. *4*, 469 (1965).

[31] *S. Fallab*, Chimia *15*, 576 (1961).

[32] Slight catalytic activity of Cu^{2+} complexes with no free coordination sites at pH $\geq$ 10.5 is probably due to partial oxidation of the ligand (cf. *e.g.* [6, 28]).

[33] *H. Sigel* and *H. Erlenmeyer*, Helv. chim. Acta *49*, 1266 (1966).

[34] The Cu^{2+} complexes with both ligands are practically completely formed in the pH range in question (pH $\geq$ 7); cf. [33].

[35] *R. Phillips*, Chem. Reviews *66*, 501 (1966).

[36] *G. L. Eichhorn, P. Clark*, and *E. D. Becker*, Biochemistry (Washington) *5*, 245 (1966).

[37] *H. Sigel* and *H. Brintzinger*, Helv. chim. Acta *47*, 1701 (1964); *H. Sigel* and *B. Prijs*, *ibid. 50*, 2357 (1967).

[38] "Apparent" because the unknown extinction of the degradation products of the nucleic bases should be subtracted from the measured extinction; however, the agreement of the k' values at various times was very good, indicating that the extinction coefficient of the degradation products is low.

[39] As expected, ternary Cu^{2+}-peroxo complexes are also formed in all three cases [33].

[40] A similar situation was found by *Kremer* [41] in a study on the hemin-catalyzed oxidation of ascorbic acid. Catalase also exhibits peroxidase properties if the H_2O_2 concentration in the reaction solution is relatively low, and an H donor is also present [42]. The reaction can thus again be directed in the desired direction by the choice of the reaction conditions.

[41] *M. L. Kremer*, Trans. Faraday Soc. *63*, 1208 (1967).

[42] *H. Aebi* and *A. Hassan*, Helv. chim. Acta *43*, 544 (1960).

nation spheres of these complexes, *i.e.* of using the metal ion-catalyzed decomposition of H_2O_2 as a "molecular probe".

3. The Catalytic Activity as a "Probe"

3.1. *N,N'*-Diglycylethylenediamine and "Homologs"

The homologous ligands *N,N'*-diglycylethylenediamine, *N,N'*-diglycyl-1,3-diaminopropane, and *N,N'*-diglycyl-1,5-diaminopentane, the complex formation of which has been studied by *Zuberbühler* and *Fallab* [43], and in which, as in polypeptides, the coordination sites are amide and amino groups, appear to be particularly suitable for use as models for the elucidation of the relation between the catalytic activity and the number of free coordination sites in Cu^{2+} complexes [44].

The decomposition of H_2O_2 is very strongly catalyzed by the Cu^{2+} complex *(6)* (see Fig. 3). The activity curve lies in the region of Cu^{2+} complexes with two free coordination sites (cf. Fig. 1). The Cu^{2+} complex *(5)*, on the other hand, is inactive, like the Cu^{2+} complexes with no free coordination sites on the central atom.

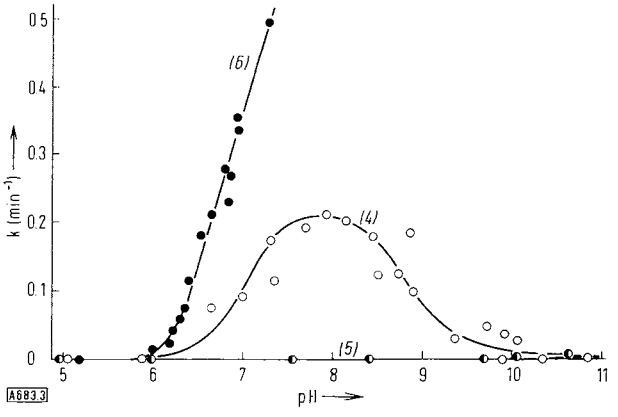
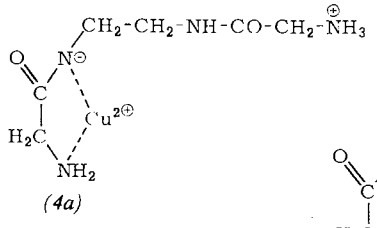


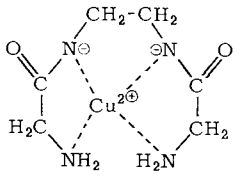
Fig. 3. Catalytic activity of the Cu^{2+} complexes (4×10^{-4} M) *(4)* (○), *(5)* (◐), and *(6)* (●), determined as the initial rate constant k (min^{-1}) of a pseudo-first order reaction with respect to H_2O_2 (8×10^{-3} M).

The activity of the Cu^{2+}-complex *(4)* reaches a maximum at pH $\approx$ 8 and then falls off to practically zero at pH $\approx$ 10; the Cu^{2+} complex *(4a)*, which has two free coordination sites, is evidently converted into the tetracoordinated complex *(4b)*.

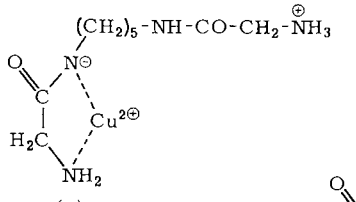
These observations [44] agree with the structures deduced from potentiometric and spectrophotometric data [43], according to which *N,N'*-diglycylethylenediamine can form Cu^{2+} complexes with two free coordination sites or with no free coordination sites, depending on the pH value. The Cu^{2+} compound formed initially without deprotonation of the amide group loses an amide proton at pH = 5.49 to form the catalytically active *(4a)*; an ammonium proton is removed



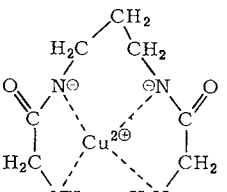
(4a)



(4b)



(6)



(5)

at pK_A = 6.51, and the proton of the second amide group is lost at pK_A = 8.21 to form the inactive *(4b)*. In the case of *N,N'*-diglycyl-1,5-diaminopentane, the primary complex loses an amide proton at pH = 5.49 to form *(6)*. The ammonium group is deprotonated at pK_A = 7.47, but according to [43] it does not coordinate, so that, in agreement with the catalytic observations, a complex with two free coordination sites exists in this range. A complex analogous to *(4b)* is formed only after deprotonation of the second amide group (pK_A = 10.30) [43]. *N,N'*-Diglycyl-1,3-diaminopropane forms the catalytically inactive Cu^{2+} complex *(5)* at pH = 5.61, with occupation of all four coordination sites; the second ammonium proton and the second amide proton are lost in a single step with $pK_{A(2H)}$ = 11.33 [43].

The pH-dependent extinction at 360 nm (extinction curves, Fig. 4), which indicates the occurrence of ternary peroxo complexes, follows a course similar to the corresponding activity curves in Figure 3 for all three ligands [44].

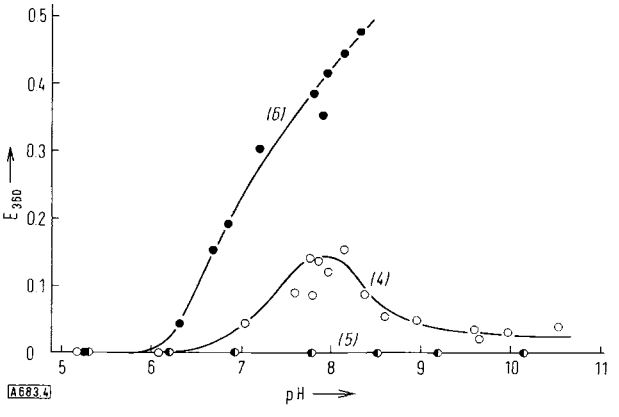


Fig. 4. Formation of ternary Cu^{2+}-peroxo complexes in media containing H_2O_2 (8×10^{-3} M), measured by the increase in extinction at 360 nm (1 cm quartz cells) as a function of the pH value for the Cu^{2+} complexes (4×10^{-4} M) *(4)* (○), *(5)* (◐), and *(6)* (●).

The results obtained with these ligands thus confirm the correlation between the catalytic activity of Cu^{2+} complexes and the number of free coordination sites.

[43] *A. Zuberbühler* and *S. Fallab*, Helv. chim. Acta *50*, 889 (1967).

[44] *H. Erlenmeyer*, *U. Müller*, and *H. Sigel*, Helv. chim. Acta *49*, 681 (1966).

3.2. Glycine Amide

The activity curve (Fig. 5)[44] of the Cu^{2+}-glycine amide (1:1) chelate *(7a)* begins, as expected, in the region of the Cu^{2+} complexes with two free coordination sites (cf. Fig. 1), but at a somewhat higher pH value than that of the complex *(6)*, after which it initially runs parallel to the latter. The somewhat later start (cf. Fig. 3) is due to the fact that the primarily formed Cu^{2+}-glycine amide complex loses its amide proton[45] to form the more active complex *(7a)*[46] at a higher pH value than the corresponding complex of *N,N'*-diglycyl-1,5-diaminopentane. The uncoordinated "residue" in *(6)* thus does not appear to influence the catalytic activity.

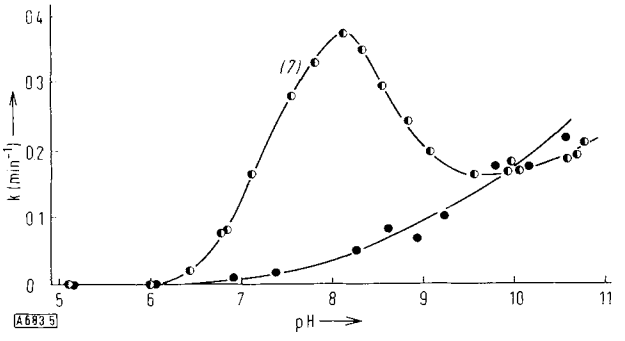
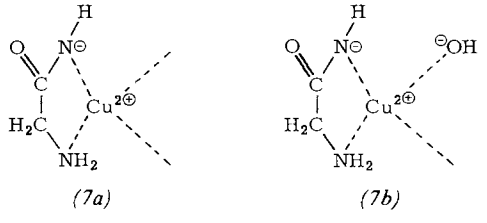


Fig. 5. Catalytic activity of Cu^{2+}-glycine amide *(7)* (◐) (4×10^{-4} M) and (for comparison) of Cu^{2+}-glycylglycine (●), determined as the initial rate constant k (min^{-1}) for the decomposition of H_2O_2, which is of pseudo-first order with respect to H_2O_2 (8×10^{-3} M).

It is surprising that this parallelism in the activities of *(6)* and *(7a)* is confined to the low pH range. The catalytic activity of the Cu^{2+}-glycine amide complex passes through a maximum at pH $\approx$ 8, then decreases until at pH $\approx$ 9.5 its activity is roughly the same as that of Cu^{2+} complexes with only one free coordination site (Fig. 5). It is therefore assumed that at pH > 8 one of the two free coordination sites is occupied by OH^-, and a complex having the structure *(7b)* is formed.



(7a) *(7b)*

These observations were confirmed potentiometrically[47]. The primary 1:1 Cu^{2+}-glycine amide complex is deprotonated with pK^{H}_{CuHL} = 7.01 and forms the complex *(7a)* with two free coordination sites. This complex is hydrolyzed with $pK^{H}_{CuL(H_2O)x}$ = 8.07 and changes into *(7b)*, which has one free coordination site.

The extinction curve of *(7)*, unlike the activity curve, has no maximum at 360 nm[44], but exhibits saturation character beyond pH $\approx$ 7. The formation of the yellow ternary complex is thus not affected by the occupation of the third coordination site by OH^-[48], *i.e.* it requires only one free coordination site for its formation, whereas the "active" complex responsible for the catalysis evidently requires two[49] (cf. also[24,33] and Section 5).

3.3. Poly-α,L-lysine Peptide

Since polyamino acids are particularly suitable for use as enzyme models[50], the Cu^{2+} complexes of poly-α,L-lysine-670, -58, and -14[51] were compared with the Cu^{2+} complexes of L-lysine and L-lysyl-α,L-lysine with respect to the catalysis of the decomposition of H_2O_2[52]. It was surprisingly found that despite the large number of potential coordination sites in the poly-α,L-lysines, the catalytic activity of their Cu^{2+} systems (Fig. 6) lies in the range of the Cu^{2+} complexes with two free coordination sites (cf. Fig. 1)[53].

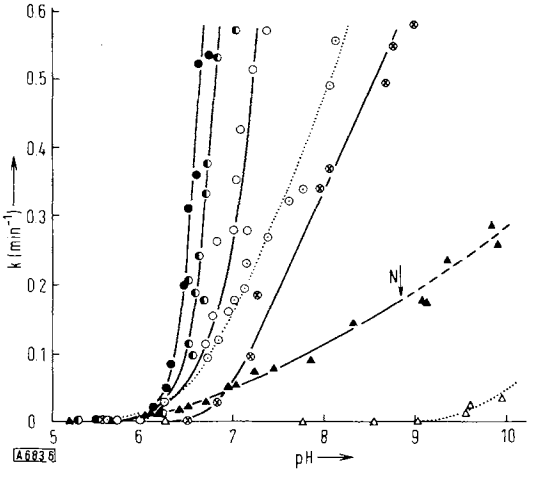


Fig. 6. Catalytic activity of Cu^{2+} systems (Cu^{2+}: lysine unit = 1:15; $[Cu^{2+}] = 4 \times 10^{-4}$ M) of poly-α,L-lysine-670 (●) and -58 (◐) and of the Cu^{2+} 1:1 systems (4×10^{-4} M) of poly-α,L-lysine-14 (○), L-lysyl-α,L-lysine (⊗), and L-lysine (▲) measured as the pseudo-first order initial rate constant k (min^{-1}) with respect to H_2O_2 (8×10^{-3} M) as a function of the pH value. The k values for the poly-α,L-lysine-14 (2:1) system (⊙) (*i.e.* 2 Cu^{2+} per ligand molecule) and the Cu^{2+}-L-lysine (1:15) system (△) are also shown (dotted curves) for comparison (see also [52]).

[45] *S. P. Datta* and *B. R. Rabin* found that the Cu^{2+} complex of glycine amide loses its amide proton; Biochim. biophysica Acta *19*, 572 (1956); cf. also *N. C. Li*, *B. E. Doody*, and *J. M. White*, J. Amer. chem. Soc. *79*, 5859 (1957).

[46] The non-deprotonated complex should have an activity similar to that of the Cu^{2+}/ glycine (1:1) system (cf. [24]).

[47] *H. Sigel*, Angew. Chem. *80*, 124 (1968); Angew. Chem. internat. Edit. *7*, 137 (1968).

[48] Up to pH $\approx$ 10.5, $[HOO^-]$ is approximately 1.2 times the corresponding $[OH^-]$ at a given pH. $pK^{H}_{H_2O_2} = 11.81$; *V. A. Kargin*, Z. anorg. allg. Chem. *183*, 77 (1929).

[49] In agreement with this the variation of the catalytic activity of tricoordinated Cu^{2+} chelates is contrary to the spectrochemical series, *i.e.* it decreases with increasing ligand field strength and complex stability, since the latter are accompanied by an increase in the difficulty of liberation of a further coordination site [24].

[50] *E. Katchalski*, *M. Sela*, *H. I. Silman*, and *A. Berger* in *H. Neurath*: The Proteins. Academic Press, New York 1964, 2nd Edit., Vol. 2, p. 405.

[51] The number added to the name indicates the degree of polymerization.

[52] *H. Sigel* and *G. Blauer*. Helv. chim. Acta *51*, 1246 (1968).

[53] Comparison of the activity curve of Cu^{2+}-L-lysine (Fig. 6) with that of the Cu^{2+}-glycylglycine (1:1) complex (Fig. 5) points to at least partial tricoordination of the Cu^{2+} in the lysine complex. This is conceivable (Stuart models), though such a complex is certainly not very stable. The third coordination site may also be occupied by OH^-, as in the Cu^{2+}-glycine amide complex (cf. Section 3.2). For the influence of the end groups and of the positive field of the polymer on the catalysis cf. [52].

As was shown in Section 2.2, ligand groups are oxidized by H_2O_2 only if they are situated in the coordination sphere of Cu^{2+} [33], and some Cu^{2+}-peptide complexes [54] are in fact degraded by H_2O_2. Molecular weight determinations were therefore carried out [52] in the Cu^{2+}-poly-α,L-lysine-58 system before and after the catalytic reaction [55]. The fact that the average molecular weight decreases by only 30–40% indicates only slight participation of the amide groups in complex formation in this pH range, as is to be expected purely on grounds of coordination chemistry [56]. The complex formation therefore probably occurs mainly by means of two ε-amino groups. This agrees with *Moriguchi*'s interpretation [58], according to which the complex formation between Cu^{2+} and poly-α,L-lysine involves amide groups only in the pH range around 12.

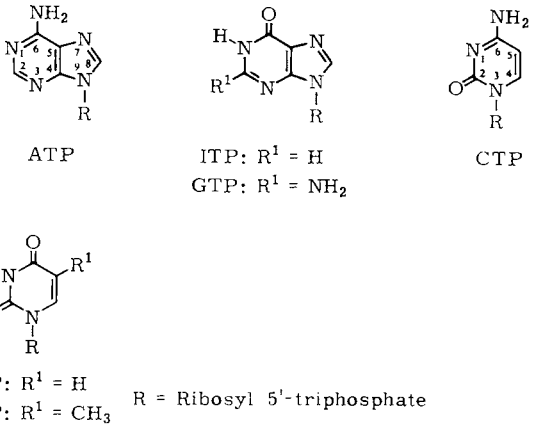
This "probe" also provides information about the complex structures of the Cu^{2+} complexes of glycylglycine amide, polymyxin B [44], and some oligomers or polymers of glycine and L-glutamic acid [52] on the basis of catalytic activity [59].

4. The Peroxidase Activity as a "Probe"

It was shown in Section 2.2 that peroxidase activity can occur only if there is an oxidizable group in the coordination sphere of the metal ion. Conversely, it will now be shown that information about the position at which a metal ion is coordinated can be obtained from the detection of peroxidase degradation of a certain group.

4.1. 5'-Triphosphates of the Ribonucleosides Adenosine, Inosine, Guanosine, Cytidine, Uridine, and Thymidine [60]

It is known (see Section 2.2) [35] that in the Cu^{2+} complex of ATP, the adenine system is coordinated to the metal ion as well as the triphosphate chain to form a macrochelate, and the adenine system is accordingly degraded by H_2O_2. *Schneider* and *Brintzinger* [61] assumed that a macrochelate of this type also occurs in the Cu^{2+}-ITP complex, and such a chelate has recently been detected in the Co^{2+}-ITP complex by *Sternlicht et al.* [62]. Information about the complex structures of the Cu^{2+}-nucleoside triphosphate complexes has now been obtained by measurement of their peroxidase activity [63,64].



The "apparent" [38] initial rate constants k' of the peroxidase degradation of the nucleic bases in the Cu^{2+} complexes of ATP (cf. Section 2.2), ITP, GTP, CTP UTP, and TTP are shown in Figure 7 as functions of the pH value. Figure 8 shows the catalytic activity; as expected, extinction curves can also be measured in every case (cf. [63]). Though the peroxidase activities (Fig. 7) of the nucleotide complexes studied differ, they indicate that the bases, as in the Cu^{2+}-ATP complex [35], take part in the complex formation to give macrochelates.

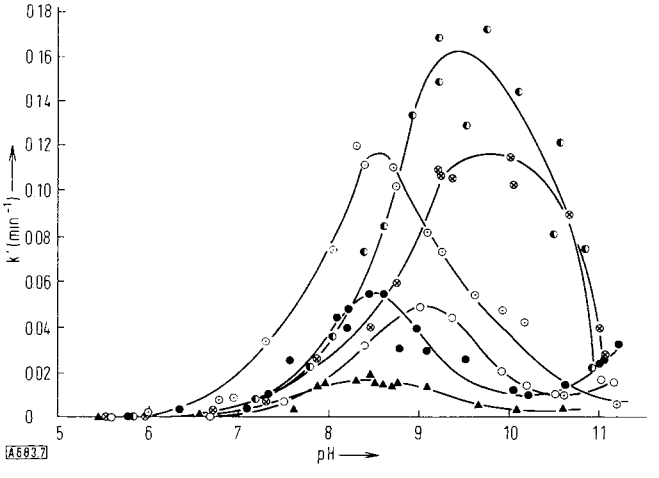


Fig. 7. Peroxidase activity ($[H_2O_2] = 8 \times 10^{-3}$ M), determined as the initial rate constant k' (min^{-1}) of the degradation of the nucleic bases, measured as a pseudo-first order reaction with respect to the ligand concentration, as a function of the pH value for the Cu^{2+} complexes (4×10^{-4} M) of ATP (○), ITP (⊗), GTP (◐), CTP (▲), UTP (●), and TTP (○). (The extinctions were measured at the maximum or in the case of pH-dependent spectra at the isosbestic point [63].)

[54] *H. Erlenmeyer, H. Sigel, H. Ch. Curtis,* and *P. Anders,* Helv. chim. Acta *49,* 19 (1966).

[55] The reaction solution stood for one day at pH = 7; other conditions as indicated in Figure 6.

[56] The participation of the amide group in the complex formation is not very probable on grounds of coordination chemistry [57]. Thus, with Cu^{2+}, glycine amide forms a complex whose amide group is deprotonated [47], whereas β-alanine amide does not [57].

[57] *P. Hemmerich, Th. Kaden,* and *H. Sigel,* unpublished.

[58] *Y. Moriguchi,* Bull. chem. Soc. Japan *39,* 2656 (1966).

[59] For Ni^{2+} complexes cf. *R. Zell* and *H. Sigel,* Helv. chim. Acta *49,* 870 (1966); *H. Sigel* and *H. Ch. Curtius,* Experientia *22,* 649 (1966).

[60] Abbreviations for the 5'-triphosphates: ATP, ITP, GTP, CTP, UTP, TTP.

[61] *P. W. Schneider* and *H. Brintzinger,* Helv. chim. Acta *47,* 1717 (1964).

[62] *H. Sternlicht, R. G. Shulman,* and *E. W. Anderson,* J. chem. Physics *43,* 3133 (1965).

[63] *H. Sigel,* Helv. chim. Acta *50,* 582 (1967).

[64] The Cu^{2+}-ATP complex is formed to an extent of more than 96% above pH = 7 [33], *i.e.* in the pH range in question. This is probably also true of the other Cu^{2+}-nucleotide complexes (cf. [63]).

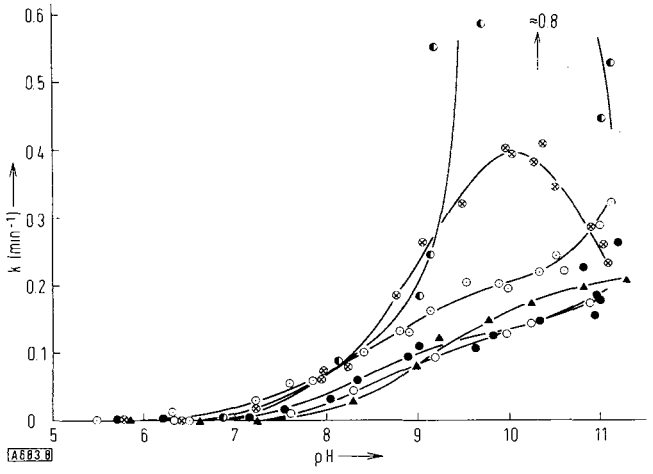


Fig. 8. Catalytic activity, determined as the initial rate constant k (min^{-1}) of the decomposition of H_2O_2, measured as a pseudo-first order reaction with respect to H_2O_2 (8×10^{-3} M), as a function of the pH value for the Cu^{2+} complexes (4×10^{-4} M) of ATP (○), ITP (⊗), GTP (◐), CTP (▲), UTP (●), and TPP (○).

The catalytic activities (Fig. 8) of the Cu^{2+} complexes of CTP, UTP, TTP, and ATP increase with rising pH over the entire range, whereas the activities of the ITP and GTP complexes pass through a maximum at pH $\approx$ 10 and then fall off again rapidly to pH $\approx$ 11. This is probably connected with the fact that the nucleic bases of ITP and GTP have two potential coordination sites, *i.e.* N-7 and the oxygen on C-6. The simultaneous coordination of Cu^{2+} to these sites and to two phosphate groups as found in the Cu^{2+}-ATP complex [35] leads to an inactive complex (cf. [63]) [66].

The fact that the base in the nucleotide complexes studied is involved in the complex formation, at equilibrium at least, should lead to a decrease in the pK_A value of the proton on N-1 in cases where this proton is present, *i.e.* in ITP, GTP, UTP, and TTP. This has in fact been conclusively demonstrated [65]. The degree of acidification [eq. (5)] [67] of the N-1 proton

$$\Delta pk_A = pK^H_{HL} - pK^H_{CuHL} \qquad (5)$$

as a result of complex formation with Cu^{2+} is approximately 2.0 pK units in all four cases; it is thus of the same order of magnitude as in the Cu^{2+} guanosine complex ($\Delta pK_A = 2.2$ [65]), in which the metal ion is coordinated only *via* the nucleic base. This confirms the participation of the nucleic bases in the complex formation in the Cu^{2+}-nucleotide complexes studied [68]. The question of the positions in the nucleic base to which the metal ion is coordinated has already been discussed [63].

[65] *H. Sigel*, European J. Biochem. *3*, 530 (1968).

[66] The fact that the peroxidase activity (Fig. 7) decreases again in every case is probably connected with the observed hydrolysis of the Cu^{2+}-nucleotide complexes [65].

[67] $K^H_{HL} = [H^+]\,[L]/[HL]$; $K^H_{CuHL} = [H^+]\,[CuL]/[CuHL]$.

[68] If the nucleic bases in the Cu^{2+}-nucleotide complexes are displaced from the coordination sphere of the Cu^{2+} by complex formation with 2,2'-bipyridyl (cf. [69]), the acidification decreases to about 0.6 pK units [65].

[69] *H. Sigel, K. Becker*, and *D. B. McCormick*, Biochim. biophys. Acta *148*, 655 (1967). For the significance of the ternary complexes cf. [70].

[70] *H. Sigel*, Chimia *21*, 489 (1967).

4.2. Native RNA, Native DNA, and DNA Denatured by Cu^{2+}

The secondary and tertiary structure of deoxyribonucleic acid (DNA) is generally accepted as being described by the helix model developed by *Watson* and *Crick* and by other authors [4]. By analogy with DNA, ribonucleic acid (RNA) is also expected to have a three-dimensionally ordered structure and definite base pairing [4]. However, the nucleic bases in this case are evidently less "protected" than in DNA. This agrees with the peroxidase activity (measured at 260 nm) [71]. The nucleic bases in the Cu^{2+}-RNA system, unlike those of the Cu^{2+}-DNA system, are degraded by H_2O_2, *i.e.* Cu^{2+} must be at least partly bonded to the nucleic bases in this case.

Degradation of the nucleic bases can however also be detected in the Cu^{2+}-DNA system if a DNA solution is allowed to stand for $1^1/_2$ days after the addition of Cu^{2+} before its peroxidase activity is measured [71]. A reference solution to which Cu^{2+} was added shortly before the measurement, on the other hand, exhibited no peroxidase activity. The Watson-Crick structure is thus destabilized by prolonged exposure to the action of Cu^{2+} (cf. also [36]), and the Cu^{2+} then penetrates into the double helix of the resulting denatured DNA. This result complements *Hiai*'s observation [72] that Cu^{2+} promotes the thermal denaturation of DNA. This type of behavior is to be expected of metal ions, since they can break H bonds by coordination.

Catalytic activity is observed in all three systems (though the magnitudes differ), as is the occurrence of ternary peroxo complexes [71].

4.3. Thermally Denatured DNA

Thermal denaturation of DNA leads to a change in its extinction at 260 nm [36, 72]. This is attributed to partial elimination of the base pairing, which should also lead to an increase in peroxidase activity. If Cu^{2+} and H_2O_2 are added to thermally denatured DNA

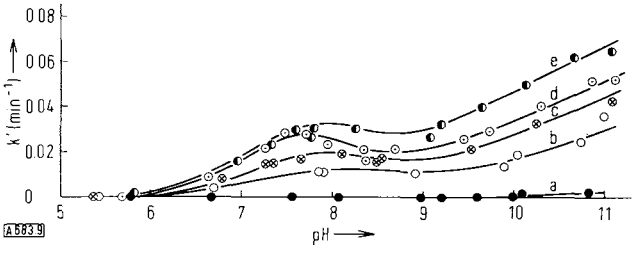


Fig. 9. Peroxidase activity of the Cu^{2+} complexes of thermally denatured DNA ([DNA] = 0.04%; $[Cu^{2+}] = 4 \times 10^{-4}$ M; $[H_2O_2] = 8 \times 10^{-3}$ M), determined as the initial rate constant k' (min^{-1}) for the degradation of the nucleic bases (pseudo-first order), measured in 1 mm quartz cells at 260 nm. DNA solutions (0.1%): (a) undenatured (●) as reference; (b) heated to 50 °C (○); (c) heated to 95 °C and kept at this temperature for 1 minute (⊗); (d) heated to 95 °C and kept at this temperature for 5 minutes (⊙); (e) heated to 95 °C and kept at this temperature for 15 minutes (◐).

[71] *H. Sigel, B. Prijs*, and *H. Erlenmeyer*, Experientia *23*, 170 (1967).

[72] *S. Hiai*, J. molecular Biol. *11*, 672 (1965).

solutions [71], it is found that the peroxidase activity increases with increasing denaturation of the DNA (Fig. 9). This confirms that the denaturation is coupled with the opening of the double helix, with the result that the bases are exposed for complex formation with Cu^{2+}. The investigation of the peroxidase activity of a Cu^{2+}-DNA system can therefore be used to distinguish between native and denatured DNA.

The catalytic activity (cf. [71]) increases to a greater degree with increasing denaturation than would be expected on the basis of consumption of H_2O_2 because of peroxidase activity. It therefore follows that the catalase activity also increases. This is probably connected with the fact that *N*-chelates are catalytically more active than *O*-chelates [23, 24]. The different charges on the complexes (*N*-chelates are generally charged positively, *O*-chelates negatively) undoubtedly affect the formation of ternary Cu^{2+}-peroxo complexes with HOO^- (cf. [70]).

4.4. Denaturation of DNA as a Function of the pH. Stabilizing Effects of LiCl, NaCl, KCl, and $MgCl_2$

0.05% aqueous DNA solutions were prepared by dissolving in each case 7.5 mg of DNA in 15 ml of H_2O at various pH values with slow stirring for 16 hours ($T = 22$ °C). After this time several samples were taken, Cu^{2+} and H_2O_2 were added, and the peroxidase activities of the samples were examined (at 260 nm) between pH 5.5 and 10.5 [73]. The resulting peroxidase activity curves (Fig. 10) clearly show the influence of the H^+ concentration on the stability of the DNA. The peroxidase activity of the samples increases with the initial H^+ concentration of the DNA solutions [74].

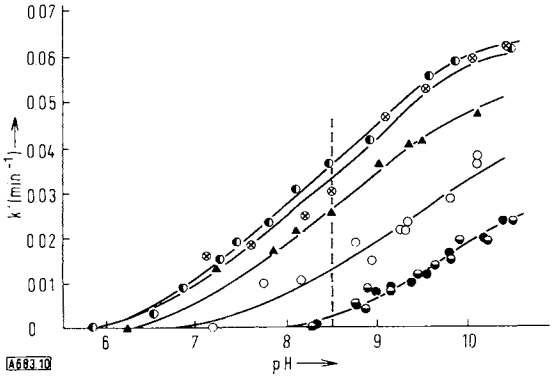


Fig. 10. Peroxidase activity of the Cu^{2+} complexes of DNA solutions (0.05%; $T = 22$ °C) aged for 16 hours at various pH values [pH = 3.0 (◐); pH = 4.0 (⊗); pH = 4.5 (▲); pH = 5.0 (○); pH = 6.0 (●), pH = 10.0 (◒)], determined as the initial rate constant (pseudo-first order) k' (min^{-1}) of the degradation of the nucleic bases. Concentration of solutions for measurement: [DNA] = 0.01%; $[Cu^{2+}] = 10^{-4}$ M; $[H_2O_2] = 8 \times 10^{-3}$ M; measured at 260 nm in 2 mm quartz cells.

If the degree of denaturation is determined at pH values between 3 and 13 by measurement of the peroxidase activity of the Cu^{2+} complexes (cf. Fig. 10) and the values k' obtained from these curves at pH = 8.5 are plotted against the pH values of the DNA solutions, one obtains a "trough-shaped" curve (Fig. 11), as was also found by *Grechko et al.* [75], who measured denaturation by the hyperchromism and the change in viscosity. It is clear from Fig. 11 that DNA suffers appreciable denaturation only in the "extreme" pH ranges. The DNA helix is very stable in solutions having pH values of 6 to 11, and the bases are thus not accessible to Cu^{2+}.

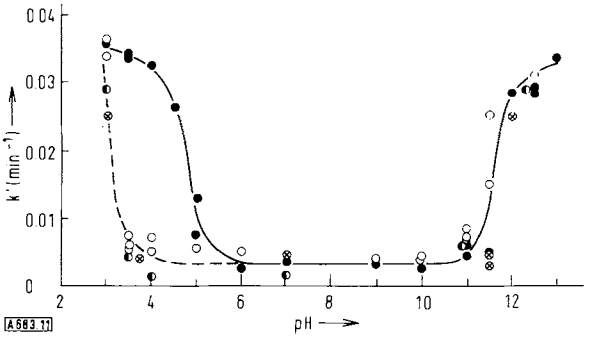


Fig. 11. Denaturation of DNA under the influence of the pH value (●) of the solution and stabilizing effect of LiCl (⊗), NaCl (○), and KCl (◐). The peroxidase activity (k') after addition of Cu^{2+} and H_2O_2 was used as a measure of denaturation, the measurements being carried out as for Figure 10. The diagram shows the k' values found from peroxidase activity curves at pH = 8.5 (cf. Fig. 10).

If the denaturation [73] is carried out in 0.05 M LiCl, NaCl, or KCl solution, the activity varies in approximately the same manner above pH $\approx$ 6. At lower pH values, however, the salts have a protective action; the increase in activity begins at a pH value about 1.5 units lower (cf. Fig. 11). The protective action of $MgCl_2$ is even more pronounced: the action of 5×10^{-4} M $MgCl_2$ is roughly equivalent to that of the monovalent salts in 0.05 M solution. This greater stabilizing action of Mg^{2+} has also been observed by *Barber* [76]. It is probably due to the greater complexing tendency of Mg^{2+} toward phosphate groups [35].

The relation between peroxidase activity and complex structure was also studied in the Cu^{2+} complex of adenosine 5′-diphosphate, in which the adenine ring is involved in the complex formation [61], and the Cu^{2+} complex of adenosine 5′-monophosphate [33], in which Cu^{2+}-adenine ring interaction (formation of a macrochelate) is also probable [33, 69, 77]. Proteins such as γ-globulin also suffer peroxidase degradation in the presence of Cu^{2+} and H_2O_2 [78]. The Cu^{2+} [54] and Ni^{2+} [79] complexes of the cyclic decapeptide polymycin B and the Ni^{2+} complexes of the linear octapeptide Val^5-angiotensin-II-Asp^1-β-amide [80] and of the tetracosapeptide β^{1-24}-corticotropin [81] are degraded similarly by H_2O_2. *Radhakrishnan* and *Meister* [82] and *Macholàn* [83] were able to show that α-amino acids in 2 *N* NaOH are primarily oxidized to keto acids by H_2O_2 in the presence of Cu^{2+}.

[73] *H. Erlenmeyer, R. Griesser, B. Prijs,* and *H. Sigel,* Biochim. biophysica Acta *157,* 637 (1968).

[74] Comparison of Figures 9 and 10 shows that more dilute DNA solutions are more susceptible to denaturation than more concentrated solutions.

[75] *V. Grechko, R. N. Maslova, L. Shkarenkova,* and *Ya. M. Varshavsky,* Abh. dtsch. Akad. Wiss. Berlin, Kl. Med. *1964,* 295.

[76] *R. Barber,* Biochim. biophysica Acta *134,* 207 (1967).

[77] *H. Sigel,* Experientia *22,* 497 (1966).

[78] *R. A. Phelps, K. E. Neet, L. T. Lynn,* and *F. W. Putnam,* J. biol. Chemistry *236,* 96 (1961).

[79] *H. Ch. Curtius, P. Anders, R. Zell, H. Sigel,* and *H. Erlenmeyer,* Helv. chim. Acta *49,* 2256 (1966).

[80] *H. Ch. Curtius, P. Anders, H. Erlenmeyer,* and *H. Sigel,* Helv. chim. Acta *51,* 896 (1968).

[81] *H. Erlenmeyer* and *H. Sigel,* unpublished.

[82] *A. N. Radhakrishnan* and *A. Meister,* J. biol. Chemistry *226,* 559 (1957).

[83] *L. Macholán,* Naturwissenschaften *46,* 357 (1959).

5. Kinetics and Mechanism of Catalase and Peroxidase Reactions

Since the direct decomposition of H_2O_2 requires an activation energy of at least 48 kcal/mole [9], thermal decomposition under conditions such that aqueous solutions can exist proceeds only catalytically. As was mentioned earlier, in the homogeneous phase catalytically active substances are mainly ions and complexes of the transition metals [9]. The relation between structure and catalytic activity has been shown for the particular case of the Cu^{2+} complexes: it was found that the complexed Cu^{2+} must have free coordination sites available to enable it to form the ternary Cu^{2+}-peroxo ligand complexes required for the catalysis. However, this gives little information about the course of the reaction.

Glasner [84] and *Erdey* and *Inczédy* [85] studied the catalysis of the decomposition of H_2O_2 by the Cu^{2+} citrate system in the alkaline range. They found that the complex [citrate-Cu−OH]$^{3-}$ acts as the catalyst, and the decomposition rate is proportional to the photometrically measured concentration of the Cu^{2+}-peroxide complex and to $[H_2O_2]^{0.5}$ [85,86]. In the oxidation of pyrocatechol in the presence of Cu^{2+} and H_2O_2, the rate depends on the concentrations of H_2O_2, pyrocatechol, and Cu^{2+} [18]. According to the kinetic studies, the oxidizing agent in this system is probably the species $[CuOOH]^+$ (cf. also [87]).

Further information was provided by the kinetic studies described below. No buffers were added in these investigations (cf. [25]), since as weak acids or bases, these would have led to complex formation with Cu^{2+}, and would thus have complicated the system.

The decrease in the H_2O_2 concentration with time was measured [25]. The slope of the tangent to this curve for time $t = 0$ gives the initial rate $v_0 = -d[H_2O_2]/dt$ of the reaction. The logarithm of v_0 was then plotted against the logarithm of the varied concentration [X]. The points obtained in this way lay on straight lines, the slopes of which gave the relation between the rate of the catalysis and the concentration of X (cf. *e.g.* [88]).

5.1. The Cu^{2+}-Ethylenediamine-H_2O_2 System

Kinetic studies at an ionic strength of $I = 0.05$ ($NaClO_4$) and $T = 22$ °C in the pH range ≈ 6–8 showed [28] that the initial rate v_0 of disappearance of H_2O_2 is proportional to $1/[H^+]$, $[H_2O_2]$, and $[Cu^{2+}\text{-en}]^2$, the catalytic activity reaching a maximum at a ratio $[Cu^{2+}]_{total}/[en]_{total} = 1{:}1.5$ (en = ethylenediamine). These results can be summarized in eq. (6), and can be interpreted by the reactions given in equations (7a) to (7d) if it is assumed that $[Cu_2en_3]^{4+}$ and $[Cu_2en_3OOH]^{3+}$ are present only in very low concentrations [28].

$$v_0 = -\frac{d[H_2O_2]}{dt} = k \cdot \frac{[\text{Cu-en}]^2 \cdot [H_2O_2]}{[H^+]} \cdot f([en]_{total}) \quad (6)$$

$$H_2O_2 \overset{K_1}{\rightleftharpoons} HOO^- + H^+ \quad (7a)$$

$$2\,[\text{Cu-en}]^{2+} + en \overset{K_2}{\rightleftharpoons} [Cu_2en_3]^{4+} \quad (7b)$$

$$[Cu_2en_3]^{4+} + HOO^- \overset{K_3}{\rightleftharpoons} [Cu_2en_3OOH]^{3+} \quad (7c)$$

$$[Cu_2en_3OOH]^{3+} \xrightarrow{k_1} \text{intermediate products} \xrightarrow[\text{(fast)}]{+\,H_2O_2} 2\,[\text{Cu-en}]^{2+} + en + O_2 + OH^- + H_2O \quad (7d)$$

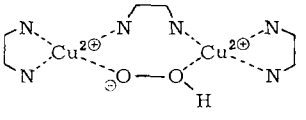
Eq. (8) can be deduced from eq. (7) as a special case of eq. (6).

$$v_0 = -\frac{d[H_2O_2]}{dt} = k_1 \cdot [Cu_2en_3OOH] = k_1 \cdot K_1 \cdot K_2 \cdot K_3 \cdot \frac{[\text{Cu-en}]^2 \cdot [H_2O_2]}{[H^+]} \cdot [en] \quad (8)$$

The maximum catalytic activity at $[Cu^{2+}]_{total}$: $[en]_{total} = 1{:}1.5$ is reflected in eq. (7b) and (9), since

$$[Cu_2en_3]^{4+} + en \rightleftharpoons 2\,[\text{Cu-en}_2]^{2+} \quad (9)$$

the maximum formation of the postulated intermediate $[Cu_2en_3]^{4+}$ (or $[Cu_2en_3OOH]^{3+}$) is to be expected at this ratio. A binuclear structure such as *(8)* can therefore be assigned to the active complex [89]. (The



(8)

secondary reactions of the species $[Cu_2en_3OOH]^{3+}$ were discussed in [28]). Prolonged action of H_2O_2 (> 20 min) on the Cu^{2+}-en system leads to oxidation products, such as glycine, that can be detected by thin layer chromatography [28].

5.2. The Cu^{2+}-Diethylenetriamine-H_2O_2 System

Experiments [28] with the Cu^{2+} complex of the tridentate diethylenetriamine (= dien) as the catalyst (cf. Section 2.1) for the decomposition of H_2O_2 in the pH range $\approx$ 7.5 to 9.5 showed that the reaction probably proceeds differently in this case. The kinetic results are summarized in eq. (10).

$$v_0 = -d[H_2O_2]/dt = k \cdot [\text{Cu-dien}]\,[H_2O_2]/\sqrt{[H^+]} \quad (10)$$

Thin layer chromatographic investigation at pH $\approx$ 9.2 showed at least four reaction products, including iminodiacetic acid, after a reaction time of only 1 to 5 minutes. This makes the interpretation difficult.

[84] *A. Glasner*, J. chem. Soc. (London) *1951*, 904.

[85] *L. Erdey* and *I. Inczédy*, Acta chim. Acad. Sci. hung. *17*, 93 (1958).

[86] Cf. [3], p. 2392.

[87] *S. Fallab*, Zeitschr. naturwiss. med. Grundlagenforsch. *1*, 333, 358 (1963).

[88] *A. A. Forst* and *R. G. Pearson*: Kinetics and Mechanism. J. Wiley, New York 1953.

[89] A similar structure is proposed by *M. T. Beck* for the binuclear species $[Fe_2(EDTA)O_2]$: Rec. chem. Progr. (1) *27*, 37, 53 (1966); cf. also *M. T. Beck*, *S. Görög*, and *Z. Kiss*, Acta chim. Acad. Sci. hung. *42*, 321 (1964).

5.3. The Cu^{2+}-2,2'-Bipyridyl-H_2O_2 System

Kinetic studies[90a] with the 1:1 complex of Cu^{2+} and 2,2'-bipyridyl (Bipy) showed that at pH ≈ 5.5 to 7.5 (natural ionic strength; T = 25 °C) the initial rate v_0 of decomposition of H_2O_2 is proportional to $1/[H^+]$, $[H_2O_2]^2$ (cf. Fig. 12), and $[Cu^{2+}\text{-Bipy}]$; v_0 decreases

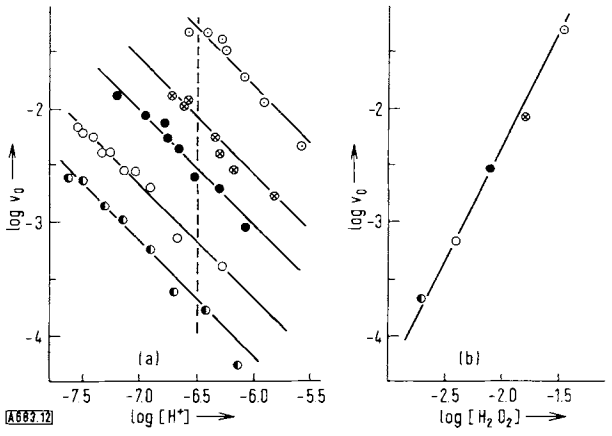


Fig. 12. (a) Catalase activity of the Cu^{2+}-2,2'-bipyridyl system ($[Cu^{2+}]$ = [Bipy] = 4 × 10^{-4} M) at various initial H_2O_2 concentrations (○ 3.2 × 10^{-2} M; ⊗ 1.6 × 10^{-2} M; ● 8 × 10^{-3} M; ○ 4 × 10^{-3} M; ◐ 2 × 10^{-3} M) as a function of the pH value, determined as the initial rate v_0 (mole l^{-1} min^{-1}) of the decomposition of H_2O_2 ($v_0 \sim [H^+]^{-1}$). (b) Evaluation of the results of (12a) at pH = 6.5 ($v_0 \sim [H_2O_2]^2$).

with increasing [Bipy] at constant $[Cu^{2+}]$. The investigations led to the kinetic equation (11) which can be explained by equations (12a) to (12d) if it is assumed

$$v_0 = -\frac{d[H_2O_2]}{dt} = k \cdot \frac{[\text{Cu-Bipy}]\,[H_2O_2]^2}{[H^+]} \qquad (11)$$

$$H_2O_2 \overset{K_1}{\rightleftharpoons} HOO^- + H^+ \qquad (12a)$$

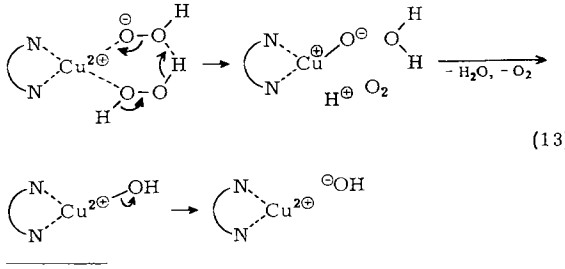
$$[Cu(Bipy)]^{2+} + HOO^- \overset{K_2}{\rightleftharpoons} [Cu(Bipy)(OOH)]^+ \qquad (12b)$$

$$[Cu(Bipy)(OOH)]^+ + H_2O_2 \overset{K_3}{\rightleftharpoons} [Cu(Bipy)(OOH)(H_2O_2)]^+ \qquad (12c)$$

$$[Cu(Bipy)(OOH)(H_2O_2)]^+ \xrightarrow{k_1} [Cu(Bipy)]^{2+} + O_2 + H_2O + OH^- \qquad (12d)$$

that $[Cu(Bipy)(OOH)]^+$ and $[Cu(Bipy)(OOH)(H_2O_2)]^+$ are present only in very low concentrations. Eq. (11) can in turn be deduced from the proposed reaction course, k being replaced by $k_1 \cdot K_1 \cdot K_2 \cdot K_3$.

The active complex and its secondary reactions can be formulated *e.g.* as in eq. (13) (cf. also [91]).



(13)

[90] a) *H. Sigel, C. Flierl*, and *R. Griesser*, J. Amer. chem. Soc. *91*, (1969) in press; b) *H. Erlenmeyer, C. Flierl*, and *H. Sigel*, J. Amer. chem. Soc. *91*, (1969), in press; c) *H. Erlenmeyer, C. Flierl*, and *H. Sigel*, Chimia *22*, 433 (1968).

[91] *L. Erdey* and *I. Inczédy*, Acta chim. Acad. Sci. hung. *7*, 93 (1955).

5.4. The Cu^{2+}-2,2'-Bipyridyl-H_2O_2-H_2N–NH_2 System

In the metal ion-catalyzed peroxidase reaction (14) of hydrazine[92] the initial rate v_0 of disappearance of

$$H_2N\text{–}NH_2 + 2\,H_2O_2 \rightarrow N_2 + 4\,H_2O \qquad (14)$$

H_2O_2[90b] in the presence of Cu^{2+}-Bipy (pH range ≈ 5–6.5; natural ionic strength; T = 25 °C) is found to be given by

$$v_0 = -\frac{d[H_2O_2]}{dt} = k \cdot \frac{[\text{Cu-Bipy}]\,[H_2O_2]\,[H_2N\text{–}NH_3^+]}{[H^+]} \qquad (15)$$

Since $H_2N\text{–}NH_2$ is protonated in this range (pK_A = 8.1[90c]), the following reaction course can be formulated:

$$H_2N\text{–}NH_3^+ \overset{K_1}{\rightleftharpoons} H_2N\text{–}NH_2 + H^+ \qquad (16a)$$

$$[Cu(Bipy)]^{2+} + H_2N\text{–}NH_2 \overset{K_2}{\rightleftharpoons} [Cu(Bipy)(H_2N\text{–}NH_2)]^{2+} \qquad (16b)$$

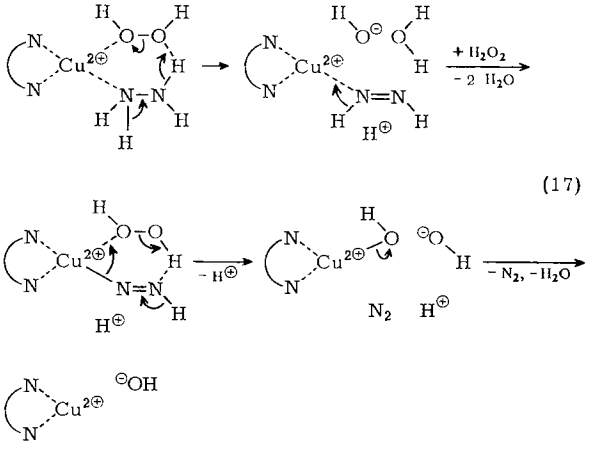
$$[Cu(Bipy)(H_2N\text{–}NH_2)]^{2+} + H_2O_2 \overset{K_3}{\rightleftharpoons} [Cu(Bipy)(H_2N\text{–}NH_2)(H_2O_2)]^{2+} \qquad (16c)$$

$$[Cu(Bipy)(H_2N\text{–}NH_2)(H_2O_2)]^{2+} \xrightarrow{k_1} \text{intermediate products} + \text{products} \qquad (16d)$$

$$\text{intermediate products} + H_2O_2 + (\text{products}) \rightarrow [Cu(Bipy)]^{2+} + N_2 + 4\,H_2O \qquad (16e)$$

This course agrees with the kinetic findings [$k = k_1 \cdot K_1 \cdot K_2 \cdot K_3$ in (15)], provided that the equilibria (16b) and (16c) are displaced to the left.

The structure of the active complex and the subsequent reaction steps can be formulated by the scheme shown in eq. (17) [cf. also eq. (13)].



(17)

The peroxidase reaction of H_2O_2 with hydroxylamine is also catalyzed by the Cu^{2+}-Bipy (1:1) complex[90b]; the principal product is probably N_2, though N_2O, NO_2^-, and NO_3^- may also be formed[93,94]. The initial rate v_0 of disappearance of H_2O_2 at pH ≈ 4.5–6.0 (natural ionic strength; T = 25 °C) is

[92] *F. A. Cotton* and *G. Wilkinson*: Anorganische Chemie. Verlag Chemie, Weinheim/Bergstr. 1967, p. 313.

[93] Cf. [3], p. 2293; cf. also Gmelins Handbuch der Anorganischen Chemie. System-Nr. 23: "Ammonium", Verlag Chemie, Berlin 1936, p. 572.

[94] *C. P. Lloyd* and *W. F. Pickering*, J. inorg. nuclear Chem. *29*, 1907 (1967); *N. Hlasivcová, J. Novak*, and *J. Zýka*, Collect. czechoslov. chem. Commun. *32*, 4403, 4410 (1967).

proportional to $1/[H^+]$, $[H_2O_2]$, and $[Cu^{2+}\text{-Bipy}]$, but is probably independent of the concentration of NH_2OH (which is, however, consumed during the reaction). The value of v_0 decreases with increasing [Bipy]. The following expression – analogous to (11) and (15) – was found for the initial rate v_0 of disappearance of H_2O_2 in the same reaction between H_2O_2 and NH_2OH using free Cu^{2+} ion as catalyst [90b]:

$$v_0 = -\,d[H_2O_2]/dt = k[Cu^{2+}]\,[H_2O_2]\,[NH_3OH^+]/[H^+].$$

A reaction course as shown in equations (12) and (16) and an active complex as shown in equations (13) and (17) can again be formulated for this system [90a,b].

If the metal ion undergoes a valency change during the catalysis in these reactions, it must be assumed that it occurs between Cu^I and Cu^{II}, and not Cu^{III}, since on the one hand Cu^{II} is reduced to yellow copper(I) oxide by both NH_2NH_2 [95] and NH_2OH [95,96] in alkaline media, and on the other Cu^I can be reoxidized to Cu^{II} by H_2O_2 [97] (cf. also [11]).

6. Conclusion

The systems discussed here give an idea of the variety of reactions that can occur on decomposition of H_2O_2, and the examples in Section 5.3 and 5.4 also clearly show the relation between catalase and peroxidase activities. Similar active complexes, with their secondary reactions [see equations (13) and (17)], can be formulated for the systems mentioned; one of the H_2O_2 molecules can be replaced by an H donor such as H_2N-NH_2 or NH_2OH (cf. [90b]). The Cu^{2+}-2,2′-bipyridyl (1:1) complex can thus catalyze both the catalase (1) and the peroxidase (2) reactions, depending on the reaction conditions. The behavior of this catalyst is thus similar to that found with enzymes (cf. [40,42]).

A similar relation to that demonstrated in this survey between the structures of Cu^{2+} complexes and their catalytic activity is also to be expected for complexes of other metal ions.

It may be assumed that the conditions that must be satisfied by a Cu^{2+} complex if it is to be capable of catalyzing the catalase or peroxidase decomposition of H_2O_2 are also applicable to enzymes containing copper.

I am grateful to Prof. Dr. H. Erlenmeyer for his numerous suggestions. I thank Prof. Dr. S. Fallab, Dr. B. Prijs, and Dr. R. Griesser for their readiness to discuss the problems that arose. Thanks are due to the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung for support of our work.

Received: April 1, 1968 [A 683 IE]
German version: Angew. Chem. *81*, 161 (1969)
Translated by Express Translation Service, London.

[95] *T. R. Bhat, D. Radhamma*, and *J. Shankar*, J. inorg. nuclear Chem. *27*, 2641 (1965).

[96] *J. H. Anderson*, Analyst *91*, 532 (1966); *89*, 357 (1964).

[97] *A. Zuberbühler*, Helv. chim. Acta *50*, 466 (1967).

Electrochromism and Solvatochromism

By W. Liptay[*]

The position and the intensity of electronic bands are influenced by an electric field. Pronounced changes in the position of absorption bands are mainly due to the dipole moment of the molecule in the ground state and the change in the dipole moment during the excitation process, and pronounced changes in intensity are due to the field dependence of the transition moment, which can be described by the transition polarizability. The effect of an external electric field on the optical absorption (electrochromism) of suitable molecules can be used to determine the dipole moment in the ground state, the change in dipole moment during the excitation process, the direction of the transition moment of the electronic band, and certain components of the transition polarizability tensor. These data largely determine the strong solvatochromism (solvent-dependence of the position and intensity of electronic bands), which is observed in particular with molecules having large dipole moments. Smaller contributions to solvatochromism result from dispersion interactions, which predominate in the case of nonpolar molecules. The models developed have been experimentally checked and verified by a combination of electro-optical absorption measurements (influence of an external electric field on absorption) and investigation of the solvent-dependence of the electronic bands.

1. Introduction

The absorption or emission spectrum of a substance in the vapor state can exhibit characteristic differences in the positions and intensities of the bands from the spectrum of the same substance in solution; these differences depend on the solvent [1–5]. This solvent-dependence of electronic bands is known as *solvatochromism*.

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[1] *A. Kundt*, Ann. physic. Chem. *4*, 34 (1878).

The optical properties of molecules can also be influenced by an external electric field; this phenomenon shall be called *electrochromism*. The fundamental cause of strong solvatochromism, such as is observed in polar dye molecules, is the same as that of electrochromism, *i.e.* the changes produced in the electronic bands by an electric field.

2. Electrochromism

Changes in optical absorption due to the action of an *external* electric field are basically attributable to three effects, which will be described in the following paragraphs.

2.1. Orientation Effect

As our example of a solute molecule, let us consider *p*-nitroaniline, which exhibits an intense long-wave absorption band (maximum at 28900 cm^{-1}, extinction coefficient = 13000 $lmole^{-1}\,cm^{-1}$, width at half height $\approx$ 6000 cm^{-1}) in benzene.

The absorption curve can be recorded with natural, unpolarized light or with linearly polarized light. In an ordinary solution the molecules are distributed isotropically, and both methods consequently give the same absorption curve, which can be represented as a plot of the extinction coefficient $\varepsilon^{sol}(\tilde{\nu})$ against the wave number $\tilde{\nu}$. The extinction coefficient is a measure of the intensity of the optical absorption at a given wavelength. The measure of the intensity of an absorption band is the transition moment $\boldsymbol{\mu}_{ga}^{sol}$ of the dissolved molecule, which is related to the molar decadic extinction coefficient ε^{sol} by the *integral absorption*:

$$\int_{\text{Band } (g\to a)} \frac{\varepsilon^{sol}(\tilde{\nu})}{\tilde{\nu}}\,d\tilde{\nu} = \frac{8\pi^3 N_A}{2303 \times 3hc}\left|\boldsymbol{\mu}_{ga}^{sol}\right|^2 \qquad (1)$$

The integral should be extended over the whole of the absorption band corresponding to the electronic excitation from the ground state g to a definite excited state a. N_A is Avogadro's number, h is Planck's constant, and c is the velocity of light. The transition moment $\boldsymbol{\mu}_{ga}^{sol}$ is a vector, which can also be represented by its absolute value $|\boldsymbol{\mu}_{ga}^{sol}|$ and a unit vector $\boldsymbol{m}$ in the direction of the transition moment.

$$\boldsymbol{\mu}_{ga}^{sol} = \left|\boldsymbol{\mu}_{ga}^{sol}\right| \boldsymbol{m} \qquad (2)$$

For a single molecule or for *an assembly of molecules having a definite orientation*, the extinction coefficient ε_{orient} with light polarized in the direction of the unit vector $\boldsymbol{e}$ is:

$$\varepsilon_{orient} = 3\,\varepsilon^{sol}\left|\boldsymbol{\mu}_{ga}^{sol}\right|^{-2}\left|\tilde{\boldsymbol{\mu}}_{ga}^{sol}\boldsymbol{e}\right|^2 = 3\,\varepsilon^{sol}\,(\tilde{\boldsymbol{m}}\boldsymbol{e})^2 = 3\,\varepsilon^{sol}\cos^2\gamma \qquad (3)$$

$\tilde{\boldsymbol{m}}\boldsymbol{e}$ is the scalar product of the unit vectors $\boldsymbol{m}$ and $\boldsymbol{e}$, and is therefore equal to the cosine of the angle γ between them. For an assembly of molecules having a definite orientation, the extinction coefficient depends on γ as indicated in eq. (3), *i.e.* on the polarization direction of the incident light wave. The direction $\boldsymbol{m}$ of the transition moment of molecules having a known orientation can therefore be determined from the dependence of the extinction coefficient on the polarization direction of the light. Partial orientation of molecules in solution can be achieved by means of an external electric field $\boldsymbol{F}_a$. The direction of the transition moment can be found from the change in optical absorption due to this field.

The total electric dipole moment $\boldsymbol{\mu}_g^F$ of a molecule in the electronic ground state g in the electric field is

$$\boldsymbol{\mu}_g^F = \boldsymbol{\mu}_g + \boldsymbol{\alpha}_g \boldsymbol{F}_e \qquad (4)$$

$\boldsymbol{\mu}_g$ is the permanent dipole moment, $\boldsymbol{\alpha}_g$ is the polarizability tensor, and $\boldsymbol{F}_e$ is the effective field strength at the position of the molecule. According to eq. (4), the dipole moment of a molecule is influenced by an electric field; the quantitative measure of the dependence is the polarizability $\boldsymbol{\alpha}_g$. For molecules having a sufficiently large permanent dipole moment, $|\boldsymbol{\mu}_g| \gg |\boldsymbol{\alpha}_g \boldsymbol{F}_e|$, and the polarizability term in eq. (4) may be disregarded. In this approximation the energy E_g^F of a dissolved molecule in the electronic ground state in the electric field is

$$E_g^F = E_g^{sol} - \tilde{\boldsymbol{\mu}}_g \boldsymbol{F}_e = E_g^{sol} - \mu_g F_e \cos\vartheta \qquad (5)$$

E_g^{sol} is the energy of the dissolved molecule in the ground state with no external field, and ϑ is the angle between the vectors $\boldsymbol{\mu}_g$ and $\boldsymbol{F}_e$. For molecules having a small permanent dipole moment, on the other hand, the term in eq. (4) that contains the polarizability $\boldsymbol{\alpha}_g$ is no longer negligible. Eq. (5) then also contains an additional term that depends on $\boldsymbol{\alpha}_g$. For the sake of simplicity, however, this will not be taken into account here or in the following equations.

According to eq. (5) the energy E_g^F depends on the direction of the dipole moment $\boldsymbol{\mu}_g$ in relation to the field $\boldsymbol{F}_e$. The orientation distribution of the molecules in a homogeneous field, *e.g.* between parallel electrodes, is therefore no longer isotropic. There will be more molecules with their dipole moments parallel to the field direction than with their dipole moments opposing the field direction. The distribution of the molecules over all possible orientations in the equilibrium state can be determined by means of Maxwell-Boltzmann statistics. The extinction coefficient ε_F of the dissolved molecules in the electric field is found from eq. (3) by multiplication by the Boltzmann factor $C \exp(-E_g^F/kT)$ and integration over all orientations.

[2] *S. E. Sheppard*, Rev. mod. Physics *14*, 303 (1942).

[3] *K. Dimroth*, S.-B. Ges. Beförd. ges. Naturwiss. Marburg *76*, No. 3, 3 (1953).

[4] *C. Reichardt*, Angew. Chem. *77*, 30 (1965); Angew. Chem. internat. Edit. *4*, 29 (1965).

[5] *N. Q. Chako*, J. chem. Physics *2*, 644 (1934).

The relative change in the extinction coefficient as a result of the orientation effect in an electric field is found to be

$$\left(\frac{\varepsilon_F - \varepsilon^{sol}}{\varepsilon^{sol}}\right)_{orient} = \frac{1}{30}\left(\frac{F_e}{kT}\right)^2 (3\cos^2\chi - 1)\left[3\left(\tilde{\boldsymbol{m}}\boldsymbol{\mu}_g\right)^2 - \mu_g^2\right] \quad (6)$$

χ is the angle between the direction of the external field $\boldsymbol{F}_a$ and the polarization direction $\boldsymbol{e}$ of the incident light, k is the Boltzmann constant, and T is the absolute temperature. The relative change in the extinction coefficient depends on the square of the field strength, the angle χ, and the angle γ between $\boldsymbol{\mu}_{ga}$ and $\boldsymbol{\mu}_g$, since $\tilde{\boldsymbol{m}}\boldsymbol{\mu}_g = \mu_g \cos\gamma$. For the case in which the transition moment $\boldsymbol{\mu}_{ga}$ of a band is parallel to the dipole moment $\boldsymbol{\mu}_g$ of the molecule, and the polarization direction $\boldsymbol{e}$ of the incident light is chosen parallel to the external field $\boldsymbol{F}_a$, it follows from eq. (6) that

$$\left(\frac{\varepsilon_F - \varepsilon^{sol}}{\varepsilon^{sol}}\right)_{orient} = \frac{4}{30}\left(\frac{\mu_g F_e}{kT}\right)^2 \approx 3 \times 10^{-4}$$

and for the case in which $\boldsymbol{\mu}_{ga}$ is perpendicular to $\boldsymbol{\mu}_g$ and $\boldsymbol{e}$ is again chosen parallel to $\boldsymbol{F}_a$, we obtain

$$\left(\frac{\varepsilon_F - \varepsilon^{sol}}{\varepsilon^{sol}}\right)_{orient} = -\frac{2}{30}\left(\frac{\mu_g F_e}{kT}\right)^2 \approx -1.5 \times 10^{-4}.$$

The extinction coefficient of an absorption band whose transition moment is parallel to the dipole moment increases in an electric field, while that of a band whose transition moment is perpendicular to the dipole moment decreases.

The numerical values given relate to *p*-nitroaniline (μ_g = 6.3 D); the field strength used was $F_a = 10^5$ V/cm, *i.e.* approximately the maximum external field strength that can be achieved in solution, and the temperature was T = 293 °K.

Extinction changes of the order of 10^{-4} due to the orientation effect are thus to be expected in a strong external electric field. To be able to measure the extinction changes with an error of $\approx 1\,\%$, an accuracy of about 10^{-6} is necessary; this can be achieved with a measuring set-up developed by *Labhart* [6, 7]. Measurements on the first intense band of *p*-nitroaniline showed an increase in the extinction coefficient in an electric field, *i.e.* the transition moment is parallel to the dipole moment.

The orientation effect, which leads to dichroism of the absorbing solutions in an electric field, was described by *Werner Kuhn* and his colleagues [8], and was to be used to determine the directions of the transition moments of electronic bands. However, at least two other effects are superimposed on the orientation effect. This hinders the simple determination of the directions of transition moments, but at the same time it allows the determination of additional characteristic molecular data.

2.2. Band Shift Effects

The electronic excitation of a molecule may be associated with a change in the dipole moment $\boldsymbol{\mu}_a - \boldsymbol{\mu}_g$ ($\boldsymbol{\mu}_a$ = dipole moment in the excited electronic state in question). The energy of a molecule in the ground state in an electric field is given by eq. (5). In the excited state,

$$E_a^F = E_a^{sol} - \tilde{\boldsymbol{\mu}}_a \boldsymbol{F}_e = E_a^{sol} - \mu_a F_e \cos\vartheta \quad (7)$$

E_a^{sol} is the energy of the dissolved molecule in the excited state with no external field. In the second part of eq. (7) and in the following equations, it is assumed for simplicity that the dipole moment $\boldsymbol{\mu}_a$ in the excited state is parallel to the dipole moment $\boldsymbol{\mu}_g$ in the ground state; this is in fact so in *p*-nitroaniline and, in general, in molecules having symmetry C_{2v}. For a given transition having the absorption wave number $\tilde{\nu}_a^{sol}$ in solution with no external field ($hc\tilde{\nu}_a^{sol} = E_a^{sol} - E_g^{sol}$), the absorption wave number $\tilde{\nu}_a^F$ in an electric field is given by

$$\tilde{\nu}_a^F = \frac{E_a^F - E_g^F}{hc} = \tilde{\nu}_a^{sol} - \frac{(\mu_a - \mu_g) F_e \cos\vartheta}{hc} \quad (8)$$

The change in the dipole moment ($\mu_a - \mu_g$) thus leads to a field-dependent shift of the band, which also depends on the angle ϑ between the dipole moment and the field direction, as illustrated in the term diagrams of Figure 1.

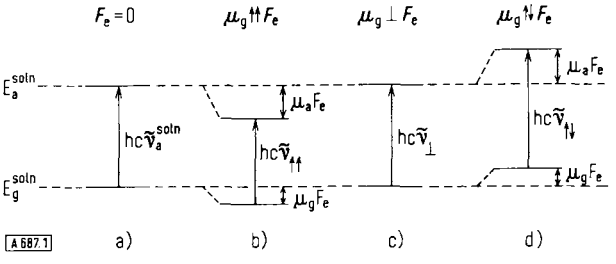


Fig. 1. Dependence of the absorption wave number on the orientation of the dipole moment with respect to the field direction ($\mu_a > \mu_g$).

Figure 1a shows the term diagram of the dissolved molecule with no external field; the difference between the two levels is proportional to $\tilde{\nu}_a^{sol}$. If the dipole moment of the dissolved molecule is oriented parallel to the field (Fig. 1b), $\cos\vartheta = 1$, so that the energy in the ground state is reduced by $\mu_g F_e$ and that in the excited state by $\mu_a F_e$. In the example considered here $\mu_a > \mu_g$; the distance between the levels E_a^F and E_g^F thus decreases, and the absorption wave number $\tilde{\nu}_{\uparrow\uparrow}$ (parallel orientation) $< \tilde{\nu}_a^{sol}$. If the dipole moment is oriented perpendicular to the field (Fig. 1c), $\cos\vartheta = 0$ and the energy levels will be the same as in the absence of an external field; thus $\tilde{\nu}_{\perp}$ (perpendicular orientation) $= \tilde{\nu}_a^{sol}$. Finally, if the dipole moment is oriented antiparallel to the field (Fig. 1d), *i.e.* $\cos\vartheta = -1$, the energy in the ground state will be increased by $\mu_g F_e$ and that in the excited state by $\mu_a F_e$; in this particular case, therefore $\tilde{\nu}_{\uparrow\downarrow}$ (antiparallel orientation) $> \tilde{\nu}_a^{sol}$.

[6] *H. Labhart*, Chimia *15*, 20 (1961).

[7] *W. Liptay, W. Eberlein, H. Weidenberg*, and *O. Elflein*, Ber. Bunsenges. physik. Chem. *71*, 548 (1967).

[8] *W. Kuhn, H. Dührkop*, and *H. Martin*, Z. physik. Chem., Abt. B *45*, 121 (1940).

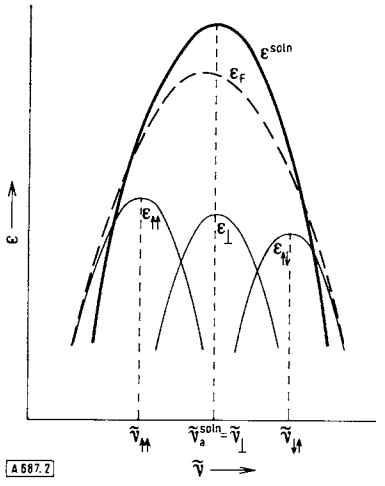


Fig. 2. Unsymmetrical broadening of an absorption band as a result of the band shift.

Figure 2 shows the absorption spectrum $\varepsilon^{sol}(\tilde{\nu})$ for the band in the absence of an external field, with a maximum at $\tilde{\nu}_a^{sol}$. For the molecules with μ_g parallel to F_e, $\tilde{\nu}_{\uparrow\uparrow} < \tilde{\nu}_a^{sol}$, *i.e.* the absorption band $\varepsilon_{\uparrow\uparrow}$ lies at lower wavenumbers. For molecules with μ_g perpendicular to F_e, the absorption band $\varepsilon_\perp$ appears at the same wavenumber as in the absence of an external field. Finally, for molecules with μ_g antiparallel to F_e, the absorption band $\varepsilon_{\uparrow\downarrow}$ is situated at higher wavenumbers than with no external field. The distribution of the molecules over the various orientations is determined by Boltzmann statistics. There are thus always more molecules with μ_g parallel to F_e than with μ_g perpendicular to F_e, and more with μ_g perpendicular to F_e than with μ_g antiparallel to F_e. The absorption component $\varepsilon_{\uparrow\uparrow}$ is therefore greater than the component $\varepsilon_\perp$, and this in turn is greater than $\varepsilon_{\uparrow\downarrow}$.

In this discussion we have picked out three possible orientations. However, the molecules are distributed monotonically over all orientations. The actual course of the absorption curve $\varepsilon_F(\tilde{\nu})$ in an external electric field is approximately as shown by the broken curve.

The band displacement effect leads to broadening of the absorption band in an external electric field. Since this broadening is unsymmetrical, the maximum of the band is also shifted. According to eq. (8) the maximum shift is $\tilde{\nu}_a^{sol} - \tilde{\nu}_{\uparrow\uparrow} = (\mu_a - \mu_g)F_e/hc$. In the example of *p*-nitroaniline $\mu_a - \mu_g \approx 8$ D, and so $\tilde{\nu}_a^{sol} - \tilde{\nu}_{\uparrow\uparrow} \approx 10$ cm^{-1}. The width of the band at half its height, on the other hand, is 6000 cm^{-1}. The shift is therefore greatly exaggerated in Figure 2, since for a 1 cm shift of the band, the width at half height should be 6 m.

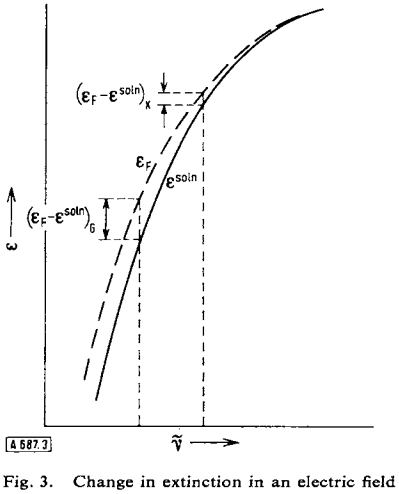


Fig. 3. Change in extinction in an electric field due to the band shift. ——: absorption curve $\varepsilon^{sol}(\tilde{\nu})$ of the dissolved molecule with no external field, - - -: $\varepsilon_F(\tilde{\nu})$ in a field.
$(\varepsilon_F - \varepsilon^{sol})_G$ represents a large change in extinction in the region of a steep rise, and $(\varepsilon_F - \varepsilon^{sol})_K$ is a small change in the region of a gradual rise.

It can be seen that the shift of the maxima of the broad absorption bands of molecules due to an external electric field, unlike the normal Stark effect in sharp spectral lines, cannot be observed directly. In the case of a constant, very small shift, the field-dependent extinction at a given wave number depends on the slope of the band, and increases with increasing steepness of the band (Fig. 3). The change in extinction due to the band shift can therefore be satisfactorily measured on steep sides of the absorption band.

To calculate the relative change in the extinction coefficient in the external electric field as a result of the band shift, it is necessary to start with equations (3) and (8), and again to average over all orientations. This gives

$$\left(\frac{\varepsilon_F - E^{sol}}{\varepsilon^{sol}}\right)_{BS} = \left(\frac{d \ln \varepsilon^{sol}/\tilde{\nu}}{d\tilde{\nu}}\right)_{\tilde{\nu}_a} \frac{F_e^2}{15\, hc\, kT} \left\{5\tilde{\mu}_g(\mu_a - \mu_g) + (3\cos^2\chi - 1)\left[3(\tilde{m}\mu_g)\tilde{m}(\mu_a - \mu_g) - \tilde{\mu}_g(\mu_a - \mu_g)\right]\right\} \quad (9)$$

The slope of the band $(d \ln(\varepsilon^{sol}/\tilde{\nu})/d\tilde{\nu})$ must be taken at the absorption wave number $\tilde{\nu}_a$ in question; since the slope is a function of $\tilde{\nu}$, the relative extinction change also depends on the wave number. The relative extinction change also varies with the square of the field strength, the angle χ, the dipole moment in the ground state, the change in the dipole moment, and the direction of the dipole moment with respect to the transition moment. In favorable cases therefore the change in the dipole moment $\mu_a - \mu_g$ and hence the dipole moment μ_a of the molecule in the excited state can be determined from the experimental quantity corresponding to the band shift. In the example of *p*-nitroaniline

$$\left(\frac{\varepsilon_F - \varepsilon^{sol}}{\varepsilon^{sol}}\right)_{BS} \approx \left(\frac{d \ln \varepsilon^{sol}/\tilde{\nu}}{d\tilde{\nu}}\right)_{\tilde{\nu}_a} \times 5$$

For a steep flank of an absorption band, the derivative of $\ln(\varepsilon^{sol}/\tilde{\nu})$ with respect to $\tilde{\nu}$ may be about 10^{-3}, so that $[(\varepsilon_F - \varepsilon^{sol})/\varepsilon^{sol}]_{BS}$ may be about 5×10^{-3}.

In the case of steep bands, the relative change in the extinction coefficient caused by the band shift may be more than ten times as great as that due to the orientation effect.

2.3. Direct Field-Dependence of the Transition Moment

If the wave function of a molecule is known, the dipole moment can be calculated by an integration process; for example the dipole moment μ_g^F of the molecule in the ground state g in an electric field is

$$\mu_g^F = \int \psi_g^{F*} \sum_i e_i r_i \psi_g^F \, d\tau \quad (10)$$

$\boldsymbol{r}_i$ are the coordinates of the positions of the nuclei and electrons of the molecule, their charges being e_i, and ψ_g^F is the wave function in the electric field. The integration must be carried out over the coordinates of all the particles over the entire space.

Similarly, the electric dipole transition moment $\boldsymbol{\mu}_{ga}^F$ for a transition between the ground state g and an excited state a in an electric field is

$$\boldsymbol{\mu}_{ga}^F = \int \psi_g^{F*} \sum_i e_i \boldsymbol{r}_i \psi_a^F \, d\tau \tag{11}$$

Thus

$$\boldsymbol{\mu}_g^F = \boldsymbol{\mu}_{gg}^F \tag{12}$$

To find $\boldsymbol{\mu}_g^F$, it is formally only necessary to replace the index a in eq. (11) by g, *i.e.* to use the wave function ψ_g^F of the ground state instead of the wave function ψ_a^F of the excited electronic state.

The dipole moment $\boldsymbol{\mu}_g^F$ in an electric field can also be expressed with the aid of the polarizability tensor $\boldsymbol{\alpha}_g$ by eq. (4). A completely analogous expression can also be given for the transition moment $\boldsymbol{\mu}_{ga}^F$ in an electric field:

$$\boldsymbol{\mu}_{ga}^F = \boldsymbol{\mu}_{ga} + \boldsymbol{\alpha}_{ga} \boldsymbol{F}_e \tag{13}$$

$\boldsymbol{\mu}_{ga}$ is the transition moment of a molecule in the absence of an external field; it corresponds to the permanent dipole moment, and will therefore be referred to as the permanent transition moment. The tensor $\boldsymbol{\alpha}_{ga}$ is a quantitative measure of the effect of an electric field on the transition moment. Owing to the analogy with polarizability, $\boldsymbol{\alpha}_{ga}$ will be referred to as the *transition polarizability* tensor. According to a quantum-mechanical perturbation calculation, its components $(\alpha_{ga})_{ij}$ are given by the following equation [9]:

$$(\alpha_{ga})_{ij} = \sum_{r \neq g} \frac{(\mu_{ra})_i (\mu_{gr})_j}{E_r - E_g} + \sum_{r \neq a} \frac{(\mu_{gr})_i (\mu_{ra})_j}{E_r - E_a} \tag{14}$$

$(\mu_{rg})_i$ and $(\mu_{ra})_i$ are the i-th components of the permanent transition moments between the states r and g and between r and a; E_g, E_a, and E_r are the energies of the states. The components of the polarizability tensor $\boldsymbol{\alpha}_g$ of a molecule can be expressed by an equation similar to eq. (14), since

$$\boldsymbol{\alpha}_g = \boldsymbol{\alpha}_{gg} \tag{15}$$

i.e. to determine the components $(\alpha_g)_{ij}$ of the polarizability, it is formally necessary only to replace the indices a by g. According to equations (14) and (15) the polarizability tensor is symmetrical: $(\alpha_g)_{ij} = (\alpha_g)_{ji}$. In general, for the transition polarizability tensor, $(\alpha_{ga})_{ij} \neq (\alpha_{ga})_{ji}$, *i.e.* the tensor is not symmetrical [9].

According to eq. (1), the intensity of an absorption band is determined by the transition moment. The transition moment can be influenced by an electric field [eq. (13)], with the result that the intensity of the band also depends on the field. For an electronic excitation with a sufficiently large permanent transition moment $\boldsymbol{\mu}_{ga}$, $|\boldsymbol{\mu}_{ga}| \gg |\boldsymbol{\alpha}_{ga}\boldsymbol{F}_e|$, and the transition polarizability tensor in eq. (13) may be neglected. In excitations of this nature, the intensity of the absorption band is practically unaffected by an electric field, as is frequently found *e.g.* in the case of *p*-nitroaniline. However, there are also electronic excitations for which the permanent transition moment is at least approximately zero, though the excitation is not forbidden by symmetry, *e.g.* in fluorenone [10]. In cases of this type the effect of an electric field on the absorption is easy to determine, even if the tensor components of $\boldsymbol{\alpha}_{ga}$ are very small. Finally, some dyes exhibit electronic excitations for which the tensor components of $\boldsymbol{\alpha}_{ga}$ are so large that the intensity is strongly dependent on the field, despite the high value of the permanent transition moment $\boldsymbol{\mu}_{ga}$ [9, 11].

To calculate the relative change in the extinction coefficient due to the direct field-dependence of the transition moment, it is necessary to start with equations (3) and (13) and average over all orientations; this gives (neglecting any change in dipole moment on excitation):

$$\left(\frac{\varepsilon_F - \varepsilon^{sol}}{\varepsilon^{sol}}\right)_{Ft} = \frac{F_e^2}{3|\mu_{ga}^{sol}|^2} \sum_{i=1}^{3} \sum_{j=1}^{3} \left\{ \left\{ \frac{2}{kT} (\alpha_{ag})_{ji} (\mu_g)_i (\mu_{ga}^{sol})_j + (\alpha_{ga})_{ij} (\alpha_{ag})_{ij} - \frac{(3\cos^2\chi - 1)}{10} \left[\frac{2}{kT} \left\{ 2 (\alpha_{ag})_{ji} (\mu_g)_i (\mu_{ga}^{sol})_j - 3 (\alpha_{ag})_{ij} (\mu_g)_i (\mu_{ga}^{sol})_j - 3 (\alpha_{ag})_{jj} (\mu_{ga}^{sol})_i (\mu_g)_i \right\} + 2 (\alpha_{ga})_{ij} (\alpha_{ag})_{ij} - 3 (\alpha_{ga})_{ii} (\alpha_{ag})_{jj} - 3 (\alpha_{ga})_{ij} (\alpha_{ag})_{ji} \right] \right\} \right\} \tag{16}$$

The relative change in the extinction thus also depends on the square of the field strength, the angle χ, the dipole moment $\boldsymbol{\mu}_g$, and the transition moment $\boldsymbol{\mu}_{ga}^{sol}$ of the dissolved molecule, as well as on the tensor $\boldsymbol{\alpha}_{ga}$ of the transition polarizability. In all the molecules studied so far, the terms of the type $(\alpha_{ga})_{ij}(\alpha_{ag})_{kl}$ are negligible in relation to the other terms.

The relative change in the extinction coefficient due to the field-dependence of the transition moment may be of the same order of magnitude as the changes due to the orientation effect and the band shift.

2.4. Electro-Optical Absorption Measurements

The measurable extinction change in the absorption spectrum of a molecule in an external electric field results from the superposition of three effects, *i.e.* the orientation effect, the band shift, and the direct effect of an electric field on the transition moment. A complete theoretical treatment leads to relations that

[9] *W. Liptay, B. Dumbacher*, and *H. Weisenberger*, Z. Naturforsch. *23a*, 1601 (1968).

[10] *W. Liptay, H. Weisenberger, F. Tiemann, W. Eberlein*, and *G. Konopka*, Z. Naturforsch. *23a*, 377 (1968).

[11] *W. Liptay, H.-J. Schlosser, B. Dumbacher*, and *S. Hünig*, Z. Naturforsch. *23a*, 1613 (1968).

permit the evaluation of experimental data [12–15]. To obtain relations of this type it is necessary to calculate the effective electric field $\boldsymbol{F}_e$ at the position of the dissolved molecule with the aid of the external electric field $\boldsymbol{F}_a$, which can be determined in the case of parallel electrodes from the applied voltage U and the distance d between the electrodes by means of the expression $F_a = U/d$. The effective field $\boldsymbol{F}_e$ in equations (5) and (6) can be expressed as the sum of a cavity field $\boldsymbol{F}_h$ and a reaction field $\boldsymbol{F}_{Rg}$ [16–17]:

$$\boldsymbol{F}_e = \boldsymbol{F}_h + \boldsymbol{F}_{Rg} \tag{17}$$

$\boldsymbol{F}_h$ and $\boldsymbol{F}_{Rg}$ can be represented as functions of $\boldsymbol{F}_a$ by means of approximations. In the approximations used, the solvent is regarded as a homogeneous dielectric continuum with the dissolved molecule situated in a cavity. In the simplest approximation the cavity is regarded as a sphere [14, 15]; however, comparison of the electro-optical absorption measurements with dielectric measurements showed that this approximation is unsatisfactory in the case of molecules whose shapes are very different from spheres, and that it is necessary to use ellipsoid-shaped cavities [9, 10]. In the calculation of the effective field $\boldsymbol{F}_e$ in eq. (7) and in the following equations, it must be borne in mind that a change in the dipole moment on excitation is associated with a change in the reaction field, *i.e.* that the reaction field of a molecule in the electronically excited state may be different from that in the ground state. According to the Franck-Condon principle, electronic excitation leads to a change only in the electronic wave function, whereas the positions of the nuclei in the Franck-Condon excited state are, to a good approximation, the same as in the ground state. To calculate the reaction field, therefore, the polarization of the solvent must be separated into electron displacement polarization and atomic and orientation polarization, only the first of these being different in the Franck-Condon excited state from that in the ground state. Finally, the anisotropic polarizability of the dissolved molecules and its change on excitation can also be taken into account. Detailed calculation shows that the change in the relative extinction coefficient in an external field for an isolated absorption band which is not superimposed by another electronic band can be represented in the following form [10, 14, 15].

$$\frac{\varepsilon_F - \varepsilon^{sol}}{\varepsilon^{sol}} = L'_\chi(\tilde{\nu}_a) F_a^2 \tag{18}$$

The quantity L'_χ, which was given explicitly in earlier publications [10, 14, 15], depends on the absorption wavenumber $\tilde{\nu}_a$, the angle χ between the polarization direction of the light and the external field direction, the dipole moment μ_g and change in dipole moment $\mu_a - \mu_g$, the transition moment μ_{ga}, and the transition polarizability tensor α_{ga}. The polarizability tensor of the dissolved molecule and its change on excitation often play a minor role. For suitable molecules, particularly molecules having (approximately) symmetry C_{2v}, the dependence of $L'\chi(\tilde{\nu}_a)$ on the wave number and on the angle χ allows the evaluation of the results of electro-optical absorption measurements and the determination of the direction of the transition moment, the dipole moments μ_g and μ_a, and certain components of the tensor α_{ga}. The dipole moment in the ground state can naturally also be obtained from dielectric measurements; comparison of the results of the two methods provides a check in particular on the electro-optical absorption measurements and the models on which they are based (cf. Table 1).

So far we have been discussing the effect of an external electric field on the optical absorption. The effect of an external electric field on emission can be treated in a similar manner [27], except that the final lifetime of a molecule in the excited state has also to be taken into account in this case, so that the excited state need not be identical with the equilibrium state.

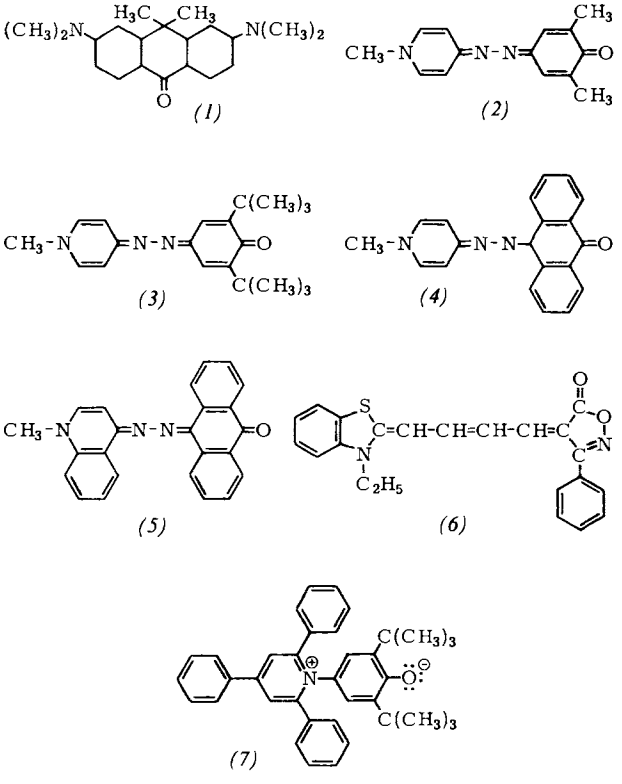


Table 1 gives the dipole moments and the directions of the transition moments that have been found so far from electro-optical absorption and emission measurements. The dipole moments μ_g, the changes in dipole moment $\mu_a - \mu_g$ on excitation, and the components $(\alpha_{ga})_{zz}$ or $(\alpha_{ga})_{yz}$ and $(\alpha_{ga})_{zy}$ of the transition polarizability are responsible for the strong solvatochromism of polar molecules (see Section 3). These quantities allow a quantitative treatment of the problem.

[12] *W. Liptay* and *J. Czekalla*, Z. Naturforsch. *15a*, 1072 (1960).

[13] *W. Liptay* and *J. Czekalla*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *65*, 721 (1961).

[14] *W. Liptay*, Z. Naturforsch. *20a*, 272 (1965).

[15] *W. Liptay*: Modern Quantum Chemistry. Academic Press, New York 1965, Vol. 3, p. 45.

[16] *L. Onsager*, J. Amer. chem. Soc. *58*, 1486 (1936).

[17] *C. J. F. Böttcher*: Theory of Electric Polarisation. Elsevier, Amsterdam 1952.

Table 1. Dipole moments and transition moment directions from electro-optical absorption and fluorescence measurements.

Compound	Solvent [a]	$\tilde{\nu}_a \cdot 10^{-3}$ (cm^{-1}) [b]	γ (°) [c]	μ_g (D) [d]	[e]	μ_a (D) [f]	[g]	$(\alpha_{ga})_{zz}$ resp. $(\alpha_{ga})_{yz}$; $(\alpha_{ga})_{zy}$ $\times 10^{24}$	Ref.
$C_6H_5-NO_2$	C	26	0	3.6	3.5	3.5		≈0	[19]
	H	36	≈90	4.2		9			[18]
C_6H_5-NO	H	31	≈60–90	3.1		12.2			[18]
C_6H_5-CHO	H	35	≈90	2.8		7.1			[18]
	H	42	≈40	2.8		6.3			[18]
p-$(CH_3)_2N-C_6H_4CN$	D	23	≈0	6.6			13		[20]
p-$H_2N-C_6H_4-NO_2$	B	29	≈0	6.3		14			[21]
	B	29	0	5.8	5.0	14		≈0	[22]
	D	28	0	6.2	6.1	15		≈0	[7]
	DME	27	0		5.7	12		≈0	[22]
p-$(CH_3)_2N-C_6H_4-NO_2$	B	26	≈0	6.9		15			[18, 21, 23]
	H	44	≈90	6.9		12			[18, 23]
	B	26	0		5.1	13		≈0	[22]
	DME	26	0		5.0	12		≈0	[22]
p-$(CH_3)_2N-C_6H_4-NO$	B	25	≈0	6.9		13			[18, 21, 23]
	H	36	≈90	6.5		13			[18, 23]
p-$(CH_3)_2N-C_6H_4-CHO$	H	36	≈0	5.6		13			[18]
1,3-$(NH_2)_2$-5-$NO_2-C_6H_3$	D	25	90	5.8	5.0	12		≈0	[7]
	D	30	0	5.8	5.2	16		≈0	[7]
1,3-$(NO_2)_2$-5-$NH_2-C_6H_3$	D	25	90	6.1	5.8	12		≈0	[7]
p-$(CH_3)_2N-C_6H_4-CH=CH-CN$	H	28	≈0	6.9		14			[21]
p-$(CH_3)_2N-C_6H_4-CH=CH-NO_2$	B	24	≈0	7.7		18			[21]
	B	19	≈0	7.7			18		[20]
4-Amino-4′-cyanobiphenyl	B	31	≈0	6.0		16			[24]
	B	25	≈0	6.0			14		[20]
4-Amino-4′-nitrobiphenyl	B	25	≈0	6.0		23			[21]
	B	18	≈0	6.0			22		[20]
4-Dimethylamino-4′-nitrobiphenyl	B	24	≈0	6.6		24			[21]
	B	19	≈0	6.6			22		[20]
4-Dimethylamino-4′-cyanostilbene	D	25	≈0	7.1		20			[21]
	D	21	≈0	7.1			21		[20]
4-Amino-4′-nitrostilbene	B	24	≈0	6.5		22			[21]
	B	18	≈0	6.5			23		[20]
4-Dimethylamino-4′-nitrostilbene	B	23	≈0	7.1		26			[21]
	B	18	≈0	7.1			25		[20]
4-Dimethylamino-4′-nitroazobenzene	B	28	≈0	8.0		25			[24]
N-(4-Dimethylaminobenzylidene)-4-nitroaniline	B	24	≈0	8.2		23			[24]
N-(4-Nitrobenzylidene)-4-dimethylaminoaniline	B	22	≈0	6.6		23			[24]
2-Amino-7-nitrofluorene	B	25	small	5.8		23			[21]
	B	20	small				19		[20]
9*H*-Carbazole	D	29	0	1.7	1.9	3.1		≈0	[7]
	D	34	90	1.7	1.6	3.1		≈0	[7]
3,6-Dinitro-9*H*-carbazole	D	28	90		6.6	14		≈0	[7]
9-Fluorenone	D	23	90	3.3		5.5		≈0	[10]
	D	31	90	3.3		4.5		3.0; 6.6	[10, 11]
	Hp	31	90	3.1		4.4		3.7; 6.2	[10, 11]
	C	31	90	3.1		4.5		3.5; 7.2	[10, 11]
	C	39	90	3.1		3.7		≈0	[10]
1-Indanone	D	34	≈10	3.6		4.4		≈0	[25]
Xanthone	D	29	0	3.8	3.0	5		≈0	[26]
(1)	D	27	90	7.3		8		≈0	[26]
	D	28	90	7.3		6		≈0	[26]
	D	31	0	7.3		9		≈0	[26]
(2)	D	19	0	12.1	11.5	20		41	[9]
(3)	D	19	0	11.5	11.0	20		37	[9]
(4)	D	20	0	11.2	10.7	21		38	[9]
(5)	D	19	≈20	8.9		16		28	[9]
(6)	D	17	0	13.0	12.7	16		120	[9]
	D	18	0	13.0	12.7	17		≈0	[9]
(7)	D	12	≈30	14.8		6		−25	[9]

[a] H = hexane, Hp = heptane, B = benzene, C = cyclohexane, D = 1,4-dioxane, DME = dimethoxyethane. [b] Average value of the wavenumber range evaluated. [c] Angle between the dipole moment in the ground state and the transition moment. [d] Dipole moment in the ground state from dielectric measurements. [e] Dipole moment in the ground state from electro-optical absorption measurements. [f] Dipole moment in the excited state from electro-optical absorption measurements. [g] Dipole moment in the excited state from electro-optical fluorescence measurements.

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3. Solvatochromism

It was shown in Section 2 that the position and intensity of an electronic band can be influenced by an electric field. In any solution, molecules having a permanent dipole moment are located in an electric field, the reaction field of the dissolved molecule, as illustrated in Figure 4. The reaction field acts on the dissolved molecule in the same way as an external electric field, *i.e.* it is capable of causing a band shift and a change in the transition moment, and hence in the intensity of the band.

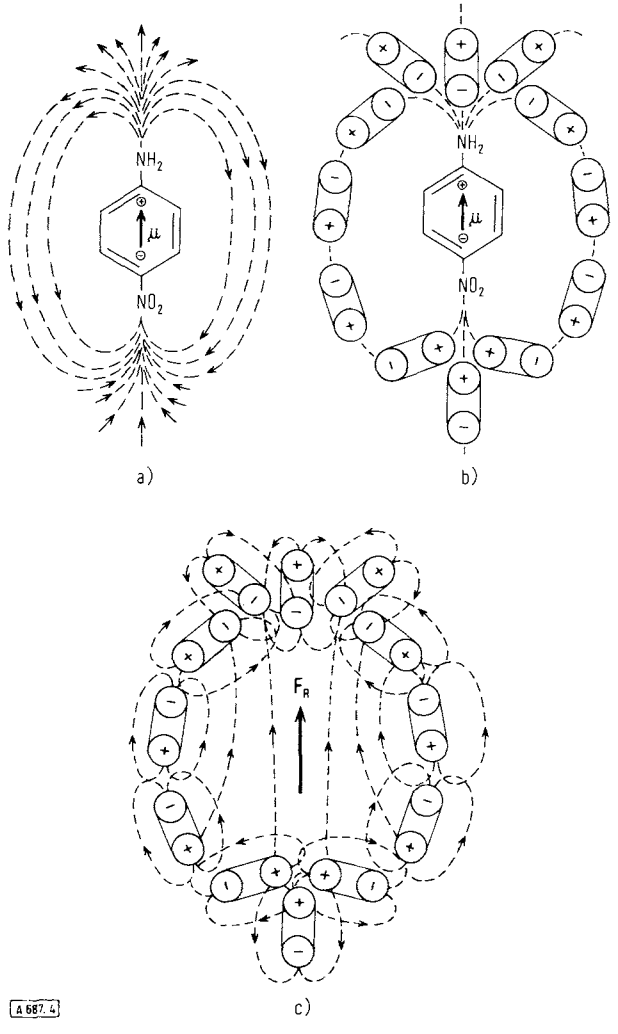


Fig. 4. Reaction field of a dissolved molecule:

(a) A molecule in the gas state with a dipole moment μ, *e.g.* *p*-nitroaniline, causes an electric dipole field in its environment, the field lines of which are shown broken.

(b) In solution, this dipole field acts on the surrounding solvent molecules. If the solvent molecules have a permanent dipole moment, they orient themselves with their dipole moment as nearly as possible parallel to the field lines. The orientation is opposed by thermal motion, so that only some of the solvent molecules are ideally oriented at any time. If the solvent molecules have no permanent dipole moment, a dipole moment is induced in the dipole field of the dissolved molecule. In the case of solvent molecules having a permanent dipole moment, the polarizability effect is superimposed on the orientation effect.

(c) If the electronic and nuclear configurations of all the solvent molecules are imagined to be frozen and the dissolved molecule then removed, a cavity surrounded by solvent molecules remains. Each of these solvent molecules has a dipole moment, which is made up from the permanent and the induced moment. Each of the dipole moments of the solvent molecules produces a dipole field in its environment, the field lines of which are shown broken. In the cavity, at the position of the dissolved molecule, the dipole fields of the solvent molecules superimpose and produce a field having the same direction as the dipole moment of the original dissolved molecule; this field is known as the reaction field $\boldsymbol{F}_R$. If the dissolved molecule is now imagined to be back in the cavity, it is clearly in an electric field.

It can be seen in Figure 4 that the reaction field depends on the nature and arrangement of the surrounding solvent molecules. The accurate determination of the (mean) reaction field, which is possible in principle by averaging methods, presents difficulties that have not yet been overcome. Useful approximations have however been developed. In the simplest approximation the solvent is regarded as a homogeneous isotropic dielectric continuum having a dielectric constant ε_{DC}. The dissolved molecules are assumed to be accommodated in this continuum in spherical cavities having a radius a, or, in a refined version, in ellipsoid-shaped cavities [9]. The dipole moment is represented by a point dipole located in the center of the spherical cavity. In this approximation, the reaction field $\boldsymbol{F}_{Rg}$ of a dissolved molecule in the electronic ground state [16,17] is given by

$$\boldsymbol{F}_{Rg} = \frac{2\,(\varepsilon_{DC}-1)}{a^3\,(2\varepsilon_{DC}+1)}\,\boldsymbol{\mu}_g' \qquad (19)$$

$\boldsymbol{\mu}_g'$ is the total dipole moment (permanent plus induced moment) of the dissolved molecule.

The changes in the position and intensity of an electronic band depend not only on the reaction field in the ground state [eq. (19)], but also on the reaction field in the excited electronic state. When the Franck-Condon principle for optical excitation processes is taken into account, the expressions for the reaction field in the excited state contain not only terms similar to that in eq. (19), but also other similar terms that depend on the refractive index n of the solution. The effect of the field on the position and intensity of electronic bands is therefore determined by the dielectric constant and the refractive index of the solution in this approximation. The effect of the reaction field is the main cause of strong solvatochromism, which is observed in particular with molecules having large dipole moments, and hence strong reaction fields. The effect of the reaction field on the electronic bands is much greater than that of an external field, for two reasons.

The first is the much greater strength of the reaction field. A molecule having an interaction radius $a = 4 \times 10^{-8}$ cm and a dipole moment of only $\mu_g' = 1$ D, in a nonpolar solvent having $\varepsilon_{DC} = 2$, has a reaction field $F_{Rg} \approx 2 \times 10^6$ V/cm; in a polar solvent with $\varepsilon_{DC} = 30$, $F_{Rg} \approx 4.5 \times 10^6$ V/cm. The maximum field strength that can be achieved with an external field, on the other hand, is not much greater than 10^5 V/cm.

Secondly, the reaction field (on average) is always parallel to the dipole moment of the dissolved molecule. In an external field on the other hand, the molecules are distributed over all possible orientations with respect to the field; at the maximum possible field strength the isotropic orientation distribution is only slightly disturbed, *i.e.* there are relatively few

more molecules with their dipole moments parallel to the field than with their dipole moments perpendicular or antiparallel to it. The contributions of the individual molecules to the change in the positions and intensities of the bands due to the external electric field thus largely cancel one another out in the average, so that the observable effects are small.

3.1. Solvent-Dependence of the Position of an Electronic Band

The solvent-dependence of the positions of electronic bands was discussed in detail in an earlier publication [28]. For a molecule having a permanent dipole moment $|\boldsymbol{\mu}_g| = \mu_{gz}$ in the electronic ground state (in the z direction) and a moment $|\boldsymbol{\mu}_a| = \mu_{az}$ parallel to it in the excited state, the solvent-dependence of the wave number $\tilde{\nu}_a^{sol}$ of the absorption maximum is given to a good approximation by the following equation

$$\tilde{\nu}_a^{sol} = \tilde{\nu}_a^{o} - \frac{(\mu_{az}-\mu_{gz})\,(F_{RM})_z}{hc} - \frac{2\,(n^2-1)}{a^3\,(2n^2+1)}\,D \qquad (20)$$

$\tilde{\nu}_a^{o}$ is the wave number of the absorption maximum in the free molecule (gas state). Eq. (20) corresponds to eq. (8), except that it also contains a term that depends on a quantity D. This term describes the solvent-dependence of the position of the absorption band due to the dispersion interactions between the dissolved molecule and the surrounding solvent molecules. For the low electronic excitations $D > 0$, so that the dispersion interactions always cause a red shift with increasing refractive index of the solution. No reliable information is available for higher excitations. The effective electric field $\boldsymbol{F}_{RM}$ in eq. (20) is the mean of the reaction fields of the dissolved molecule in the ground state and in the Franck-Condon excited state [28], *i.e.* the primary state after the excitation process. For the particular case in question the z component of $\boldsymbol{F}_{RM}$ is:

$$(F_{RM})_z = \frac{1}{a^3}\left[\frac{\varepsilon_{DC}-1}{2\,\varepsilon_{DC}+1}\left(1-\frac{2\,\alpha_{gz}(\varepsilon_{DC}-1)}{a^3\,(2\,\varepsilon_{DC}+1)}\right)^{-1} 2\mu_{gz} + \frac{n^2-1}{2\,n^2+1}\left(1-\frac{2\,\alpha_{gz}\,(n^2-1)}{a^3\,(2n^2+1)}\right)^{-1}(\mu_{az}-\mu_{gz})\right] \qquad (21)$$

ε_{DK} is the dielectric constant of the solution and n is its refractive index. α_{gz} is the z component of the polarizability tensor $\boldsymbol{\alpha}_g$ of the molecule in the ground state, transformed to principal axes. Any polarizability change on excitation is disregarded. Relations for cases in which $\boldsymbol{\mu}_g$ is not parallel to $\boldsymbol{\mu}_a$ and in which the polarizability change on excitation is taken into account are given in [28].

The solvent-dependence of the position of an electronic band can, according to eq. (20) with the aid of eq. (21), be represented by a function that depends on the properties of the dissolved molecule (μ_{gz}, μ_{az}, α_{gz}, a, D) and on the dielectric constant and the refractive index of the solvent. Since there is no correlation between the dielectric constant and the refractive index of polar solvents, at least two parameters that depend on the solvent are necessary for the general description of the solvent-dependence of electronic bands. A general description involving only one solvent-dependent parameter such as has repeatedly been sought [4], is fundamentally impossible. In the case of a dissolved nonpolar molecule, however, $\boldsymbol{F}_{RM}$ disappears, leaving only the term containing the refractive index n in eq. (20), so that the solvent-dependence of the wave number can now be described by a single parameter (*e.g.* by n). For molecules having a large dipole moment in the ground state and a large change in moment, the solvent-dependence due to the term in n is small, and the effect of the solvent on the wave number approximately depends only on ε_{DC}.

The dipole moments in the ground and excited states can be determined for suitable molecules from electro-optical absorption and dielectric measurements. The polarizability α_{gz} may be determined independently or estimated, and the quantity D may be estimated [28] or determined by matching of the experimental data. Using an estimated value a and the values ε_{DC} and n, it is then possible to calculate $[a^3(F_{RM})_z(\mu_{az}-\mu_{gz}) + 2\,hcD(n^2-1)/(2\,n^2+1)]$ *via* eq. (21) for various solvents. A plot of $\tilde{\nu}_a^{sol}$ as a function of this expression should give a straight line, from which $\tilde{\nu}_a^{o}$ and a can be obtained. This value a is then used to repeat the evaluation until a used for the calculation of the bracketed expression in eq. (21) agrees, within the limits of accuracy, with the value of a obtained as the result.

Corresponding experimental studies were carried out on *trans*-4-dimethylamino-4′-nitrostilbene [28], fluorenone [10], and some dyes [11]; the results satisfied the linear relation with reasonable accuracy, and so confirmed the above models. The solvent-dependence of the wave number of the absorption maxima of electronic bands can be described, both for an increase and for a decrease in the dipole moment on excitation, by eq. (20) with the aid of eq. (21). The solvent-dependence of the position of an absorption band is determined mainly by the dipole moment of the dissolved molecule in the ground state and the change in the dipole moment on excitation. An increase in the dipole moment on electronic excitation leads to a red shift, and a decrease in the dipole moment to a blue shift of the band with increasing dielectric constant of the solution. This change in position, which depends on the dielectric constant, is superimposed on a shift that depends on the refractive index. The latter shift is due to dispersion interactions and the change in the dipole moment on excitation, and, at least at low electronic excitations, always leads to a red shift with increasing refractive index of the solution. In the case of apolar molecules with $\mu_g = \mu_a = 0$ the reaction field $\boldsymbol{F}_{RM} = 0$ and the second term in eq. (20) disappears. The solvent-dependence is then mainly due to the dispersion interactions. These interactions can cause a strong red shift on transfer of the molecule from the

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gas state into solution, but because of the smaller range of variation of the refractive index of the solvent, only a weak red shift is generally observed with increasing refractive index of the solvent, *e.g.* in the case of aromatic hydrocarbons [28]. For molecules having only a small dipole moment in the ground state and a large change in dipole moment on excitation, the reaction field $\boldsymbol{F}_{RM}$ may be largely determined by the term in eq. (21) that depends on the refractive index. This will also lead to a strong red shift of the absorption band on transfer of the molecule from the gas state into solution, and a weaker red shift with increasing refractive index of the solvent, as is found *e.g.* in the case of electron donor-acceptor complexes.

3.2. Solvent-Dependence of the Intensity of Electronic Bands

In addition to the solvent-dependence of the extinction coefficient, many molecules give a change in the width of the absorption band, with the result that the total intensity varies only slightly with the solvent [29,30]. Electro-optical absorption measurements have sometimes [9,10] shown a considerable field-dependence of the transition moment. Owing to the solvent-dependence of the reaction field, the intensities of the absorption bands were also expected to depend on the solvent in these cases, and this was in fact confirmed experimentally [10,11]. A detailed treatment of the problem [31] showed that the intensity of an optical absorption can be described with the aid of the integral absorption (see eq. (1)); the solvent dependence of the integral absorption is due to the solvent-dependence of the transition moment:

$$\overset{sol}{ga} = \boldsymbol{\mu}_{ga} + \boldsymbol{\alpha}_{ga}\,\boldsymbol{F}_{RM} + \frac{2\,(n^2-1)}{a^3\,(2\,n^2+1)}\,\boldsymbol{W}_{ga} \qquad (22)$$

$\boldsymbol{\mu}_{ga}$ and $\boldsymbol{\mu}_{ga}^{sol}$ are the transition moments in the free molecule (permanent transition moment) and in the dissolved molecule respectively; $\boldsymbol{\alpha}_{ga}$ is the transition polarizability tensor, the components of which are given by eq. (14). Eq. (22) corresponds closely to eq. (13), except that it also contains a vector $\boldsymbol{W}_{ga}$, which may be interpreted as the effect of the dispersion interaction on the transition moment. The effective electric field $\boldsymbol{F}_{RM}$ is again the mean of the reaction fields in the ground state and in the Franck-Condon excited state. For the special case of $\boldsymbol{\mu}_g$ parallel to $\boldsymbol{\mu}_a$ (in the z direction), $|\boldsymbol{F}_{RM}| = (F_{RM})_z$ is represented by eq. (21). The vector $\boldsymbol{W}_{ga}$ should generally be very small, so that for molecules having a large reaction field $\boldsymbol{F}_{RM}$, *i.e.* for molecules having a large dipole moment, the last term in eq. (22) may be ignored; for molecules having no dipole moment or having a small dipole moment, $\boldsymbol{\mu}_a^{sol}$ and hence also the integral absorption should depend only to a small extent on the solvent [29,30]. For molecules having a dipole moment, the integral absorption depends on the reaction field, which can be calculated for various solvents from the data obtained in electro-optical and dielectric measurements (cf. Section 3.1). The theoretical models have been checked and verified experimentally by means of suitable plots [10,11]. It was found that some molecules exhibited an increase and others a decrease in the integral absorption with increasing field strength, and hence with increasing reaction field [11]. The magnitude of the increase or decrease in the integral absorption is determined according to eq. (22) by the transition polarizability tensor $\boldsymbol{\alpha}_{ga}$. The behavior of a given electronic band cannot generally be predicted from other simple molecular quantities. Electronic excitations associated with a very large increase in the dipole moment may be expected to show an increase in the integral absorption, while excitations associated with a very large decrease in the dipole moment may be expected to show a decrease in the integral absorption with increasing field strength. However, this single rule is not generally valid [11].

The possibility of simple observation of the solvent-dependence of the integral absorption of an electronic band depends not only on the transition polarizability $\boldsymbol{\alpha}_{ga}$ (or more precisely the product $\boldsymbol{\alpha}_{ga}\boldsymbol{F}_{RM}$ in eq. (22)) but also on the permanent transition moment $\boldsymbol{\mu}_{ga}$. If $\boldsymbol{\mu}_{ga}$ is large, the solvent-dependence of the integral absorption can be observed only if the components of the tensor $\boldsymbol{\alpha}_{ga}$ are sufficiently large. If on the other hand $\boldsymbol{\mu}_{ga}$ is very small or zero, the solvent-dependence of the intensity of the absorption band is clear even when the components of $\boldsymbol{\alpha}_{ga}$ are small.

Particularly interesting relations are found in fluorenone [10]. The direction of the dipole moment will be referred to as the z axis. Solutions of this molecule give an absorption band at about 31000 cm^{-1} with a transition moment direction in the molecular plane parallel to the y axis. The maximum extinction coefficient ε_{max} and the integral absorption of this band are strongly solvent-dependent [dimethylformamide (ε_{DC} = 36.7): ε_{max} = 1320; ether (ε_{DC} = 4.4): ε_{max} = 685; heptane (ε_{DC} = 1.97): ε_{max} = 410]. The absorption band can no longer be observed in the gas state, and ε_{max} is certainly less than 50. Fluorenone thus has an absorption band whose intensity is almost zero in the free molecule. The intensity recorded in solution is due to the perturbation of the molecule by its reaction field. The permanent transition moment, and hence the integral absorption of the band in the free molecule, is not zero on symmetry grounds, but disappears purely by chance. The appearance of a field-induced absorption band with a transition moment in the y direction as a result of a reaction field in the z direction will be explained in more detail.

In the molecular orbital (MO) scheme the absorption band in question can be interpreted, on the basis of the experimentally observed transition moment directions and SCF–MO approximation calculations, as resulting from the excitation $\varphi_5 \rightarrow \varphi_8$ of an electron from the fifth (filled) π-MO φ_5 into the eighth (empty) π-MO φ_8. φ_5 belongs to the irreducible representation A_2 of the point group C_{2v}, and φ_8 to the representation B_1; the atomic orbital coefficients c_{5p} and c_{8p} of the MOs in the LCAO approximations are illustrated in Figures 5a and 5b. In the simple MO approximation the transition moment in question $\boldsymbol{\mu}_{ga} = e\sqrt{2}\int \varphi_5\varphi_8\,\boldsymbol{r}\,d\tau$. In the LCAO–MO approximation the equation simplifies further, the integral reducing to a sum: $\boldsymbol{\mu}_{ga} = e\sqrt{2}\sum_{p=1}^{14} c_{5p}c_{8p}\boldsymbol{r}_p$,

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where r_p are the position vectors of the atoms p. To obtain the transition moment μ_{ga}, it is necessary to form the products $c_{5p}c_{8p}r_p$ and carry out the summation over all the atoms (p = 1 to 14). Similarly the components of the transition moment $(\mu_{ga})_x$, $(\mu_{ga})_y$, and $(\mu_{ga})_z$ in the directions of the three coordinates are obtained on replacement of the position vectors r_p by their components x_p, y_p, and z_p.

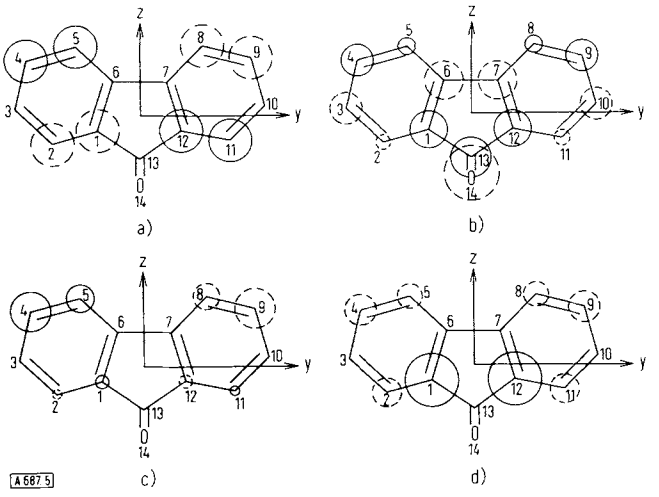


Fig. 5. Representation of the molecular orbitals φ_5 and φ_8 and of the components $(\mu_{ga})_z$ and $(\mu_{ga})_y$ of the transition moment of fluorenone (for practical reasons, the numbering of the skeletal atoms is different from that normally used):

(a) Atomic orbital coefficients c_{5p} of the fifth π-MO φ_5 (representation A_2).

(b) Atomic orbital coefficients c_{8p} of the eighth π-MO φ_8 (representation B_1).

(c) Products $c_{5p}c_{8p}z_p$ (representation B_2).

(d) Products $c_{5p}c_{8p}y_p$ (representation A_1).

The areas of the circles are proportional to the magnitude of the orbital coefficient (c_{5p}, c_{8p}) or of the product ($c_{5p}c_{8p}z_p$, $c_{5p}c_{8p}y_p$) for the atom p in question. Continuous circles denote positive signs, and broken circles negative signs.

The products $c_{5p}c_{8p}z_p$ are shown in Figure 5c. Since the xz plane of the molecule is a plane of symmetry, the magnitudes of the coefficients c_{5p} and c_{8p} on equivalent atoms, *e.g.* on atoms 1 and 12 or 4 and 9, must be the same, and so also must the magnitudes of the products $c_{5p}c_{8p}z_p$. The signs of the product $c_{5p}c_{8p}z_p$ for equivalent atoms are always dissimilar, *i.e.* $c_{54}c_{84}z_4 = -c_{59}c_{89}z_9$. The sum, and hence the z component of the transition moment, must therefore be zero. The z component of the transition $\varphi_5 \rightarrow \varphi_8$ is forbidden in the electric dipole approximation by the symmetry of the molecule and the irreducible representation of the MOs involved. It can similarly be shown that the x component of the permanent transition moment is also zero.

Figure 5d shows the products $c_{5p}c_{8p}y_p$. The y component of the transition moment is proportional to the sum of the areas, and will generally be finite. The optical electronic excitation $\varphi_5 \rightarrow \varphi_8$ is therefore generally allowed with a transition moment direction parallel to the y axis. The y component of the transition moment is zero only when the coefficients c_{5p} and c_{8p} are just such that the sum of the negative terms (sum of the negative areas in Fig. 5d; atoms 2 to 11) is equal to the sum of the positive terms (sum of the positive areas in Fig. 5d; atoms 1 and 12). The optical electronic excitation $\varphi_5 \rightarrow \varphi_8$ is then forbidden, but this is accidental, and is not due to symmetry relations. According to experimental studies, this situation occurs, at least to a good approximation, in the case of the fluorenone absorption in question in the free unperturbed molecule.

The electrons in the molecule are displaced by an external electric field or by the reaction field of the dissolved molecule. On orientation of the molecule with the dipole moment parallel to the electric field, the atomic orbital coefficients of atoms 1, 2, 11, 12, 13, and 14 will increase, while those of atoms 4, 5, 6, 7, 8, and 9 will decrease. The contributions to the integral $(\mu_{ga})_y$, *i.e.* the areas for the corresponding atoms (Fig. 5d), will thus change, the sum of the positive areas increasing and the sum of the negative areas decreasing, so that a finite transition moment in the y direction arises in an electric field in the z direction.

Similar variations of the transition moments and hence of the integral absorptions of electronic bands have also been found for some dye molecules [11].

3.3. A Relation between the Solvent-Dependence of the Position and the Solvent-Dependence of the Integral Absorption of Electronic Bands

A plot of the wave number $\tilde{\nu}_a^{sol}$ of the absorption maximum of an electronic band of a dissolved molecule as a function of $[a^3(F_{RM})_z(\mu_{az} - \mu_{gz}) + 2\,hcD\,(n^2 - 1)/(2\,n^2 + 1)]$ should, according to eq. (20) and eq. (21), be linear. It is in fact found that the experimental points for the various solvents deviate more or less strongly from linearity, and some solvents, such as dioxane and benzene, are quite irregular. The reason for the pronounced scatter is the fact that the reaction field based on the continuum model is only a rough approximation, which fails in particular in the cases of dioxane and benzene [10]. The same deviations are therefore to be expected, and are in fact found experimentally, in suitable plots of the integral absorption as a function of the field F_{RM} in accordance with equations (1), (21), and (22). The relations (20) with (21) and (1) with (21) and (22) can be checked only with the aid of a large number of solvents, so that individual deviations cancel out in the "mean".

According to eq. (20) and equations (1) and (22), both the position of the absorption band and the integral absorption depend on the average value of the reaction field F_{RM}. The reaction field can be eliminated by combination of equations (1), (22), and (20).

In a plot of $\tilde{\nu}_a^{sol}$ against a function of the integral absorption, which is possible in various cases, the deviations due to the poor approximation of the reaction field should be eliminated, as has been confirmed experimentally [10, 11].

The theory of the effect of an external field on electronic bands can be checked and confirmed by comparison of the results of electro-optical absorption measurements, electro-optical fluorescence measurements [16, 20], and dielectric measurements [9, 10]. These methods allow the measurement of the dipole moments of suitable molecules in the ground and excited states and certain components of the transition polarizability tensor. These quantities are responsible for the strong solvatochromism of polar molecules, and allow a quantitative description of the solvent-dependence of both the positions and the intensities of absorption bands. An independent check on the models was provided by various plots of the absorption wave number against functions of the integral absorption. Another possible cause of a strong dependence of the integral absorption on an external field and on the

solvent would be an equilibrium between isomers having sufficiently different dipole moments, *e.g. cis-trans* isomers. In such cases the relative quantities of the isomers could be strongly field-dependent, and hence also solvent-dependent. Since the absorption bands of isomers are usually different, the extinction of the solution would then depend on the field and on the solvent. Investigations on a number of dyes that exhibit an extremely strong solvent-dependence have indicated that this possibility is very unlikely, though it cannot be completely ruled out [11].

We are grateful to the Fonds der Chemischen Industrie, the Deutsche Forschungsgemeinschaft, and the Stiftung Volkswagenwerk for their support of the experimental and theoretical studies.

Received: May 27, 1968 [A 687 IE]
German version: Angew. Chem. *81*, 195 (1969)
Translated by Express Translation Service, London

Steps in Precipitation Reactions

By K. H. Lieser [*]

The combined application of various methods of investigation (e.g. nephelometry, conductivity measurements, electron microscopy, isotope exchange, BET surface area determinations, paper chromatography, coprecipitation) lead to a refined insight into the course of precipitation reactions. The formation of a new solid phase within a solution can, in the case of ionic crystals, be formally described as proceeding via a number of steps – nucleation, growth, ripening, and recrystallization (aging) – which overlap in time. The precipitation of hydroxides is a more complex process since additional chemical reactions (e.g. hydrolysis, condensation reactions) take place within the newly formed solid phase.

1. Introduction

Precipitation is a fundamental chemical operation for the separation and purification of substances. It is well known that precipitations very often give the desired result only if certain well-established procedures are rigidly adhered to, though in many cases the basis of these procedures, which have been evolved empirically, are still far from clear.

The principal process in a precipitation reaction is the formation of a new solid phase from a solution. It is convenient to distinguish the following steps: nucleation, growth, ripening, and recrystallization (aging). However, this well-established distinction is only formal, since the various steps overlap in time.

The following discussion deals mainly with the precipitation of salts (particularly sparingly soluble salts). Precipitation of hydroxides is a more complex process, since chemical reactions (*e.g.* elimination of water, conversion of basic salts into hydroxides) also occur during formation of the solid phase, depending on the pH value and time. Consequently, there are as yet hardly any theoretical schemes for the general treatment of the precipitation of hydroxides; the principal features of this process will be discussed in a separate section.

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2. Steps in a Precipitation Reaction

2.1. Nucleation

The formation of submicroscopic particles (nuclei) of the new phase from a supersaturated solution is particularly interesting, but relatively difficult to observe experimentally. It generally begins only when a certain supersaturation has been reached, and proceeds very rapidly. The questions that arise in connection with the formation of a new phase have already been considered in detail by *Tammann* [1], *Ostwald* [2], and *Volmer* [3]. The kinetics of precipitation reactions have also been described by *Nielsen* [4].

Nucleation can be either homogeneous (spontaneous) or heterogeneous. Homogeneous or spontaneous nucleation occurs without the participation of other substances, by combination of the dissolved ions or molecules to form larger particles. Heterogeneous nucleation begins on small particles of foreign matter (seeds), on which ions or molecules are deposited (*e.g.* by adsorption) until a nucleus has been formed.

[1] *G. Tammann*: Kristallisieren und Schmelzen. J. A. Barth, Leipzig 1903.

[2] *W. Ostwald*: Die wissenschaftlichen Grundlagen der analytischen Chemie. W. Engelmann, Leipzig 1897.

[3] *M. Volmer*: Kinetik der Phasenbildung. Th. Steinkopff, Dresden 1939.

[4] *A. E. Nielsen*: Kinetics of Precipitation. Pergamon Press, Oxford 1964.

The seeds may be present in the solution as impurities, and can be removed by filtration. They are often more numerous in fresh than in aged solutions. Thus freshly prepared and unfiltered solutions generally contain a considerably greater number of seeds, and so give finer precipitates [5,6]. The seeds may also come from the walls of the vessel or from a glass rod [7,8]. Scratching the wall of the container with a glass rod is a well known method of initiating crystallization. Ultrasonic treatment has a similar effect [9].

In spontaneous nucleation, the number of nuclei is very strongly dependent on the concentration of the ions or molecules in the solution. Thus it is well known that finer precipitates are obtained from more concentrated than from dilute solutions.

Relatively high supersaturations are often observed in the absence of seeds. The supersaturation S is defined by

$$S = \frac{c - c_s}{c_s} \tag{1}$$

The ratio $c/c_s = S + 1 = S'$ is known as the supersaturation ratio. c is the actual concentration and c_s is the saturation concentration (solubility). The occurrence of supersaturation can be explained thermodynamically by means of the surface tension. The change in free enthalpy ΔG is given by the difference in the chemical potentials μ of the substance in question per molecule in the dissolved (μ_1) and in the solid (μ_2) state and by the surface tension σ:

$$\Delta G = -n(\mu_1 - \mu_2) + \sigma F \tag{2}$$

n is the number of molecules in a nucleus. If the nuclei are assumed to be spherical, then $F = n^{2/3} \cdot f$ [$f = (3v)^{2/3} \cdot (4\pi)^{1/3}$; v = volume of a molecule] and

$$\Delta G = -n(\mu_1 - \mu_2) + n^{2/3} f \sigma \tag{3}$$

The curve in Figure 1 shows ΔG as a function of the number of molecules in a nucleus. For small values of n, ΔG is always positive, *i.e.* very small nuclei redissolve. A metastable equilibrium exists at the maximum

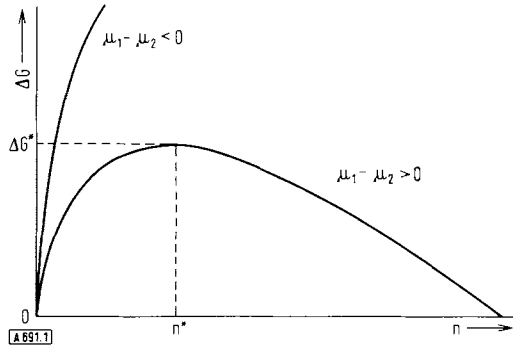


Fig. 1. Free enthalpy ΔG as a function of the number of molecules n in a nucleus (n^* = number of molecules in a critical nucleus).

[5] *E. J. Bogon* and *H. V. Moyer*, Analytic. Chem. *28*, 473 (1956).

[6] *L. Erdey*, *É. Gere*, and *L. Polos*, Acta chim. Acad. Sci. hung. *26*, 43 (1961).

[7] *A. E. Nielsen*, Acta chem. scand. *11*, 1512 (1957).

[8] *M. Kahlweit*, Z. physik. Chem. N.F. *25*, 1 (1960).

[9] *G. Schmid* and *A. Jetter*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *56*, 760 (1952).

of the curve (d $\Delta G/dn = 0$); this corresponds to the critical state for nucleation (denoted hereafter by an asterisk).

A nucleus in which the number of molecules $n = n^*$ is known as a critical nucleus, and particles in which the number of molecules $n < n^*$ are called subnuclei or embryos. Whereas all nuclei having $n < n^*$ redissolve, nuclei with $n > n^*$ grow into crystals. A homogeneously supersaturated solution is therefore thermodynamically in a metastable state, which can persist for a very long time. A precipitate can form only when the energy barrier ΔG^* has been overcome; in homogeneous nucleation, for example, this can occur as a result of random free enthalpy variations in small regions of the solution.

Information about the radius of a critical nucleus and the number of molecules that it contains can be obtained from the following argument. For spherical particles,

$$F = \frac{3V}{r} \tag{4}$$

Since dV/dn = v (volume of one molecule), it follows from eq. (2) that

$$\frac{d\Delta G}{dn} = -(\mu_1 - \mu_2) + \frac{2v\sigma}{r} \tag{5}$$

In the metastable equilibrium, d $\Delta G/dn = 0$, and the radius of the critical nucleus is therefore

$$r^* = \frac{2v\sigma}{\mu_1 - \mu_2} \tag{6}$$

The number of molecules in a critical nucleus is

$$n^* = \frac{V^*}{v} = \frac{2\sigma F^*}{3(\mu_1 - \mu_2)} \tag{7}$$

The free enthalpy of the critical nucleus is

$$\Delta G^* = -n^*(\mu_1 - \mu_2) + \sigma F^*$$
$$\Delta G^* = -\frac{2\sigma F^*}{3} + \sigma F^* = \frac{\sigma F^*}{3} \tag{8}$$

The surface area F^* of the critical nucleus is found with the aid of eq. (7) to be

$$F^* = 3\beta \frac{\sigma^2 v^2}{(\mu_1 - \mu_2)^2} \tag{9}$$

where β is a geometric shape factor:

$$\beta = \frac{4F^3}{27V^2} \tag{10}$$

[β = 16.76 (sphere), 20.22 (icosahedron), 22.20 (dodecahedron), 27.71 (octahedron), 32 (cube), 55.43 (tetrahedron)].

The difference in the chemical potentials is given by the ratio of the activities a in the solution (a_1) and in the solid (a_2):

$$\mu_1 - \mu_2 = kT \ln \frac{a_1}{a_2} \tag{11}$$

If the concentration and saturation concentration are used as approximations for the activities, it follows, with the aid of eq. (1), that

$$\mu_1 - \mu_2 = kT \ln (S + 1) \tag{12}$$

and from equations (7), (9), and (12):

$$n^* = 2\beta \frac{\sigma^3 v^2}{[kT \ln (S^* + 1)]^3} \tag{13}$$

S^* = critical supersaturation

Eq. (13) permits the rough calculation of the number of molecules in a critical nucleus. Measured values for the surface tension σ are available in only a few cases; it is of the order of 100 erg/cm^2. From σ and the critical supersaturation S^*, we obtain n^* values of the order of 100, *i.e.* a critical nucleus consists of about 100 molecules and has a diameter of the order of 100 Å.

The radius of a nucleus in a supersaturated solution is given by the Gibbs-Kelvin equation [10]

$$r = \frac{2v\sigma}{kT \ln (S + 1)} \tag{14}$$

which follows from equations (6) and (12). According to this equation at a certain supersaturation S, only particles of one particular size are present in the solution, this size decreasing with increasing supersaturation (Fig. 2).

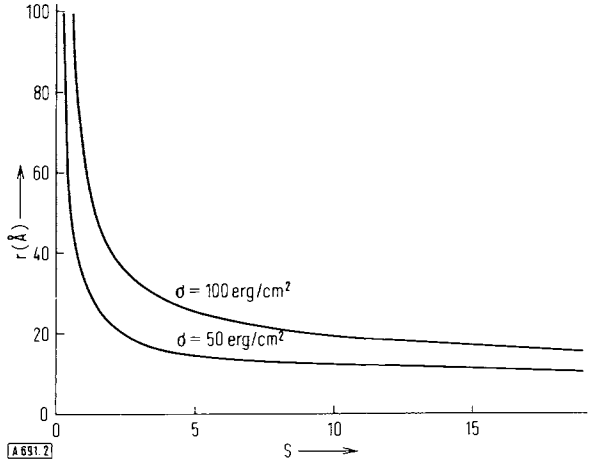


Fig. 2. Radius of the nuclei in a supersaturated solution as a function of the supersaturation S on the basis of the Gibbs-Kelvin equation for various surface tensions.

The calculation provides no details on the concentration of subnuclei in a supersaturated solution, which is very strongly dependent on the supersaturation (cf. Fig. 3). The number of critical nuclei also changes extremely rapidly with the supersaturation, so that S^* can be determined relatively accurately by experiment. Slightly below this critical supersaturation, the number of critical nuclei is still very small (*i.e.* the nucleation rate is very low), whereas only slightly above the critical supersaturation the number of critical nuclei is so large that precipitation begins almost instantaneously.

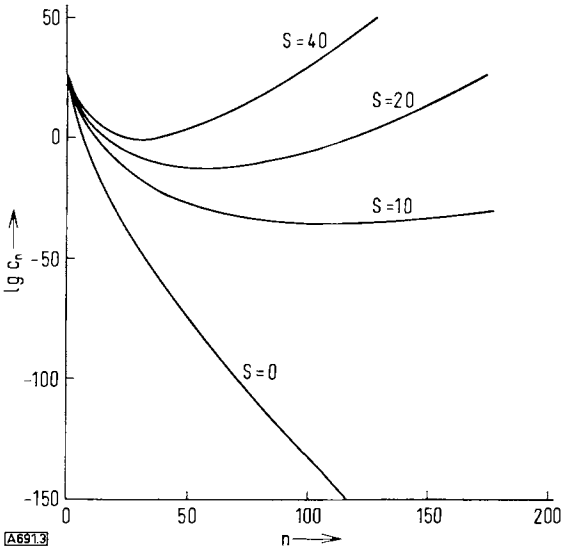


Fig. 3. Concentration of subnuclei in a supersaturated solution on the basis of theoretical considerations (n = number of molecules in a subnucleus, S = supersaturation; calculated for $\beta = 40$, $\sigma = 50$ erg/cm^2, $v = 10^{-22}$ cm^3, $c_s = 2.5 \times 10^{-6}$ mole · l^{-1}) after *Nielsen* [4].

The first equation for the nucleation rate was given by *Volmer* and *Weber* [11], and later by *Becker* and *Döring* [12]; further theoretical treatments were given by *Nielsen* [4], and *Kahlweit* [8]. The nucleation rate J (number of nuclei formed per cm^3 per sec) can be expressed by

$$J = J_0 \exp[-\Delta G^*/kT] \tag{15}$$

It follows with the aid of equations (8), (9) and (12) that

$$\log J = \log J_0 - \frac{A}{[\log (S + 1)]^2} \tag{16}$$

where

$$A = \frac{\beta \sigma^3 v^2}{(kT \ln 10)^3} \tag{17}$$

As an approximation

$$\log J \approx 30 - \frac{A}{[\log (S + 1)]^2} \tag{18}$$

The nucleation rate according to this equation can be found from a diagram (Fig. 4) [4]. For spontaneous (homogeneous) nucleation, the experimental values of J as a function of the supersaturation S lie on a curve having a constant value for A; it is therefore possible to calculate the surface tension σ with the aid of eq. (17).

Figure 4 shows that the nucleation rate for relatively wide ranges can be approximately given by a relation of the form

$$J = k_m c^m \tag{19}$$

[10] *J. W. Gibbs*: Scientific Papers. Yale University Press, New Haven 1957, p. 258; *W. Thomson*, Proc. Roy. Soc. Edinburgh 7, 63 (1870).

[11] *M. Volmer* and *A. Weber*, Z. physik. Chem., Abt. A *119*, 277 (1926).

[12] *R. Becker* and *W. Döring*, Ann. Physik *24*, 719 (1935).

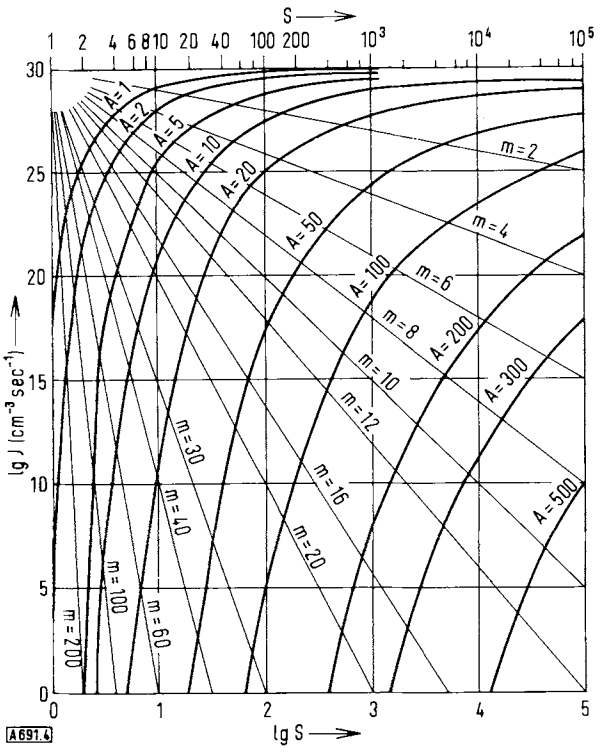


Fig. 4. Nucleation rate (number of nuclei formed per cm^3 sec^{-1}) as a function of the supersaturation for various values of A [cf. eq. (17) and (20)].

The exponent m corresponds to the slope d log J/d log c of the experimental curve, and also provides information about the size of a critical nucleus; it is found from equations (16) and (13) that

$$\frac{\mathrm{d}\log J}{\mathrm{d}\log c} = m = \frac{\mathrm{d}\ln J}{\mathrm{d}\ln (S+1)} = \frac{2\beta\sigma^3 v^2}{[kT]^3[\ln (S+1)]^3} = n^* \quad (20)$$

The surface tension can finally also be determined with the aid of this equation.

2.2. Growth

Once a critical nucleus has been formed, it can grow into a crystal in various ways. Like dissolution, this growth proceeds in small steps, *i.e.* by deposition of single ions or molecules, and not by combination of larger particles.

The first detailed theoretical treatment of crystal growth was due to *Kossel*[13] and *Stranski*[14]; the basic model is shown schematically in Figure 5.

According to this model of stepwise growth, there are non-equivalent sites on the surface of a crystal. A site marked (1) is preferred, while the edges and corners of the crystal are less favorable. The first step in the formation of a new layer has particularly unfavorable energy requirements. The particle (2), which is a surface nucleus, forms a new layer by two-dimensional growth. It is also possible that more than one surface

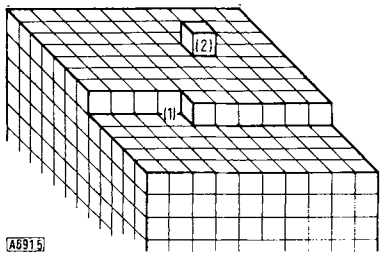


Fig. 5. Model of crystal growth according to *Kossel* [13] and *Stranski* [14].

nucleus is deposited, and in this case the zones formed by the two-dimensional growth of these nuclei overlap. If the formation of surface nuclei is very fast, a new layer is started before the growth of the last layer is complete, *i.e.* the (polynuclear) growth takes place in several layers simultaneously one upon another (cf. Fig. 6). If the formation of surface nuclei is very slow, one layer is generally formed after the last is complete (mononuclear growth); this type of growth is therefore strongly inhibited. At low supersaturations, the deposition of an ion or molecule as a surface nucleus is very unlikely, so that mononuclear growth cannot occur.

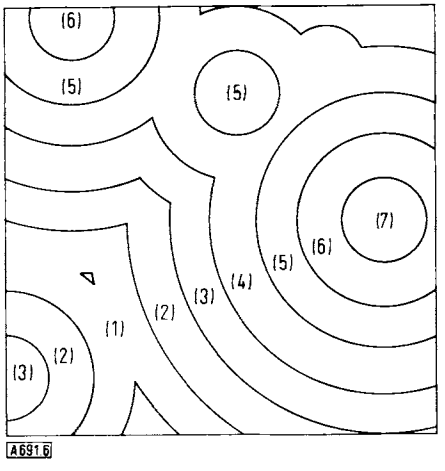


Fig. 6. Polynuclear growth (schematic; the numbers denote superimposed layers).

As an alternative to stepwise growth, *Frank*[15] proposed growth on screw dislocations (Fig. 7), where there are always energetically favorable sites for the deposition of ions or molecules. The screw dislocation is retained as a crystal imperfection, and is continuously propagated in the form of a spiral as growth proceeds.

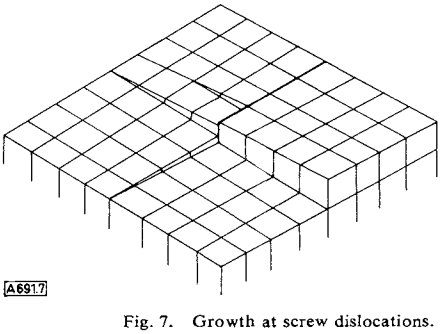


Fig. 7. Growth at screw dislocations.

[13] *W. Kossel*, Nachr. Ges. Wiss. Göttingen, math.-physik. Kl., 135 (1927); Ann. Physik *21*, 455 (1934); *33*, 651 (1938).

[14] *I. N. Stranski*, Z. physik. Chem., Abt. A *136*, 259 (1928).

[15] *F. C. Frank*, Discuss. Faraday Soc. *5*, 48 (1949).

The formation of surface nuclei is no longer necessary, and growth at screw dislocations can therefore occur even at low supersaturations. In agreement with this model, spiral growth at screw dislocations has in fact been observed in many cases.

Various consecutive processes may be important to the crystal growth:

(a) diffusion of the ions or molecules from the solution onto the surface; (b) adsorption of the ions or molecules on the surface; (c) transition on the surface; (d) transport on the surface to a suitable site.

Process (b) is very much faster than the other processes, since it is not inhibited. The processes (c) and (d) are generally indistinguishable, and are therefore known collectively as the surface reaction. The rate-determining step for the growth of the crystals may thus be the diffusion or the surface reaction.

If the diffusion is rate-determining, the growth rate of a crystal is given by

$$\frac{dn}{dt} = 4\pi D(c-c_s)r \qquad (21)$$

This yields the relation given by *Neumann* [16] for the radius of a particle as a function of time:

$$r(t) = \sqrt{2DV(c-c_s)t} \qquad (22)$$

V is the molar volume and D is the diffusion coefficient. Eq. (22) is valid only when $V(c - c_s) \ll 1$.

If on the other hand the surface reaction is rate-determining, it may be assumed that the growth rate of a crystal is proportional to the area and to the concentration difference [8], and one then obtains

$$\frac{dn}{dt} = 4\pi r^2 k(c-c_s) \qquad (23)$$

and

$$r(t) = kV(c-c_s)t \qquad (24)$$

Equations (21) to (24) are applicable provided that the linear growth of a crystal can be followed as a function of time. If growth and ripening overlap, as is usually the case in the precipitation of sparingly soluble ionic crystals, dn/dt and dr/dt may be positive or negative for a given crystal.

In many cases we are interested in the decrease in concentration in the solution as a result of crystal growth, which can be described by a kinetic equation

$$J = -\frac{dn_L}{dt} = k_m c^m \qquad (25)$$

n_L is the number of ions or molecules per cm³ of solution. However, *Marc* [17] showed that the growth rate for readily and moderately soluble substances satisfies the equation

$$J = k_m (c - c_s)^m \qquad (26)$$

[16] *K. Neumann* in [3], p. 209.

[17] *R. Marc*, Z. physik. Chem., Abt. A *61*, 385 (1908).

The exponent m is usually known as the order of the growth reaction. This is correct in the sense used in chemical kinetics for a relation of the form of eq. (25), but not for an emipirical relation of the type of eq. (26).

The progress of crystal growth can also be described by the change in the supersaturation; the characteristic quantity used [4] is

$$\alpha = 1 - \frac{S}{S_0} \qquad (27)$$

S_0 is the supersaturation at time $t = 0$. For spherical particles of (average) radius r and a constant number of particles,

$$r = r_e \alpha^{1/3} \qquad (28)$$

r_e is the (average) radius of the crystals at the end of the experiment. For the case where diffusion is rate-determining, *Nielsen* [4] derived from this relation

$$t = K_D I_D \qquad (29)$$

where

$$K_D = \frac{r_e^2}{3VD(c_0 - c_s)} \qquad (30)$$

and I_D is the "diffusion chronomal"

$$I_D = \int_0^{\alpha} \frac{dx}{x^{1/3}(1-x)} \qquad (31)$$

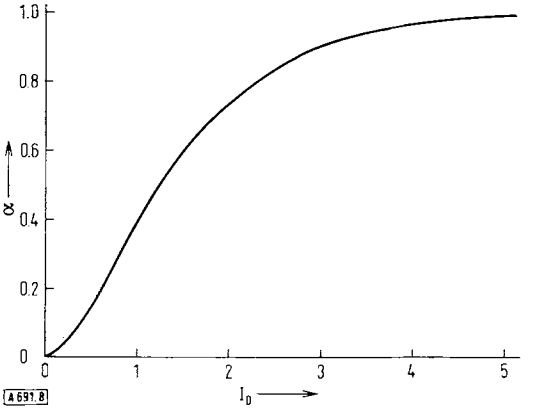


Fig. 8. Diffusion chronomal after *Nielsen* [4] [cf. eq. (27) to (31)].

Figure 8 shows α as a function of I_D. This diagram can be used for the evaluation of measurements, *e.g.* by reading off I_D for the experimental value of α and plotting it as a function of time. If the diffusion is rate-determining, as was assumed in the derivation of eq. (29), this procedure should give a straight line, the slope of which $(1/K_D)$ should according to eq. (30) give reasonable values for the diffusion coefficient D. For aqueous electrolytes, D is of the order of 10^{-5} cm² sec⁻¹ at room temperature.

For the case in which the surface reaction is rate-determining, *Nielsen* [4] uses the quantity

$$\alpha = 1 - \frac{c}{c_0} \qquad (32)$$

and with the aid of eq. (28) he obtains the following relations for mononuclear or polynuclear growth.

$$t = K_m I_m \text{ and } t = K_p I_p \qquad (33)$$

The "chronomals" I_m and I_p are shown in Figures 9 and 10 as functions of α. The indices 1, 2, 3, *etc.* indicate the order of the reaction: *e.g.* I_{p_3} is the "chronomal" for a third order polynuclear reaction. The practical application is similar to that of the "diffusion chronomal" I_D. If the graph of I_m or I_p against time gives a straight line, the "chronomal" used corresponds to the mechanism and the order of the reaction.

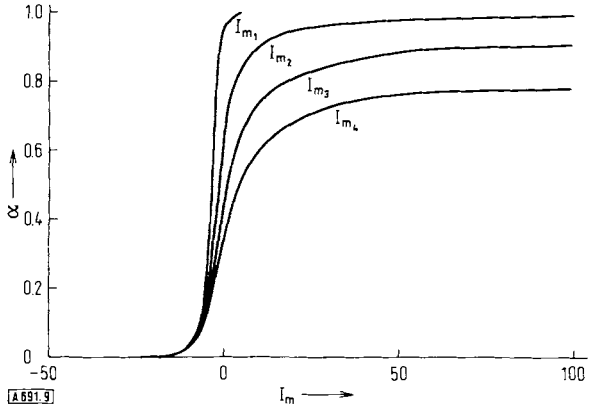


Fig. 9. Chronomals I_m for mononuclear growth after *Nielsen* [47] [cf. eq. (32) and (33)].

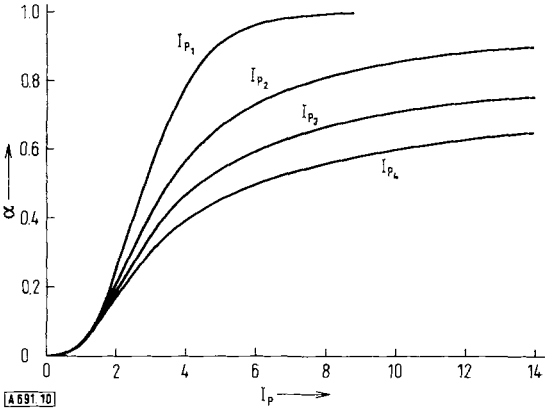


Fig. 10. Chronomals I_p for polynuclear growth after *Nielsen* [4] [cf. eq. (32) and (33)].

In this evaluation of experimental data with the aid of "chronomals", it is again assumed that the number of particles is constant and that the growth can be approximately described on the assumption of spherical particles. These two conditions are frequently not satisfied in practice. The greatest difficulty is the fact that the number of particles and the state of order are continously changing as a result of ripening processes.

2.3. Ripening

The small crystals formed by nucleation and growth in the solution are generally very imperfect; they contain many defects and crystal imperfections, and are not in thermodynamic equilibrium with the solution. The deviation from thermodynamic equilibrium increases with increasing supersaturation of the solution, *i.e.* with increasing rate of formation of the small crystals. The thermodynamically stable final state of a precipitation reaction would be a perfect single crystal, since the free enthalpy, and in particular the surface free enthalpy, is then at a minimum. It is well known that this state is never reached in a precipitation reaction, the product of which is always a large number of crystals of different sizes having greater or smaller numbers of defects and imperfections. In general, the higher the supersaturation, the smaller are the crystals and the greater is the number of imperfections. With decreasing supersaturation, the small, highly imperfect crystals show a steadily growing tendency to redissolve and to form larger, less imperfect crystals. Processes that lead to a thermodynamically more stable state, *i.e.* to larger, less imperfect crystals, are known as ripening. According to *Ostwald* [2], small crystals pass into solution during ripening, while the larger crystals continue to grow (Ostwald ripening). Another theory [18] involves the combination of small particles and growth of the resulting composite particles into larger crystals (cementation).

Information about the size of the crystals that are in equilibrium with the solution at a certain supersaturation is obtainable with the aid of the Gibbs-Kelvin equation (14) (cf. Fig. 2). However, this equation contains only the surface tension and the supersaturation as parameters, and does not include the degree of disorder of the crystal by defects and crystal imperfections. The influence of these quantities cannot be disregarded, but it cannot be accurately determined at present. The ripening leads to a change in the size disorder, and the degree of disturbance decreases, as shown qualitatively in Figures 11 and 12.

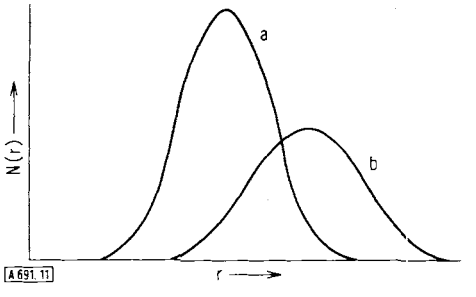


Fig. 11. Change in the crystal size distribution as a result of ripening (schematic) a: Before ripening, b: after ripening.

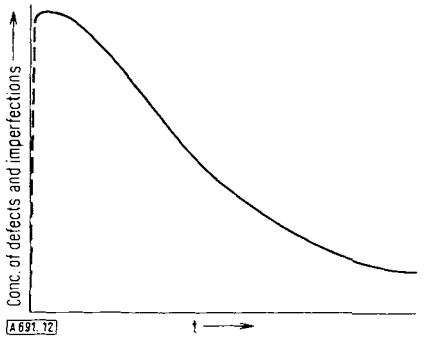


Fig. 12. Change in the concentration of defects and imperfections as a result of ripening (schematic).

[18] *J. Kolthoff*, Chem. Weekbl. *29*, 362 (1931); Proc. Kon. nederl. Akad. Wetensch. Ser. *40*, 82 (1937).

If we consider the Ostwald ripening mechanism, only some of the crystals formed in any stage of a precipitation reaction have a chance to grow further. The remaining crystals redissolve. This is true in particular during the growth stage, since the supersaturation in the solution often changes very markedly in this stage.

The rate of Ostwald ripening is subject to the same considerations as the rate of growth of the crystals. The ripening may be divided into the following processes:

(a) dissolution of ions or molecules from small crystals, (b) diffusion of the dissolved particles from the surfaces of the small crystals into the solution, (c) diffusion of the particles out of the solution onto the surfaces of larger crystals, (d) adsorption of the ions or molecules on the surfaces of the larger crystals, (e) transition to the surface, (f) transport on the surface to a suitable site.

As in the case of growth, the diffusion (b and c) or the surface reaction (a, e, and f) could be the rate-determining step.

2.4. Recrystallization

Recrystallization processes differ from ripening in that they extend over a longer period and become noticeable only after growth. The number of crystals and their size generally show little change. The supersaturation is usually zero or very small. The crystals and the solution are in a dynamic equilibrium, which leads to a continuous exchange of matter. This does not cause any externally recognizable changes, but can be followed radiochemically over a period of many months.

A crystal formed and grown at a high supersaturation usually has many internal defects and disorders. It is therefore relatively far removed from the equilibrium state, even when it is comparatively large. If it remains in contact with the solution for a long time, it has the opportunity to change into a less disturbed crystal by recrystallization. Thus it is well known that in the quantitative separation of substances by precipitation, better results are obtained by allowing the precipitate to stand for some time in contact with the mother liquor.

The experimental observation of recrystallization has not progressed very far, and no theory yielding information about the effects of various parameters (concentration of the ions of the substance itself and of foreign ions, temperature) has not yet been developed.

3. Methods of Investigation

3.1. General

Many methods are available for the investigation of precipitation reactions. In the measurement of the nucleation rate, the number of nuclei is determined as a function of time. The results are unambiguous unless the number of nuclei is simultaneously decreased by ripening. The crystal growth is usually followed by means of the change in the conductivity or concentration of the solution. It is important, for the evaluation of the results, that the number of crystals must remain constant during this process. Otherwise the growth of individual selected crystals must be followed directly, *e.g.* by observation under a microscope or by weighing.

The following methods of investigation may be considered: counting the nuclei or crystals, measurement of the linear growth of the crystals, weighing the crystals, measurement of the decrease in concentration in the solution, nephelometry, conductivity measurement, electron microscopy, isotopic exchange, determination of the surface area by the BET method, paper chromatography, and coprecipitation.

Each of these methods provides part of the picture. For a comprehensive study of a precipitation reaction it is best to use as many different methods as possible and to compare the results critically.

The first four methods listed need no explanation. The application of the others will be illustrated by examples.

3.2. Nephelometry

Figure 13 shows the results for the precipitation of barium sulfate. The nephelometric measurement gives a good picture of the course of precipitation. Nucleation becomes evident only after an induction period of about 4 minutes; the crystal growth then begins, as is shown by a steep increase in turbidity. The turbidity reaches a maximum after about 45 minutes, and then decreases slightly. This decrease is due to ripening, which is superimposed on the crystal growth.

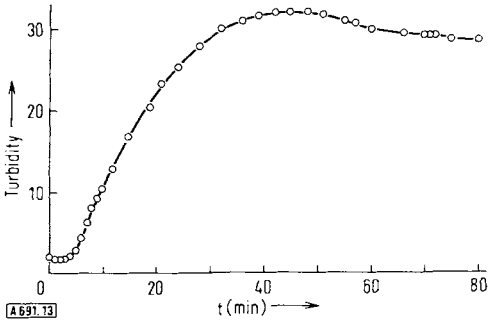


Fig. 13. Relative turbidity on mixing of equal volumes of 4×10^{-4} M solutions of $Ba(NO_3)_2$ and Na_2SO_4 as a function of time.

3.3. Conductivity Measurement

If ions in a solution form complexes or nuclei, the electrical conductivity of the solution must decrease. A pronounced decrease in conductivity is to be expected in the growth stage. The conductivity component due to the ions that are involved in a precipitation reaction is obtained by subtraction of the final conductivity after the precipitation from the value found at the time in question[19]. In the example in Figure 14 it is possible to distinguish three sections. At the beginning of the precipitation, an initial period of 0.2 to 0.5 min is recorded during which there is no change in conductivity. This initial

[19] *K. H. Lieser* and *A. Fabrikanos*, Z. physik. Chem. N.F. *22*, 406 (1959).

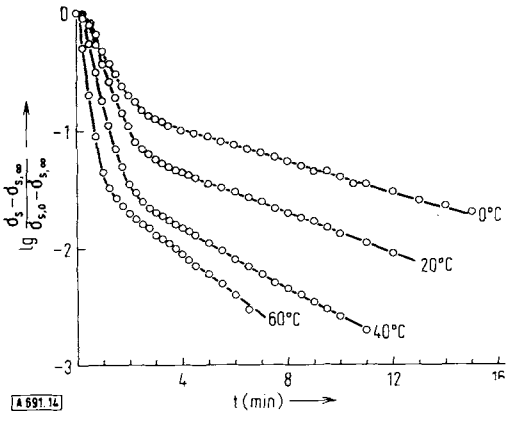


Fig. 14. Relative conductivity of the ions involved in the precipitation process on mixing of equal volumes of 2×10^{-3} M solutions of $Ba(NO_3)_2$ and Na_2SO_4 at various temperatures as a function of time.

period is not the same as the induction period found in nephelometric measurements. No new phase can be recognized optically during the induction period. During the initial period, no change is observed even in the submicroscopic range, *i.e.* no complexes or high molecular weight aggregates are formed to any appreciable extent in the solution. After the initial period the conductivity falls off rapidly with a half life of about 0.2 to 0.6 min. The decrease is exponential, and is due to the growth. The flatter part of the curve (half life about 2 to 5 min) corresponds to ripening. The assignment of the sections of the conductivity curves is in agreement with other experiments.

3.4. Electron Microscopy

The electron microscope makes it possible to observe the shape and size of the nuclei and crystals during the precipitation reaction even in the submicroscopic range.

Fixation of a given state can be achieved by the following technique[20]. The precipitation process in a sample is arrested within a few seconds by quenching on a support in an aluminum block cooled with liquid air. Ice can be removed by vacuum sublimation. Foreign substances can be completely excluded in many cases by suitable choice of the reagents used for the precipitation (so that apart from the precipitation product, only volatile substances are present).

Some examples of electron micrographs are given in Figures 15 to 17.

1 min after the start of precipitation of $BaSO_4$ by mixing 0.1 M solutions of its ions, very small particles are present and the crystals are very irregularly developed (Fig. 15a). 9 min later the content of small particles has decreased appreciably, and 3 hours after the start of precipitation (Fig. 15d) one finds crystals that, though rather more regular, are practically no larger. The investigation of the relatively dense precipitates is facilitated by ultrasonic treatment. With more dilute starting solutions ($\approx 10^{-3}$ M), the precipitation follows an entirely different course (Fig. 16). After 1 min only very small crystals are present, and these grow relatively slowly into larger crystals. After a long time the small crystals have disappeared, and all the crystals present (which are more or less well developed) are significantly larger than those obtained by precipitation from more concentrated solutions (cf. Fig. 16d and 15d). A temperature rise accelerates growth and ripening, and so leads to better-developed crystals (Fig.17). The size of the crystals is not greatly influenced by the temperature rise. The various stages of the precipitation (nucleation, growth, and ripening) are clearly recognizable in the electron micrographs in every case.

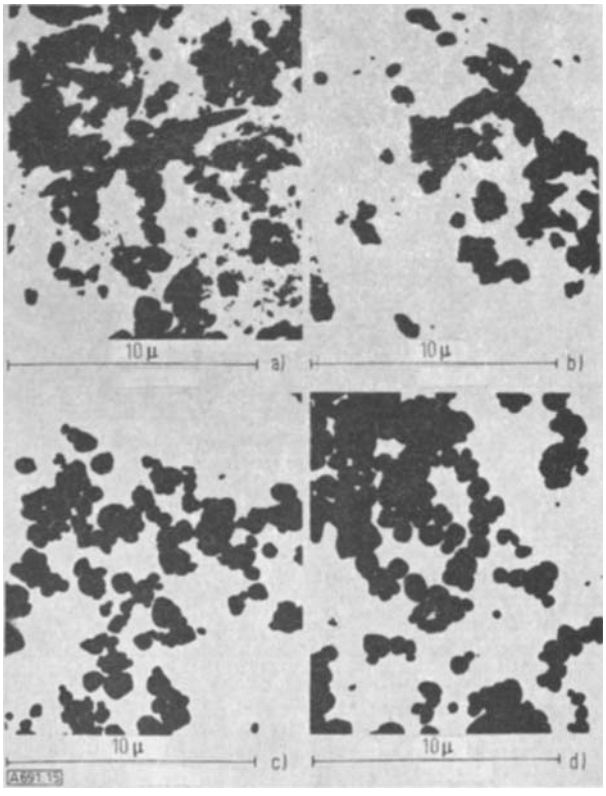


Fig. 15. Electron micrographs during the precipitation of $BaSO_4$ after mixing of equal volumes of 0.1 M solutions of $Ba(NO_3)_2$ and Na_2SO_4 at 20 °C. (a) 1 min, (b) 10 min, (c) 1 hour, (d) 3 hours after the start of precipitation.

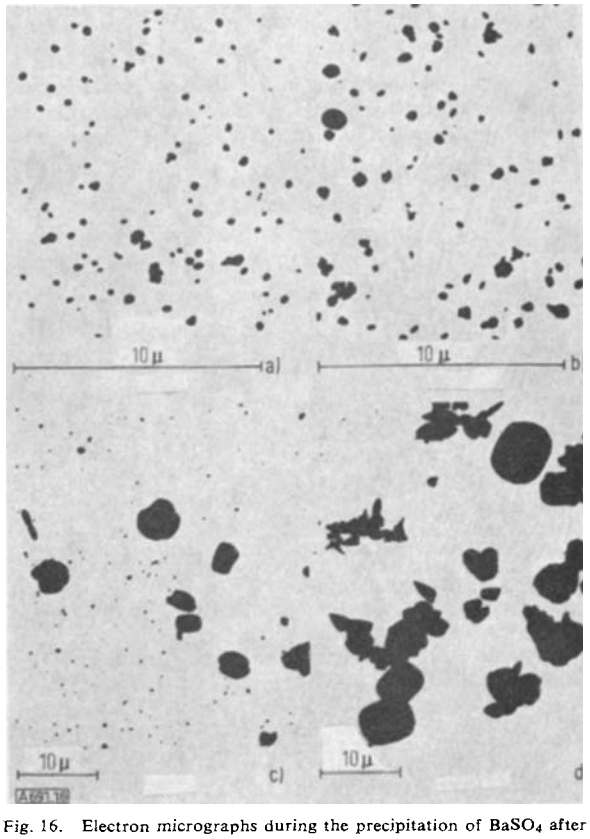


Fig. 16. Electron micrographs during the precipitation of $BaSO_4$ after mixing of equal volumes of 10^{-3} M solutions of $Ba(NO_3)_2$ and Na_2SO_4 at 20 °C. (a) 1 min, (b) 2 min, (c) 8 min, (d) 20 min after the start of precipitation.

[20] *A. Fabrikanos* and *K. H. Lieser*, Z. physik. Chem. N.F. *34*, 16 (1962).

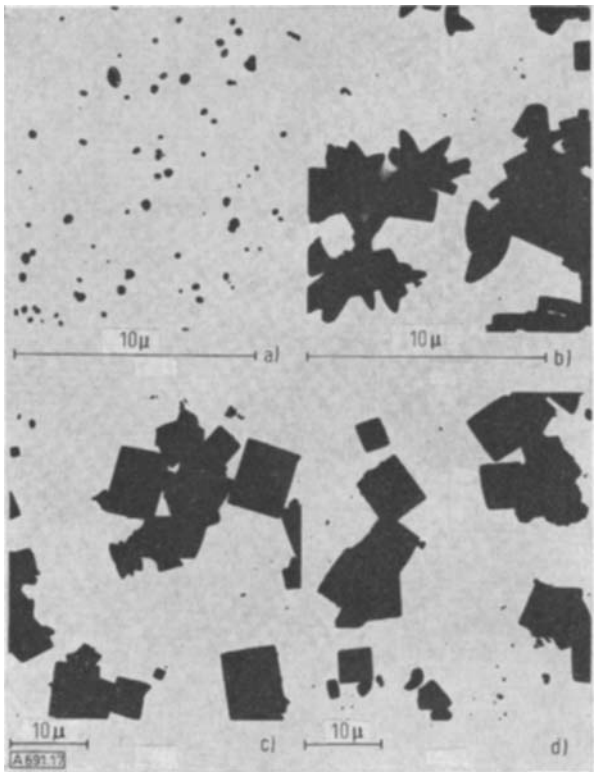


Fig. 17. Electron micrographs during the precipitation of $BaSO_4$ after mixing of equal volumes of 10^{-3} M solutions of $Ba(NO_3)_2$ and Na_2SO_4 at 50 °C. [(a) 2 min, (b) 4 min, (c) 8 min after the start of precipitation] and at 80 °C [(d) 30 min after the start of precipitation].

3.5. Isotopic Exchange

Radionuclides having sufficiently high specific activities are the most suitable for the investigation of ion exchange processes.

When a solid is introduced into a solution containing exchangeable radioactively labeled ions, the activity in the solution is observed to decrease in two steps under suitable experimental conditions (Fig. 18). The fast step a, which has

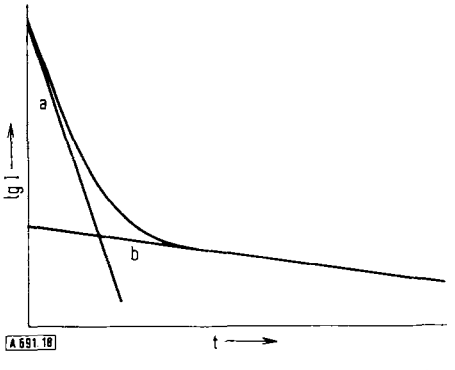


Fig. 18. Activity decrease as a function of time for isotope exchange on the surface of ionic crystals. a: Isotope exchange with the ions that were present on the surface of the solid phase at the beginning of the experiment. b: Isotope exchange with the ions that have reached the surface by recrystallization.

a half-life of the order of 1 min, is due to ion exchange of the labeled ions in the solution with the ions present on the surface of the solid at the beginning of the experiment. The surface of the solid is constantly being renewed as a result of recrystallization; labeled ions are transported into the interior of the crystal, while unlabeled ions pass to the surface. The exchange process continues until the labeled ions are uniformly distributed (apart from isotope effects) throughout the entire solid and the solution. The slow step b is caused by recrystallization. The slope of the curves in Figure 18 is a measure of the rate of the steps, and provides information about their kinetics [21]. The intercept on the ordinate is a measure of the isotopic exchange on the surface and allows the determination of the surface area of the solid. According to a relation that was first derived by *Paneth* [22, 23],

$$F = \left(\frac{I_0}{I} - 1\right) fcV\, N_L \qquad (34)$$

where I_0 and I are the number of counts per unit time in the solution before and after exchange with the surface, c is the concentration of the exchanging ions in the solution, V is the volume of the solution, N_L is the Loschmidt number, and f is the area equivalent to an exchangeable ion. The latter can be roughly calculated from the molecular weight M and the density ρ by means of the relation

$$f = \left(\frac{M}{\rho N_L}\right)^{2/3} \qquad (35)$$

or from X-ray data.

If suitable labeled ions (in the carrier-free state if possible) enter the solution during a precipitation, they take part in the precipitation reaction. The transport of matter within a short period dt is given by

$$dm = -dm_1 + dm_2 \qquad (36)$$

dm_1 is the quantity separating out from the solution, and dm_2 is the quantity passing into solution from the solid phase. Similarly, for the activity a (given by the number of labeled ions N and their decay constant λ, $a = \lambda N$) we obtain

$$da = -da_1 + da_2 \qquad (37)$$

By introduction of the specific activity in the solution $A = a/m$ we obtain at the time t_0 at which the activity is added

$$A_0 = \frac{a_0}{m_0} \qquad (38)$$

and at the time $t_0 + dt$

$$A_0 + dA = \frac{a_0}{m_0 + dm_2} \qquad (39)$$

(The specific activity in the solution is not affected by the quantity $-dm_1$ separating out from the solution.) It follows from equations (38) and (39) that

$$\frac{1}{A_0}\left(\frac{dA}{dt}\right)_{t_0} = -\frac{1}{m_0}\left(\frac{dm_2}{dt}\right)_{t_0} \qquad (40)$$

If the quantity separating out from the solution is assumed to be proportional to the surface area of the solid

$$\frac{dm_2}{dt} = \text{const} \times F \qquad (41)$$

we obtain the equation

$$-\frac{m_0}{A_0}\left(\frac{dA}{dt}\right)_{t_0} = \text{const} \times F \qquad (42)$$

[21] *K. H. Lieser, Ph. Gütlich,* and *I. Rosenbaum,* Radiochim. Acta *4*, 216 (1965).

[22] *F. Paneth* and *W. Vorwerk,* Z. physik. Chem., Abt. A *101*, 445 (1922).

[23] *K. H. Lieser* and *W. Hild,* Z. anorg. allg. Chem. *320*, 117 (1963).

The relative change in the specific activity at time $t = t_0$ is thus a measure of the surface area. If the activity is introduced at various times t_0 after the start of the precipitation, it is possible to follow the change in the relative surface area during precipitation as a function of time.

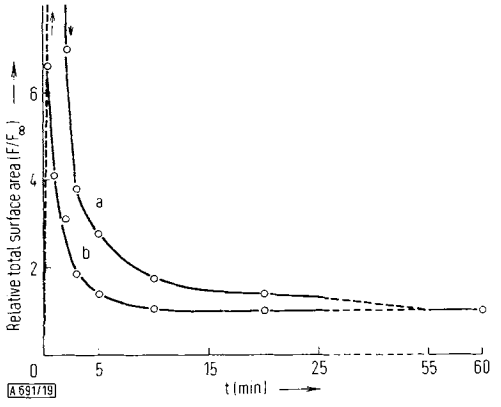


Fig. 19. Relative total surface area of the solid phase $BaSO_4$ as a function of time. (a) Precipitation by mixing of equal volumes of 10^{-3} M solutions of $Ba(NO_3)_2$ and Na_2SO_4; (b) as (a) but with 10^{-2} M solutions.

Figure 19 shows the relative total surface area of the solid phase during the precipitation of barium sulfate as found in this way. The course of the curves at the beginning of the precipitation is interesting, since the surface area of even very small particles is measured in this way. The total area of the solid phase is zero at first. Nucleation then leads to a large number of small particles having a large total area (steep ascent of the curve), from which growth and ripening yield a smaller number of crystals with a smaller total area. In the discussion of these curves we are faced with the question of when we can speak of a new phase.

The relative average crystal size $\bar{r}$ can also be calculated from the relative total area:

$$\bar{r} \sim \frac{\bar{m}}{F} \tag{43}$$

$\bar{m}$ is the quantity of solid. The average crystal size found in this way during the precipitation of barium sulfate from solutions at various concentrations is shown in Figure 20.

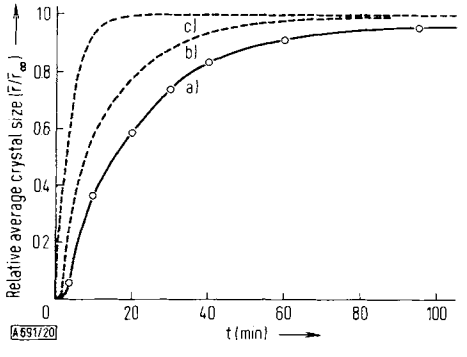


Fig. 20. Relative average crystal size on precipitation of $BaSO_4$ from solutions having various concentrations: (a) by mixing of equal volumes of 4×10^{-4} M solutions of $Ba(NO_3)_2$ and Na_2SO_4; (b) as (a), but with 10^{-3} M solutions; (c) as (a), but with 10^{-2} M solutions.

3.6. Determination of the Surface Area by the BET Method

The total surface area of a solid phase can be determined not only by isotopic exchange using equation (31) but also by the method devised by *Brunauer, Emmett,* and *Teller*[24] (BET method), which is based on the low-temperature adsorption of nitrogen. This method can be used for the study of precipitation reactions only if the processes to be studied are slow and if enough of the solid phase is available, since the BET method requires the isolation of relatively large samples (> 1 g), which must be dried under the mildest possible conditions. The BET method is therefore primarily suitable for the investigation of recrystallization.

Figure 21 shows the specific surface area of freshly precipitated barium sulfate as a function of time[25]. The precipitation from concentrated solutions shows a pronounced maximum

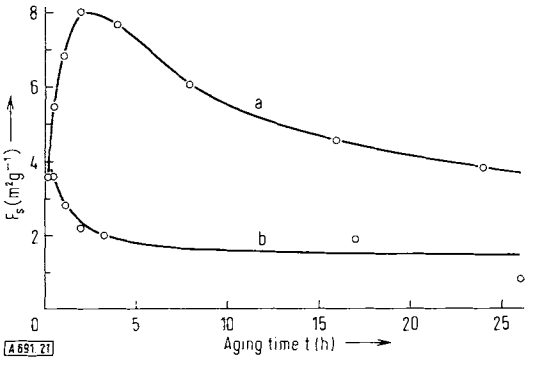


Fig. 21. Change in the specific surface area of the solid phase $BaSO_4$ as a result of recrystallization after precipitation by mixing of equal volumes of 10^{-1} M (a), and 10^{-3} M (b) solutions of $Ba(NO_3)_2$ and Na_2SO_4 at 20 °C.

that is not observed in precipitation from very dilute solutions. It can be seen from the diagram that recrystallization can cause marked changes in the solid phase, which extend over a period of about 1 day at room temperature, and take place at a correspondingly higher rate at higher temperatures (cf. Fig. 22)

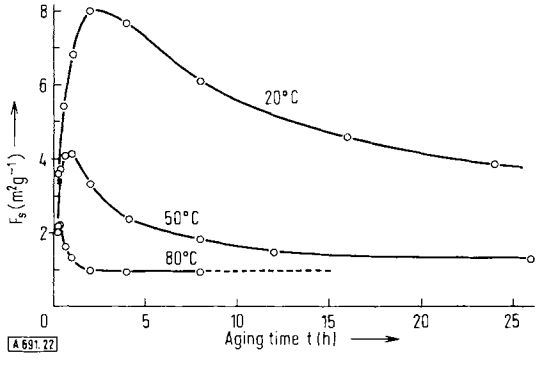


Fig. 22. Change in the specific surface area of freshly precipitated $BaSO_4$ (by mixing of equal volumes of 0.1 M solutions of $Ba(NO_3)_2$ and Na_2SO_4) as a function of temperature.

3.7. Paper Chromatography

Information about the course of a precipitation reaction can often be very easily obtained by paper chromatography. Thus the compound formed on precipitation may be radioactively labeled, samples then being taken from the suspension of solid phase in solution during the precipitation and developed on paper with an electrolyte solution having the same composition.

[24] *S. Brunauer, P. H. Emmett,* and *E. Teller*, J. Amer. chem. Soc. *60*, 309 (1938).

[25] *Ph. Gütlich* and *K. H. Lieser*, Z. physik. Chem. N.F. *46*, 257 (1965).

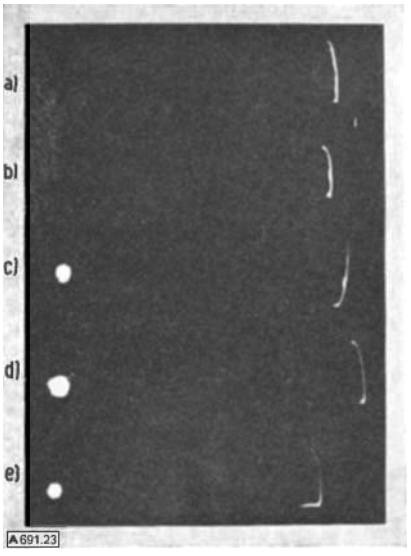


Fig. 23. Autoradiograms of paper chromatograms during the precipitation of $BaSO_4$ after mixing of 4×10^{-4} M solutions of $Ba(NO_3)_2$ and Na_2SO_4. Sample (a) 2 min, (b) 6 min, (c) 20 min, (d) 50 min, (e) 150 min after the start of precipitation.

Figure 23 shows a series of autoradiograms of paper chromatograms demonstrating the progress of precipitation of barium sulfate. No solid is present at the start, and all the barium ions migrate with the solvent front. No intermediate complexes (subnuclei) can be detected. The content of solid phase increases during the precipitation process. The chromatogram can also be evaluated quantitatively with the aid of a counter (cf. Fig. 24).

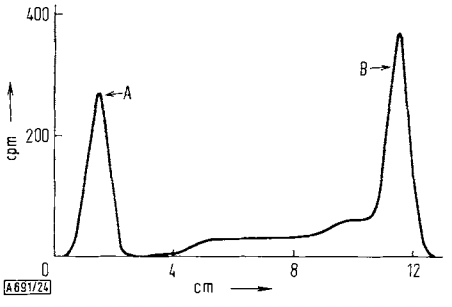


Fig. 24. Activity distribution on a paper chromatogram. A: Start, B: Solvent front.

The same principle can also be used with high-voltage electrophoresis for the investigation of precipitation reactions.

3.8. Coprecipitation

Important information can also be obtained from the behavior of foreign substances in a precipitation reaction. This is particularly true of a microcomponent, *i.e.* a foreign substance that is present in an extremely low concentration in comparison with the principal component (macrocomponent). Radiochemical methods are particularly useful for the elucidation of the behavior of microcomponents. The first detailed investigations on coprecipitation were carried out by *Hahn*[26].

Two processes may be responsible for the coprecipitation of a microcomponent, *i.e.* (1) formation of solid solution and (2) occlusion or adsorption. The tendency to form solid solutions depends on whether the macrocomponent and the microcomponent have similar ionic radii and the same charge. If these conditions are satisfied and the microcomponent is less soluble than the macrocomponent, the microcomponent is generally enriched in the solid phase. A more interesting microcomponent for the investigation of precipitation reactions is one that is occluded in or adsorbed on the solid phase. The occlusion of a microcomponent may result from chemical reactions with the macrocomponent or from adsorption during precipitation. In the latter case one should expect partial separation of the microcomponent during ripening.

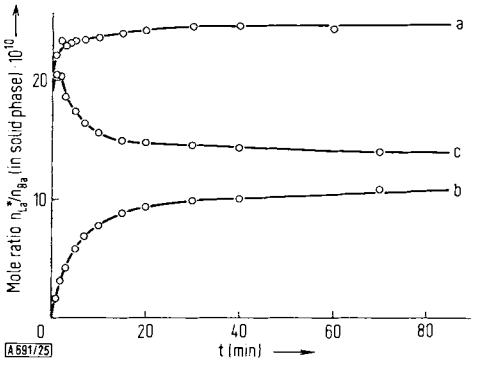


Fig. 25. Behavior of carrier-free lanthanum ions during the precipitation of barium sulfate by mixing of 10^{-3} M solutions of $Ba(NO_3)_2$ and $NaSO_4$. a: Addition of the labeled La^{3+} ions before the start of precipitation; b: addition of La^{3+} after completion of precipitation; c: occluded La^{3+} ions.

This is in fact observed. Figure 25 shows the behavior of carrier-free lanthanum ions during the precipitation of barium sulfate. The molar ratio La^{3+}/Ba^{2+} is of the order of 10^{-8} in this example. If the radioactively labeled La^{3+} ions are added before the start of precipitation, they may be occluded in or adsorbed on the surface (curve a). If on the other hand the La^{3+} ions are not introduced into the solution until the precipitation is complete, only adsorption on the surface occurs (curve b). The difference between curves a and b (curve c) shows the behavior of the occluded lanthanum ions. A proportion of these ions (about 1/3) is carried out of the solid phase again in the course of about 30 minutes. This is due to ripening, which proceeds as Ostwald ripening.

4. Experimental Results

4.1. Nucleation

A freshly supersaturated solution at first contains only ions (ion pairs) or molecules, whereas it later contains mainly nuclei or crystals. Between these there must be more or less stable intermediates known as subnuclei; these can also be described as high molecular weight complexes or aggregates of molecules. The reactions that take place during the formation of a crystal from cations A^+ and anions B^- can be summarized in the following scheme:

$$A^+ + B^- \rightleftharpoons AB \overset{A^+,\,B^-}{\rightleftharpoons} (AB)_n \overset{A^+,\,B^-}{\rightleftharpoons} (AB)_n^* \rightarrow \text{crystal} \quad (44)$$

The complexes $(AB)_n$ may contain an excess of cations or of anions (*e.g.* $[(AB)_nA_m]^{m+}$), depending on the concentrations in solution.

Radiochemical measurements show that the concentration of dissolved molecules or ion pairs AB and

[26] *O. Hahn* and *L. Imre*, Z. physik. Chem., Abt. A *144*, 161 (1929); *O. Hahn*: Applied Radiochemistry. Cornell University Press, Ithaca, N.Y., 1936.

of high molecular weight complexes $(AB)_n$ in saturated solutions is relatively small. It is about 2% of the total concentration in the saturated solution for silver halides [27], a few tenths of one percent for barium sulfate [28], and a few percent for strontium sulfate [28].

According to classical theory [3, 12] there should always be a certain amount of high molecular complexes $(AB)_n$ present in quasistationary equilibrium immediately after the saturation point has been reached; according to *Nielsen* [4] there is a certain delay before these complexes are formed.

On the basis of existing knowledge of the rates of ionic reactions [29], it must be assumed that the reversible reactions that lead to the formation of the complexes $(AB)_n$ are very fast, at least in the low molecular weight range. At higher molecular weights, inhibitions similar to those observed in crystal growth may occur.

The principal questions in the investigation of nucleation are as follows:

(a) What is the critical supersaturation or the critical supersaturation ratio?

The critical supersaturation ratio Γ is defined [30] as

$$\Gamma = \sqrt{\frac{K_{su}}{K_s}} \tag{45}$$

(K_{su} and K_s are the solubility products in the supersaturated and in the saturated states respectively); some examples of experimental values are $\Gamma = 4$ for silver chloride [8] and 7.1 for barium sulfate [31]. As is shown by the existing data, the critical supersaturation is higher for 2,2-electrolytes such as barium sulfate, strontium sulfate, and calcium oxalate than for 1,1-electrolytes such as the silver halides. The values also depend on the precipitation conditions [8, 31].

(b) How does the nucleation rate vary with the supersaturation?

The nucleation rate increases very rapidly with increasing supersaturation. This relationship, which is illustrated in Figure 4, has frequently been confirmed experimentally [4, 8] and is also clearly seen from electron micrographs (cf. Figs. 15 and 16).

(c) Can the nucleation intermediates indicated in eq. (44) be detected?

From the assumption that the solubility product is an upper ion concentration limit, and that even in the presence of a solid phase, the ion concentration cannot be increased indefinitely beyond this limit, it follows that highly supersaturated solutions must contain detectable quantities of subnuclei. Attempts to detect these subnuclei by paper chromatography or high-voltage electrophoresis have been unsuccessful. This negative result is further confirmed by conductivity measurements (Table 1).

Table 1. Conductivity before and after mixing equal volumes of $Ba(NO_3)_2$ and K_2SO_4 solutions having equal conductivities.

$c_{Ba^{2+}}$ [a] (mole · l^{-1})	σ_c [b] (Ω^{-1} cm^{-1})	$c_{Ba^{2+}}$ [c] (mol · l^{-1})	Saturation ratio (c/c_s)	σ_c [c] (Ω^{-1} cm^{-1})	Reaction time (min)
8×10^{-5}	1.09×10^{-5}	4×10^{-5}	4	2.08×10^{-5}	—
1.6×10^{-4}	4.12×10^{-5}	0.8×10^{-4}	8	4.09×10^{-5}	—
2.0×10^{-4}	5.12×10^{-5}	1.0×10^{-4}	10	5.12×10^{-5}	45
2.72×10^{-4}	7.03×10^{-5}	1.36×10^{-4}	13.6	7.03×10^{-5}	20
4.0×10^{-4}	10.15×10^{-5}	2.0×10^{-4}	20	10.1×10^{-5}	7
5.0×10^{-4}	12.7×10^{-5}	2.5×10^{-4}	25	12.6×10^{-5}	5

[a] Before mixing. [b] Specific conductivity of the starting solutions. [c] After mixing.

Barium nitrate and potassium sulfate solutions having equal conductivities were mixed and the conductivity of the mixture was then measured immediately. If no high molecular weight complexes are formed, the conductivity should not decrease (provided that the change in the activity coefficients of the ions on mixing can be neglected). It can be seen from Table 1 that there is no appreciable decrease in conductivity after mixing even at a supersaturation ratio of 25.

Contrary to the classical theory of nucleation [3, 12] which postulates that the concentration of subnuclei ought to be ≈ 2 orders of magnitude greater than that calculated from the maximum error of the conductivity measurements, the experimental results indicate that subnuclei are not present in appreciable quantities. The solution contains almost exclusively ions. The reaction in accordance with eq. (44) has not yet progressed appreciably from left to right. The concentration of the ions is higher by the factor given by the supersaturation ratio than in the saturated solution. The inhibition of the nucleation begins in the region of the higher molecular weight complexes $(AB)_n$ or in the critical nucleus $(AB)_{n^*}$. This inhibition may be due to the need for the components of the high molecular weight complexes to arrange themselves into the precursor of a crystal.

4.2. Growth

The growth of the crystals can be described by the variation of the average crystal size with time (Fig. 20).

If the crystals are to be sorted according to size, it is recommended that at least two separation methods be used and the results compared. For example, very small crystals that are retained by a membrane filter migrate with the solvent front in paper chromatography (cf. Fig 26).

It is found that for barium sulfate, strontium sulfate, and calcium oxalate, the rate of crystal growth is determined over a wide concentration range by the surface reaction, and not by diffusion in the solution [32–34]. In the case of potassium perchlorate, on the other hand, the rate-determining step is the diffusion in the

[27] *K. H. Lieser*, Z. anorg. allg. Chem. *292*, 97 (1957).

[28] *K. H. Lieser*, Z. anorg. allg. Chem. *335*, 225 (1965).

[29] *M. Eigen* in *A. Weissberger*: Technique of Organic Chemistry. Interscience, New York 1963, Vol. VIII/2, pp. 793 and 895.

[30] *V. K. La Mer* and *R. H. Dinegar*, J. Amer. chem. Soc. *73*, 380 (1951).

[31] *A. Fabrikanos* and *K. H. Lieser*, Z. physik. Chem. N.F. *36*, 232 (1963).

[32] *K. H. Lieser* and *A. Fabrikanos*, Z. physik. Chem. N.F. *22*, 278 (1959).

[33] *K. H. Lieser* and *H. Wertenbach*, Z. physik. Chem. N.F. *34*, 1 (1962).

[34] *G. Papakostidis*, *A. Fabrikanos*, and *K. H. Lieser*, Z. physik. Chem. N.F. *62*, 168 (1968).

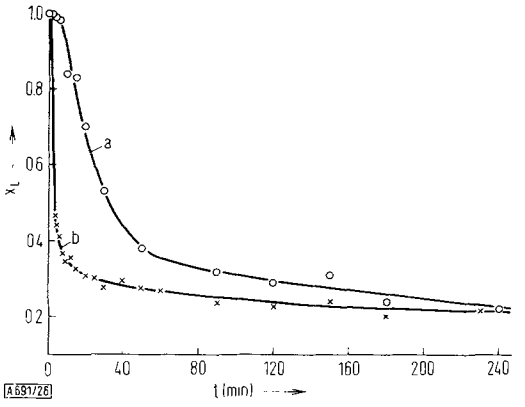


Fig. 26. Fraction of dissolved barium sulfate as a function of time after mixing of 4×10^{-4} M solutions of $Ba(NO_3)_2$ and Na_2SO_4. a: Separation by paper chromatography; b: separation by a membrane filter.

solution [35]. The inhibition of the crystal growth may be due to various factors. The following possibilities are conceivable:

(a) The ions have to overcome a potential barrier to become incorporated into the crystal lattice and to lose at least part of their solvation shell.

(b) Only a few sites on the surface are suitable for the deposition of an ion.

(c) A surface nucleus must be formed first.

Experiments in which crystals whose ripening process is complete are used and the supersaturation is such that no new nucleation is possible are particularly useful for the study of crystal growth. Experiments with calcium oxalate and strontium sulfate show clearly that even under these conditions the surface reaction is rate-determining. It is interesting to note that the growth of these crystals and the isotopic exchange on their surface have the same half life. The same processes are evidently rate-determining in both cases. This suggests, however, that the inhibition of growth is due to the factors mentioned under (a), *i.e.* to a potential barrier for the incorporation of the ions into the crystal lattice or to the removal of water of hydration.

4.3. Ripening

Ripening can be followed very easily by radiochemical methods, since in ripening by the Ostwald mechanism small crystals redissolve while larger crystals continue to grow. This is accompanied by transport of matter, which must lead to a change in the specific activity in the solution.

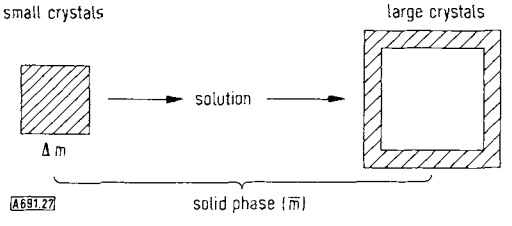


Fig. 27. Scheme of Ostwald ripening.

[35] *G. Tappe* and *M. Kahlweit*, Z. physik. Chem. N.F. *30*, 90 (1961).

Let $t = 0$ be the start of precipitation and t_0 the time at which the activity is introduced. According to eq. (38), the specific activity in the solution at time t_0 is $A_0 = a_0/m_0$. To facilitate understanding, Ostwald ripening is formally divided into two steps in Figure 27.

In the first step of ripening, a quantity Δm of small crystals is dissolved. The specific activity in the solution consequently changes to

$$A = \frac{a_0}{m_0 + \Delta_m} \tag{46}$$

In the second step the quantity Δm is deposited on larger crystals. This does not lead to a change in the specific activity in the solution. Based on the total quantity $\bar{m}$ of solid phase present at time t_0, the ratio $\Delta m/\bar{m}$ is a measure of Ostwald ripening.

$$\frac{\Delta m}{\bar{m}} = \frac{m_0}{\bar{m}} \frac{A_0 - A}{A} \tag{47}$$

$\Delta m/\bar{m}$ is the fraction of the solid phase that is dissolved and redeposited between the time t_0 of introduction of the activity and the end of the precipitation process. The ripening in fact proceeds, not in two independent steps, but continuously in very many small successive steps. However, this does not affect the validity of the treatment.

Experimental $\Delta m/\bar{m}$ values are given Table 2 for the precipitation of barium sulfate. It can be seen that *e.g.* of the solid that is present 2 minutes after the start of precipitation from 0.01 M solutions, about 37% have undergone Ostwald ripening, *i.e.* have redissolved, before the end of the precipitation. Ripening thus leads to extensive changes in the solid phase, which are associated with appreciable matter transport through the solution. The values for $\Delta m/\bar{m}$ observed at the end of the precipitation are a measure of the isotopic exchange on the surface of the solid phase.

Table 2. Fraction of the solid phase that participates in exchange of matter between the solid phase and the solution as a result of Ostwald ripening between the indicated time t_0 after the start of precipitation and the end of the precipitation of $BaSO_4$.

t_0 (min)	$\frac{\Delta m}{\bar{m}}$		t_0 (min)	$\frac{\Delta m}{\bar{m}}$	
	[a]	[b]		[a]	[b]
0.5	1.0	(0.5)	10	0.069	0.056
1	0.65	0.42	20	0.035	0.041
2	0.30	0.37	30	0.035	0.041
3	0.23	0.16	60	—	—
5	0.103	0.15	65	0.019	—

[a] Precipitation from 10^{-3} M solutions. [b] Precipitation from 10^{-2} M solutions.

The process of Ostwald ripening is thus detected and quantitatively determined in this way. No cementation takes place in the systems studied so far (alkaline earth metal sulfates, calcium oxalate).

4.4. Recrystallization

Recrystallization with the aid of the mother liquor can also be followed radiochemically. Clear differences are found in the recrystallization rates. For example, the half life of the recrystallization in the precipitation of barium sulfate is 80 min for 10^{-2} M solutions, 2000 min for 10^{-3} M solutions, and 6000 min for 4×10^{-4} M solutions.

Since precipitation from concentrated solutions yields very imperfect crystals (cf. Fig. 15), the half-life of the recrystallization is a sensitive measure of the perfection of the crystals. The lower the supersaturation at which the crystals are formed, the less imperfect they are and the smaller is their tendency to recrystallization.

Conclusions concerning recrystallization can also be drawn from the behavior of foreign ions that form solid solutions with the solid phase. The ease with which these foreign ions are incorporated into the solid phase increases as their solubility decreases and as their ionic radius approaches that of the ions of the solid phase. Thus barium ions are incorporated preferentially during the recrystallization of strontium sulfate, whereas calcium ions are not [36].

The specific surface area of the solid phase [25] passes through a maximum during recrystallization only in precipitations from relatively concentrated solutions (cf. Fig. 21). To explain this maximum, which is observed at various temperatures (cf. Fig. 22), it must be assumed that the crystals formed under these conditions are so strongly disordered that they break down during recrystallization to give smaller crystals, which then recombine and grow into larger crystals again. This process may be due to crystal imperfections that are gradually healing.

The results of these investigations explain the well known analytical practice of leaving a precipitate in contact with the mother liquor for 24 hours before filtration.

5. Some Characteristics of the Precipitation of Hydroxides

The precipitation of hydroxides differs from the precipitation of ionic crystals in the following respects:

(a) Hydroxide precipitates are generally amorphous.

(b) The treatments proposed by *Kossel* [13] and *Stranski* [14] cannot be applied to hydroxides, *i.e.* the nucleation and growth cannot be described merely by the deposition of ionic or molecular units, since chemical reactions also occur (*e.g.* reactions between OH groups with loss of water).

(c) The course of the precipitation of hydroxides depends not only on concentration, temperature, and time, but also on the pH value.

The precipitation of hydroxides is therefore a very much more complicated process than the precipitation of an ionic crystal. Though simple models exist, *e.g.* for the course of the chemical reaction and the formation of basic salts as intermediates, there are as yet no more advanced schemes for the quantitative treatment of the precipitation of hydroxides.

Information about the effects of time and pH can be obtained from radio paper chromatography [37]. Figure 28 shows the pH dependence of the quantity of high molecular weight condensation products that remains at the start of the chromatogram for the precipitation of cerium(III) hydroxide. The vertical arrows show the effect of time. The experimental values obtained immediately after the adjustment of

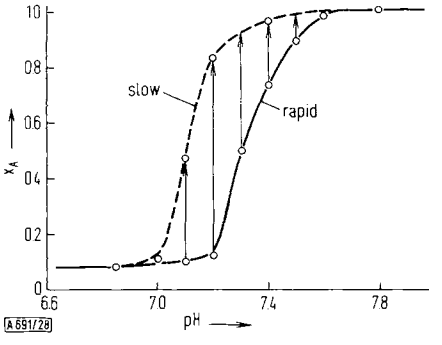


Fig. 28. Fraction of high molecular weight condensation products remaining at the start of the paper chromatogram for the precipitation of cerium(III) hydroxide as a function of the pH value and of time.

the pH (fast precipitation) are given as well as the limiting values found after several hours at a constant pH value. This diagram clearly shows the characteristic features of a hydroxide precipitation, *i.e.* the start of the precipitation of the hydroxide and the aging of the hydroxide at constant pH value.

The corresponding diagram for the precipitation of iron(III) hydroxide is shown in Figure 29.

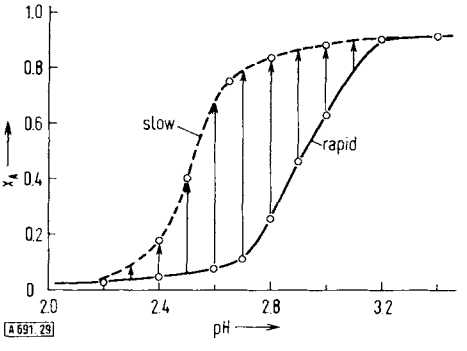


Fig. 29. Fraction of high molecular weight condensation products remaining at the start of the paper chromatogram for the precipitation of iron(III) hydroxide as a function of the pH value and of time.

Though this method does not provide new fundamental information, it does yield quantitative information on the course of the hydroxide precipitation. Intermediates can also be detected on the paper chromatograms in the region between the start and the solvent front (cf. Fig. 24); however, these intermediates cannot be identified.

[36] *W. Hild* and *K. H. Lieser*, Z. anorg. allg. Chem. *331*, 133 (1964).

[37] *A. Fabrikanos* and *K. H. Lieser*, Z. physik. Chem. N.F. *51*, 130 (1966).

The dependence of the precipitation of hydroxides on pH and time can be discussed on the basis of the scheme shown in Figure 30. Important processes involved in the precipitation are hydrolysis reactions, which lead to hydroxo complexes and hydroxides, and condensation reactions in which products having higher molecular weights are formed. The hydrolysis reactions are relatively fast, whereas the condensation reactions are slow. It is therefore not surprising that the path followed varies according to whether the pH change is fast or slow. The products may also be different. Thus the probability of occlusion of foreign substances (particularly of hydroxides being formed at higher pH values) is considerably greater when the pH change is fast. Diagrams of the types shown in Figures 29 and 30 therefore yield important information for the practical precipitation of hydroxides.

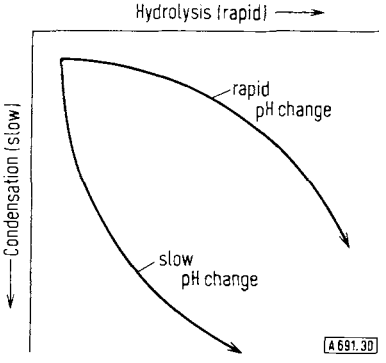


Fig. 30. The course of hydroxide precipitation.

Received: May 24, 1968 [A 691 IE]
German version: Angew. Chem. *81*, 206 (1969)
Translated by Express Translation Service, London.

COMMUNICATIONS

Tetrakis(cyclopentadienyl)protactinium(IV)

By *F. Baumgärtner, E. O. Fischer, B. Kanellakopulos,* and *P. Laubereau* [*]

Tetrakis(cyclopentadienyl)protactinium(IV) *(1)* is the first complex of protactinium to contain purely aromatic ligands. Surprisingly, the central atom is tetravalent in this complex. In its synthesis, Pa_2O_5 (110 mg) was first chlorinated by a $Cl_2/CCl_4/Ar$ mixture for 3 h at 600 °C. The yellowish white chlorination product that was collected as sublimate was treated immediately with $Be(C_5H_5)_2$ (2.6 g) at 65 °C. After a reaction time of 45 h, the excess of $Be(C_5H_5)_2$ was removed from the dark green reaction mixture by vacuum sublimation (80 °C/10^{-3} torr). Benzene-extraction of the residue for 110 h with exclusion of air afforded chloride-free *(1)* in the form of orange-yellow crystals (yield calculated with respect to Pa_2O_5: 54%).

The appearance of the molecular ion peak at *m/e* 491 and of a fragmentation pattern analogous to that of the corresponding compound $Th(C_5H_5)_4$ [1] in the mass spectrum (Varian MAT CH-5, electron energy 70 eV, sample temperature ~20 °C) confirm the presence of $Pa(C_5H_5)_4$.

Compound *(1)* is moderately soluble (*ca.* 1.1 mg/ml) in benzene, forming a pale yellow solution. Unlike $Th(C_5H_5)_4$ it cannot be sublimed, but decomposes above 210 to 230 °C similarly to $U(C_5H_5)_4$ [2] and $Np(C_5H_5)_4$ [3].

The IR spectrum of *(1)* (KBr disk) demonstrates the presence of exclusively symmetrical five-membered rings in that it contains characteristic bands at 784 and 811 (γ_{CH}), 1008 (δ_{CH}), 1445 (ω_{CC}), and 3078 cm^{-1} (ν_{CH}). It can also be deduced from the positions and the intensities of the bands that compound *(1)* possesses a molecular structure that is analogous to those of the other tetrakis(cyclopentadienyl) complexes of 5f elements.

Received: November 28, 1968 [Z 926 IE]
German version: Angew. Chem. *81*, 182 (1969)

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[3] *F. Baumgärtner, E. O. Fischer, B. Kanellakopulos,* and *P. Laubereau*, Angew. Chem. *80*, 661 (1968); Angew. Chem. internat. Edit. *7*, 634 (1968).

Alkali-Metal (Diphenylphosphino)dithioformates and (Diphenylthiophosphinyl)dithioformates

By *R. Kramolowsky* [*]

Metal dithiocarbamates have been much investigated in the past and have been used for analytical and industrial purposes. However, of the related phosphinodithioformates only one triphenyltin [1] and one phenylzinc derivative [2] of (diphenylphosphino)dithioformic acid have so far been recorded, and only then in a brief manner [3].

Alkali-metal (diphenylphosphino)dithioformates can be prepared by reaction of alkali-metal diphenylphosphides *(1)* with CS_2 in tetrahydrofuran (THF) at about −50 °C under nitrogen, and have been isolated as dioxane adducts *(2)* in 70–90% yield.

$$(C_6H_5)_2PM + CS_2 \xrightarrow[\text{2. ether/dioxane}]{\text{1. THF}}$$

(1)

(M = Li, Na, K)

$$(C_6H_5)_2P\text{-}C(=S)S^{\ominus}\,M^{\oplus}\cdot 1\ \text{dioxane}$$

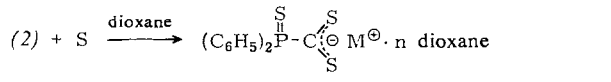
(2)

These pale orange-yellow compounds *(2)* form pale red, stable solutions in polar solvents such as acetone, THF, and alcohol, but aqueous solutions decompose after a short time. In acetone they show their ionic character by pronounced conductivity (M = K, equivalent conductivity at 25 °C: Λ_c = 90.5 Ω^{-1} cm^2 $mole^{-1}$; v = 569.0 l·$mole^{-1}$).

Barium bis[(diphenylphosphino)dithioformate] is obtained by double decomposition of *(2)* with anhydrous $Ba(NO_3)_2$ in liquid ammonia. This salt is readily soluble in boiling NH_3

but crystallizes from this solvent at −70 °C in pale red, shiny leaflets; it resembles the alkali-metal salts *(2)* closely in its solubility properties and in being easily hydrolyzed.

In dioxane solution the alkali-metal (diphenylphosphino)dithioformates add sulfur even at room temperature, forming the hitherto unknown alkali-metal (diphenylthiophosphinyl)-dithioformates, which crystallize as dioxane adducts *(3)* in almost quantitative yield.



(2) + S $\xrightarrow{\text{dioxane}}$ $(C_6H_5)_2\overset{S}{\overset{\|}{P}}-C^{\ominus}\begin{matrix}\nearrow S\\ \searrow S\end{matrix}$ $M^{\oplus}\cdot$ n dioxane

(3)

M = Li; n = 3
M = Na; n = 1
M = K; n = 2

The ionic structure of these compounds *(3)* is shown by their solubility in polar organic solvents and by their high conductivity in acetone (M = K, equivalent conductivity at 25 °C: $\Lambda_c = 124.5\ \Omega^{-1}\ cm^2\ mole^{-1}$; $v = 551.0$ l·mole^{-1}).

In the IR spectra of *(2)* (in acetone) a broad, very intense band at 1009–1011 cm^{-1} can be assigned to the ν_{as}SCS vibration; in the case of *(3)*, ν_{as}SCS appears shifted to shorter wavelengths at 1046 (vs), the νP=S being as expected at 645 cm^{-1} (vs).

When aqueous solutions of nickel(II) salts are treated with alcoholic solutions of *(2)*, ocher-colored nickel(II) bis[(diphenylphosphino)dithioformate] *(4)* is precipitated; this dissolves to red solutions in organic solvents such as chloroform, carbon tetrachloride, acetone, and benzene; the result of cryoscopic molecular-weight determination indicates that this salt *(4)* exists as monomer in 1,2-dibromoethane and it has no electrical conductivity in acetone solution. It is diamagnetic, whence it can be assumed to be a square-planar chelate complex with low-spin configuration of the nickel(II) ion.

Experimental:

All operations are carried out under pure nitrogen. Solutions of *(1)* in THF are obtained as follows:

(a) for M = Na or K: by heating diphenylphosphine (10 ml, 10.6 g, 57 mmoles) and sodium (1.5 g) or potassium (3 g) in THF (75 ml) under reflux; or (b) for M = Li: by dissolving lithium diphenylphosphide-dioxane (16.0 g, 57 mmoles) [5] in THF (75 ml).

Either of these solutions is added dropwise, with stirring at −50 °C over 1 h, to a solution of CS_2 (3.5 ml, 4.4 g, 57 mmoles) in THF (100 ml). The THF is then mostly removed in a high vacuum, the oily residue is taken up in ether, and the ethereal solution is treated with dioxane (10 ml). The dioxane-adducts *(2)* crystallize slowly at 0 °C and are purified by dissolution in dioxane and precipitation by ether (yield 70–90%).

Received: March 29, 1968; revised December 20, 1968 [Z 928a IE]
German version: Angew. Chem. *81*, 182 (1969)

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[2] *J. G. Noltes*, Recueil Trav. chim. Pays-Bas *84*, 782 (1965).

[3] Reaction of $(C_6H_5)_2PH$ with CS_2 gives a mixture of compounds, of which only $(C_6H_5)_2PCH_2P(S)(C_6H_5)_2$ and $(C_6H_5)_2P(S)CH_2P(S)(C_6H_5)_2$ [4] have so far been isolated (*R. Kramolowsky*, unpublished work), and not the compound $[(C_6H_5)_2PH_2]^+[(C_6H_5)_2PCSS]^-$ as formulated by *C. Dörken* [Ber. dtsch. chem. Ges. *21*, 1505 (1888)].

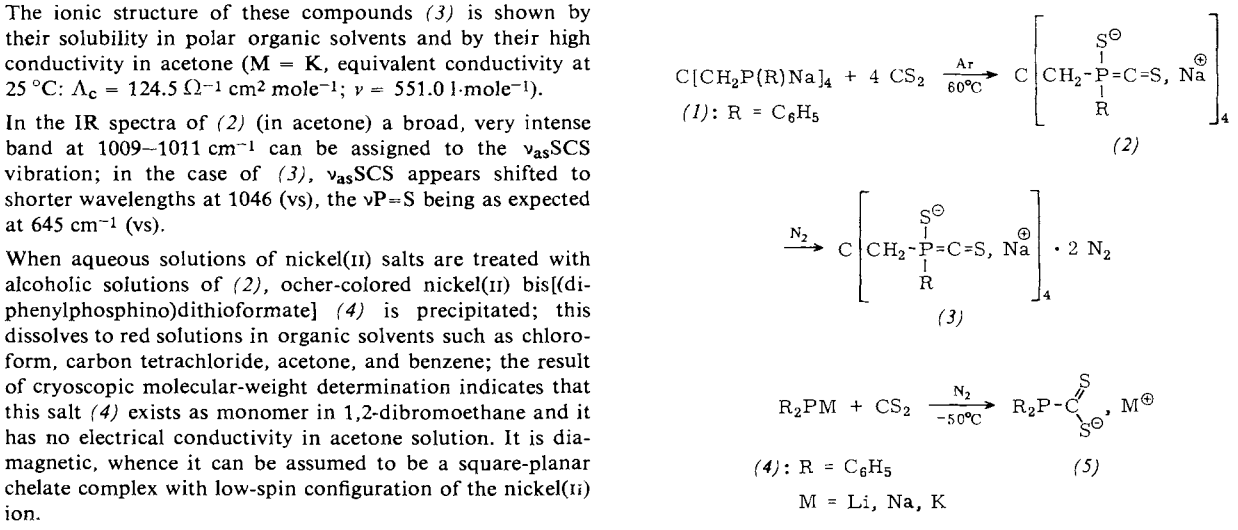
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A Salt-Like Organic Complex Containing Molecular Nitrogen [1]

By *J. Ellermann, F. Poersch, R. Kunstmann*, and *R. Kramolowsky* [*]

Reaction of a 1:4 (molar) mixture of tetrakis[(phenylsodiophosphino)methyl]methane *(1)* [2] and CS_2 in tetrahydrofuran (THF) at 60 °C under argon gives tetrasodium neopentanetetrayltetrakis[phenyl(thiocarbonyl)phosphoranethiolate] *(2)*, which is ocher-colored and soluble in polar solvents. This product absorbs molecular nitrogen greedily and within 24 h gives a quantitative yield of the yellowish-brown complex *(3)* with the stoichiometric proportions *(2)*: $N_2 \approx 1{:}2$. The complex *(3)* is also formed directly and more rapidly by analogous reaction of *(1)* with CS_2 under nitrogen. It is remarkable that the alkali-metal (diphenylphosphino)-dithioformates *(5)* [3] that are formed from alkali-metal diphenylphosphides *(4)* and CS_2 at −50 °C do not react with N_2 [3].



$C[CH_2P(R)Na]_4 + 4\ CS_2 \xrightarrow[60°C]{Ar} C\left[CH_2-\overset{S^{\ominus}}{\overset{|}{P}}=C=S,\ Na^{\oplus}\right]_4$

(1): R = C_6H_5 *(2)*

$\xrightarrow{N_2} C\left[CH_2-\overset{S^{\ominus}}{\overset{|}{P}}=C=S,\ Na^{\oplus}\right]_4 \cdot 2\ N_2$

(3)

$R_2PM + CS_2 \xrightarrow[-50°C]{N_2} R_2P-C\begin{matrix}\nearrow S\\ \searrow S^{\ominus}\end{matrix},\ M^{\oplus}$

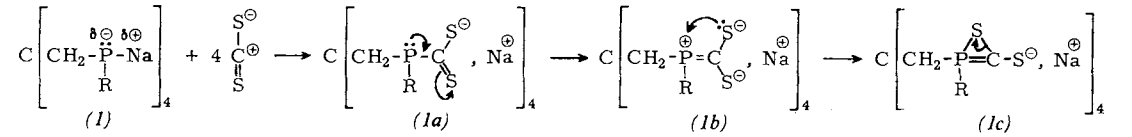
(4): R = C_6H_5 *(5)*
M = Li, Na, K

That the reactions of *(1)* and *(4)* with CS_2 lead to different types of product may be due primarily to the different reaction temperatures. Absorption of only two moles of N_2 per mole of *(2)* indicates that, like numerous other compounds containing the neopentane skeleton [4–6], the compound *(2)* functions as a twice bidentate reagent and chelating agent and that it binds N_2 in a spirocyclic 1:2 complex *(3)*.

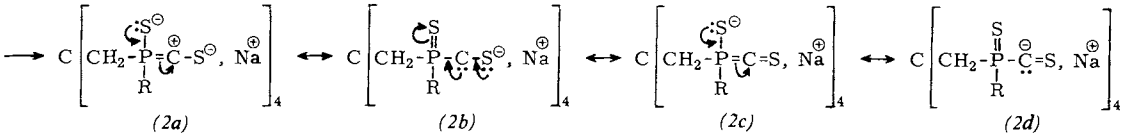
We suggest that, in the first step of the reaction, CS_2 is inserted into the polar P–Na bonds. *(1a)* can pass into *(2a)* by the regrouping *(1a)* of electrons and the rearrangement *(1b,c)*. The possibility of mesomeric stabilization between a carbonium *(2a)*, a carbene *(2b)*, a thiocarbonyl *(2c)*, and a carbanion structure *(2d)* explains both why *(2)* can be obtained as intermediate and why it is very reactive – sufficiently so to fix molecular nitrogen. As a working hypothesis we assume that *(3a)* is thus formed and stabilizes itself by mesomerism with *(3b)* and *(3c)*.

Like N_2, the isoelectronic CN^- also forms a 1:2 complex with *(2)*; from CO and *(2)* is obtained a compound that contains CO as a carbonyl group (ν>C=O: 1708 cm^{-1}). Reaction of the salt *(1)* with CO_2 gives $C[CH_2P(C_6H_5)-COONa]_4$ which is inert to N_2.

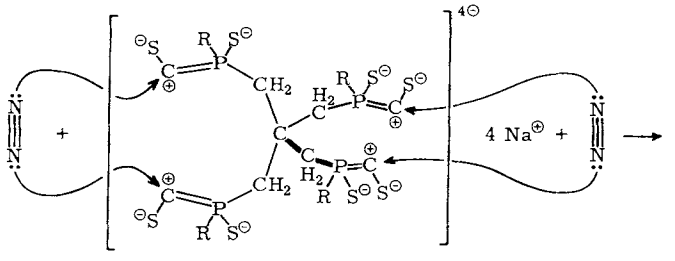
The composition and ionic character of compounds *(2)* and *(3)* are proved by elemental analyses and measurements of conductivity in dimethylformamide (DMF). The IR spectrum of *(3)* (as KBr disk) includes, besides the absorptions due to the neopentane skeleton and the phenyl groups, the following intense bands (cm^{-1}): νN=N 2090; νP–C$\begin{matrix}\nearrow S\\ \searrow N\end{matrix}$ 1166, 1050, and 902; νP=S 633. The bands at 2090 and 900 cm^{-1} are not present in the IR spectrum of *(2)*. The bond order of the N≡N bonds in *(3)* can be calculated by Siebert's method [7] from the νN≡N as being 2.6, *i.e.*, of the mesomeric



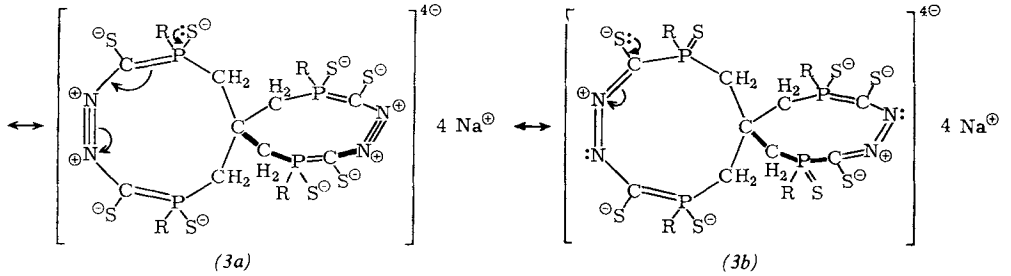
(1) (1a) (1b) (1c)



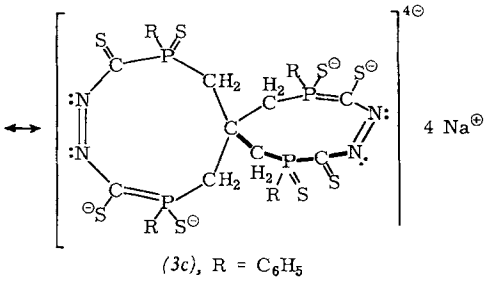
(2a) (2b) (2c) (2d)



(2a)

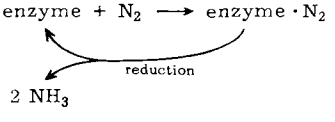


(3a) (3b)



(3c), R = C_6H_5

forms *(3a–c)* the greatest weight attaches to *(3a)*. Since the salt *(3)* decomposes on vaporization, no molecule ion appears in its mass spectrum; the fragment ions that occur can thus serve only as indications for the correctness of structure *(3)*. The fragment of greatest relative intensity, at m/e = 155 [CH_3–P(S)–C_6H_5], indicates the occurrence of this grouping in *(3)*; its composition is proved by the isotope peak for ^{34}S at m/e = 157. The assumption that a 1,2-shift of the phenyl group on the P–S bond occurs before further fragmentation is supported by observation of ions m/e = 109/111 (S–C_6H_5). Other fragments correspond to the tropylium cation [$C_7H_7^+$: m/e = 91; from CH_2–P(S)–C_6H_5 by elimination of PS^+ ?] and the C_6H_5 unit and their subsequent products. Similarly, expected ions from *(3)* can be seen with the composition PS (m/e = 63/65), CS (m/e = 44/46), C_4H_5 [m/e = 53; the residue of the neopentane skeleton after elimination of CH_3–P(S)–C_6H_5], N_2 (m/e = 28; second-largest relative intensity), Na (m/e = 23).



On the basis of our findings it seems possible that N_2 could be fixed also by enzymes that contain no transition-metal catalyst [8]. The extent to which compound *(3)* can be used as a model substance in this connection remains to be determined by future investigations.

Experimental:

Compound *(1)* (773 mg, 1.31 mmoles) and CS_2 (398 mg, 5.23 mmoles) in argon-saturated THF (25 ml) are warmed under argon for 4 h at 60 °C. When the solution is concentrated to *ca.* 10 ml in a high vacuum and then treated with light petroleum (40 ml), the product *(2)* is precipitated; it is washed with light petroleum (4 × 10 ml) and dried in a high vacuum (yield 85%), then having m.p. from 180 °C (dec.) and Λ (20 °C, DMF) = 182 Ω^{-1} cm^2 mole^{-1}, v = 7200 l · mole^{-1}. The product *(2)* dissolves readily in DMF, moderately in THF, ethanol, acetone, acetonitrile, dioxane, and halogenated hydrocarbons. All operations are conducted under argon; on contact with N_2 the salt *(3)* is formed. This is obtained directly by heating *(1)* (726 mg, 1.23 mmoles) with CS_2 (380 mg, 5 mmoles) in THF (20 ml) in a nitrogen atmosphere under reflux [working up as for *(2)*; yield 80–85%]; it has m.p. from 208 °C (dec.) and Λ (20 °C, DMF) = 154 Ω^{-1}cm^2 mole^{-1}, v = 7000 l · mole^{-1}. *(3)* dissolves readily in DMF,

ethanol/H_2O, and THF, and moderately to only slightly in acetone, acetonitrile, dioxane, CS_2, and halogenated hydrocarbons.

Received: December 19, 1968 [Z 928b IE]
German version: Angew. Chem. *81*, 183 (1968)

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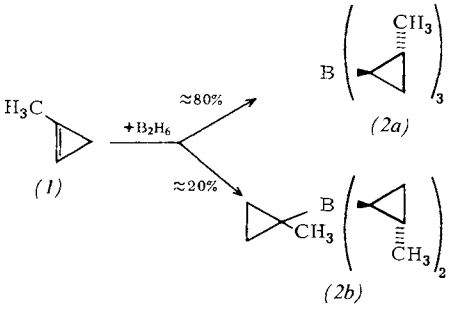
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trans-2-Methylcyclopropanol from 1-Methylcyclopropene

By *R. Köster*, *S. Arora*, and *P. Binger*[*]

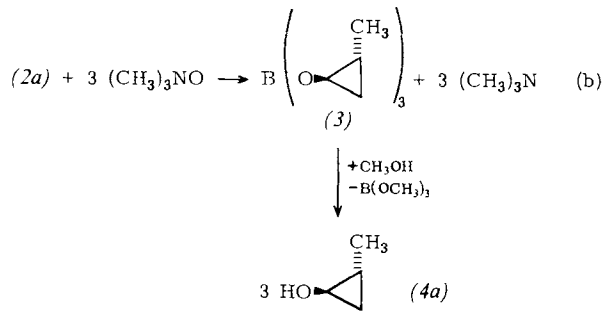
Reaction of 1-methylcyclopropene[1] *(1)* and diborane in pentane according to (a) proceeds *via cis* BH addition[2] to give a yield of more than 80% of tris(*trans*-2-methylcyclopropyl)borane *(2a)* [b.p. 37–40 °C/0.001 torr, molecular weight (mass spectrometric) 176 (B_1)] containing only a few (≈ 7%) 1-methylcyclopropyl groups as *(2b)* (gas chromatography). With tetraethyldiborane, compound *(1)* forms almost pure diethyl(*trans*-2-methylcyclopropyl)borane.



(a)

In diethyl ether the formation of polymeric organoboranes of unknown structure causes the yield of *(2)*[**] formed in (a) to fall to 65–70%. ^{1}H-NMR spectrum of *(2)* (undiluted): τ = 9.0 (D, $J < 2$ Hz), 9.2 (M), 9.6 (M), 10.9 ppm (M) in the intensity ratio 3:2:1:1.

Compound *(2)* reacts with trimethylamine *N*-oxide[3] in boiling toluene according to (b) giving tris(*trans*-2-methylcyclopropyloxy)borane *(3)* in 70% yield. ^{1}H-NMR spectrum



(b)

of *(3)*: τ = 6.70 (M), 9.09 (D, J = 2.5 Hz), 9.33 (M), 9.79 ppm (M) in the intensity ratio 1:3:2:1.

In a reaction analogous to (b), tricyclopropylborane[4] can also be oxidized to tricyclopropyloxyborane. Owing to the sensitivity of cyclopropanols[5], no useful results are obtained on treatment with aqueous hydrogen peroxide.

Transesterification of *(3)* with methanol leads to a 75% yield of sterically uniform *trans*-2-methylcyclopropanol *(4a)*, which contains at most *ca.* 5% of 1-methylcyclopropanol *(4b)* as a reaction product of *(2b)*. The structure of *(4a)* follows from *cis*-hydroboration[2] and from the agreement of its ^{1}H-NMR spectrum with a computer-simulated spectrum (LAOCOON I)[6]. ^{1}H-NMR spectrum of *(4a)* (undiluted): τ = 4.50 (S), 6.96 (M), 9.0 (D, J = 2.5 Hz), 9.15 (M), and 9.76 ppm (M) in the intensity ratio 1:1:3:2:1.

Tris(trans-2-methylcyclopropyloxy)borane (3)

Compound *(2)* (4.8 g, 27.2 mmole) [prepared from *(1)* and diborane in pentane] is diluted with anhydrous toluene (50 ml), and anhydrous trimethylamine *N*-oxide (6.25 g, 83.5 mmole) is added portion-wise to the solution at 80 °C. On boiling for 30 min, 4.8 g (99%) of $N(CH_3)_3$ is evolved. The excess of *N*-oxide is filtered off and the filtrate distilled under vacuum to yield compound *(3)* (4.2 g, 70%) having b.p. 74–75 °C/2 torr, n_D^{20} = 1.4288.

trans-2-Methylcyclopropanol (4a)

Removal of the azeotropic mixture $(CH_3O)_3B/HOCH_3$ (b.p. 54 °C) and of methanol from a solution of *(3)* (4.8 g, 21.4 mmole) in absolute methanol (30 ml) by distillation over a 25-cm packed column (*ca.* 3 theoretical plates) affords the compound *(4a)* [4 g, b.p. 34–36 °C/12 torr, molecular weight (mass spectrometric) 72]; gas chromatogram: 87.5% of *(4a)*, 5.7% of methylcyclopropanol *(4b)*, 1% of isobutanol, 0.1% of butyraldehyde, 4.6% of CH_3OH.

Received: January 2, 1969 [Z 929a IE]
German version: Angew. Chem. *81*, 185 (1969)

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[**] Compound *(2)* in the text refers to the mixture of *(2a)* and *(2b)* obtained according to equation (a).

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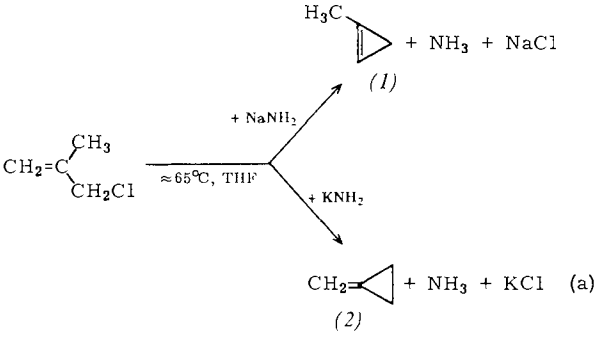
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Methylenecyclopropane from Methallyl Chloride

By *R. Köster*, *S. Arora*, and *P. Binger*[*]

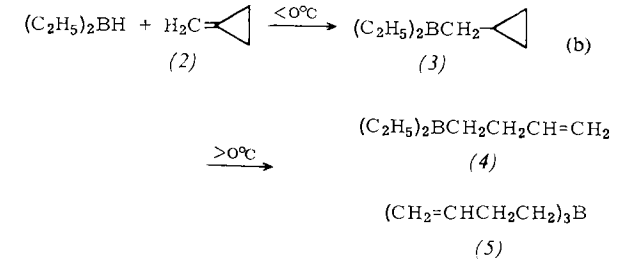
In continuation of previous experiments on cyclopropylborane[1] we have carried out the hydroboration[2] of 1-methylcyclopropene *(1)*. Compound *(1)* is now readily ac-

cessible by treatment of methallyl chloride with *sodium* amide in boiling tetrahydrofuran[3]. Surprisingly, however, reaction with *potassium* amide under otherwise identical conditions proceeds *via* route (a) to give a 36% yield of methylenecyclopropane *(2)*, as the only C_4H_6 hydrocarbon, instead of *(1)*.



After removal of oligomers, *e.g.* C_8H_{12} and $C_{12}H_{18}$, compound *(2)* is obtained in 97% purity (IR[4], ^{1}H-NMR[5], and mass spectra[5]). Thus the preparation of *(2)* by equation (a) is superior to all previously known methods[4–6]. Compound *(2)* is also formed quantitatively when *(1)* is passed through a suspension of KNH_2 in boiling THF, so that *(1)* cannot be ruled out as an intermediate in reaction (a).

Compound *(2)* and tetraethyldiborane react together according to equation (b) at −10 to 0 °C to give diethyl(cyclopropylmethyl)borane *(3)*, which rapidly isomerizes at room temperature to diethyl-3-butenylborane *(4)* [IR spectrum: 1637 ($\nu_{C=C}$), 990 ($\gamma_{=CH}$), 910 cm^{-1} ($\gamma_{=CH_2}$)] in a manner analogous to cyclopropylmethyllithium[7] and cyclopropylmethylmagnesium[8]. However, in the presence of pyridine the cyclopropylmethyl group of *(3)* remains intact.



Reaction of *(2)* with diborane at room temperature proceeds according to equation (b), yielding mainly tris(3-butenyl)borane *(5)*, since the cyclopropylmethyl groups of tris(cyclopropylmethyl)borane rearrange rapidly at temperatures above 0 °C. ^{1}H-NMR spectrum of *(5)* (undiluted): τ = 4.16 (M), 5.11 (M), 5.16 (M), 7.79 (M), 8.66 ppm (T, J = 8 Hz) in the intensity ratio 1:1:1:2:2.

Compound *(5)* is not completely homogeneous since hydroboration of *(2)* also gives rise to isomeric C_4H_7 groups (< 10%), presumably by inverse BH addition, which can be detected in the ^{1}H-NMR spectrum as 1-methyl-1-cyclopropyloxy groups [τ = 8.62 (S), 9.35 (M), and 9.59 ppm (M) in the intensity ratio 3:2:2] after oxidation of *(5)* by trimethylamine *N*-oxide.

Methylenecyclopropane (2)[9]

Methallyl chloride (101 g, 1.12 mole) is added dropwise over a period of 1 h to KNH_2 (64.8 g, 1.17 mole) in boiling anhydrous tetrahydrofuran (250 ml). Compound *(2)* and NH_3 are evolved and are carried by a stream of argon through 5 N H_2SO_4 (250 ml, weight increase = 14.4 g (76%) of ammonia) into a cold trap (−80 °C). A single recondensation affords 21.7 g (36%) of product; gas chromatogram: 97% of *(2)* and 3% of isobutene.

Received: January 2, 1969 [Z 929b IE]
German version: Angew. Chem. *81*, 186 (1969)

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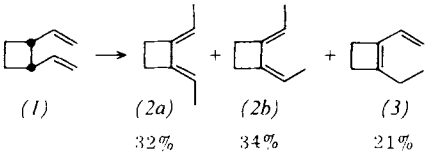
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[9] *Note added in proof* (February 7, 1969): In the meantime we have achieved a yield of up to 65% of C_4H_6 hydrocarbons (gas chromatogram: 38% of *(1)*, 62% of *(2)*) with $NaNH_2$ in boiling dioxane.

Preparation and Properties of 1,2-Diethylidenecyclobutane

By *P. Heimbach* and *R. Schimpf*[*]

The readily accessible *cis*-1,2-divinylcyclobutane *(1)*[1], which is formed catalytically in 40% yield from butadiene, undergoes ready isomerization on treatment with potassium *tert*-butoxide in dimethyl sulfoxide[2] at 40–60 °C to give *(2a)* and *(2b)* – two of the three conceivable isomers of 1,2-diethylidenecyclobutane – as well as 1-ethyl-2-vinylcyclobutene *(3)*. *trans*-1,2-Divinylcyclobutane can also be isomerized to *(2a)*, *(2b)*, and *(3)*. Compounds *(2a)* and *(2b)* were not separated by distillation.



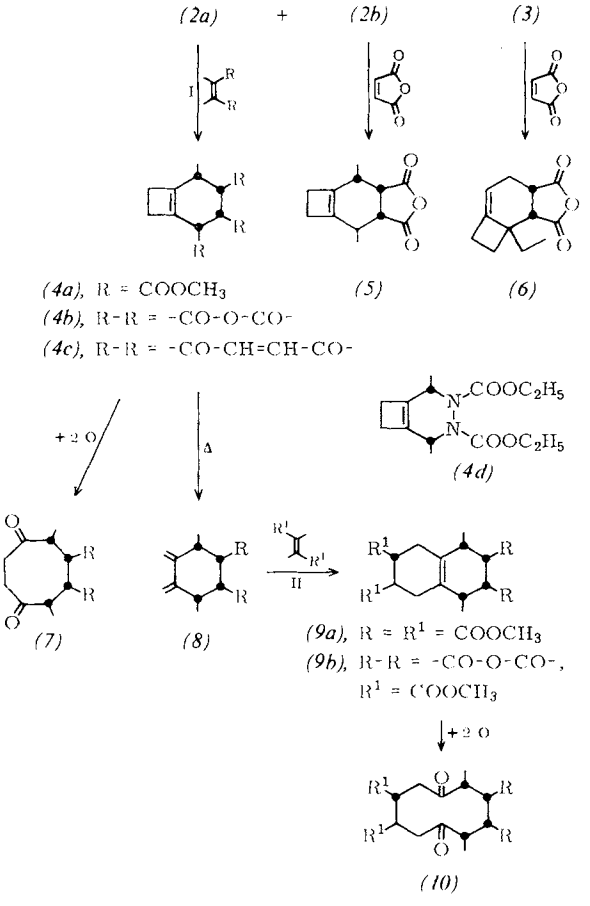
In a competing reaction, *(1)* rearranges to *cis,cis*-1,5-cyclooctadiene[3]. Since both reactions are of first order with respect to compound *(1)*, thermal rearrangement of *(1)* to *cis,cis*-1,5-cyclooctadiene can be strongly suppressed by working with high concentrations of potassium *tert*-butoxide. Moreover, *cis,cis*-1,5-cyclooctadiene undergoes partial isomerization to *cis,cis*-1,3-cyclooctadiene under the reaction conditions given above.

The equilibrium set up between *(2a)*, *(2b)*, and *(3)* in the presence of the basic catalyst can be utilized, *inter alia*, to isolate *(3)*, the isomer having the lowest boiling point, in a yield in excess of 60%, by means of a spinning-band column. Like 1,2-dimethylenecyclobutane[4–6], *(2a)* and *(2b)* can react with maleic anhydride in two steps. Compound *(3)* reacts with one mole of maleic anhydride to give *(6)*.

(2a) is considerably more reactive than *(2b)*; consequently, when a mixture of the two isomers is allowed to react under mild conditions it is only *(2a)* that actually undergoes reaction. *(2b)* can subsequently be drawn off and subjected to reaction under more drastic conditions. (Pure *(2b)* can be obtained in this way.)

The steric uniformity of the products obtained from *(2a)* or *(2b)* and the dienophile I does not depend on the reactivity of the dienophile[7].

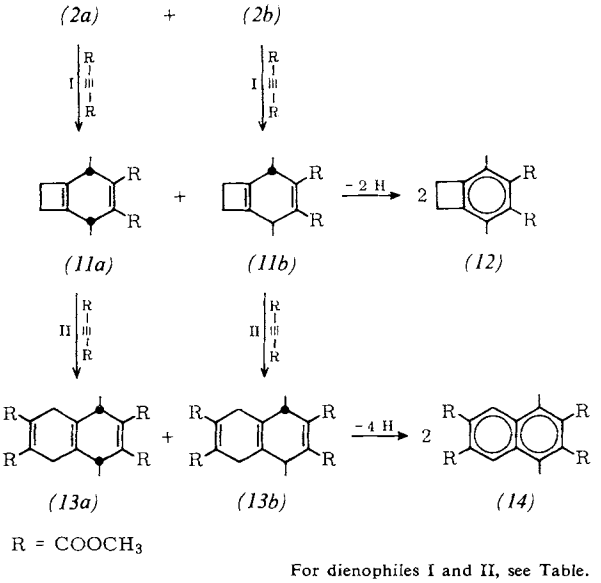
A particular advantage lies in the fact that the four-membered ring of the primary product *(4)* opens at 140 °C to give



For dienophiles I and II, see Table.

a 1,3-diene again. The same applies to *(5)*. We were able to establish the presence of *(8)* by IR and NMR spectrometry. It can react further with the dienophile II.

Treatment of *(4)* and *(9)* with ozone and subsequent catalytic hydrogenation of the intermediate product leads to *(7)* and *(10)*, respectively, both substances being substituted in a sterically uniform manner. *(5)* reacts similarly. If, for example, dimethyl acetylenedicarboxylate is used as dienophile *(2a)* + *(2b)* afford the cyclohexadiene derivatives *(11a)* and



For dienophiles I and II, see Table.

(11b) as well as *(13a)* and *(13b)* (the formal products of the normal Birch reduction). These compounds can be oxidized to *(12)* and *(14)*, respectively, by *p*-chloranil.

A selection of the new compounds is given in Table 1.

Isomerization of (1):

Compound *(1)* (222.1 g, 2.05 mole) and DMSO (282 g) containing 47.6 g of 61.5% potassium *tert*-butoxide (remainder butanol) are stirred together vigorously for 5 h at 60 °C (± 2 °C) under a protective gas. The mixture is worked up in the following way: All volatile products are distilled off at a pressure of 10^{-4} torr, first at a bath temperature of 20 °C (F_I = 211.4 g) and then at 60 °C (F_{II} = 286.4 g). DMSO and *tert*-butanol are removed from the fractions by washing twice with water: organic phase F_I = 199.1 g; F_{II} = 16.7 g. Chromatographic analysis showed the reaction product to have the following composition: 2.7 g of *(1)* (= 98.8% conversion), 46.5 g of *(3)* = 21.2%; 75.6 g of *(2b)* = 34.4%; 68.8 g of *(2a)* = 31.4%; 4.6 g of *cis,cis*-1,3-cyclooctadiene = 2.1%; 14.0 g of *cis,cis*-1,5-cyclooctadiene = 6.4% (total rearrangement 8.5%), 3.6 g of other olefins = 1.6%; residue

Table 1. New compounds prepared from *(2a)* + *(2b)*. The IR, ^{1}H-NMR, and mass spectra are in accord with the structures given.

Diene or starting material	Dieneophile or reactant I	Dieneophile or reactant II	*T* (°C)	Product	B.p. (°C/torr)	M.p. (°C) (n_D^{20})	Yield (%)
(2a) [a]	Dimethyl maleate	–	80	*(4a)*	49–50/10^{-4}	90–90.5	85
(2a) [a]	Maleic anhydride	–	0	*(4b)*		39.5–40	100
(2a) [a]	*p*-Quinone	–	40	*(4c)*		68–69	78
(2a) [a]	Diethyl azodicarboxylate	–	20	*(4d)*	70/10^{-4}	(1.4780)	95
(2b)	Maleic anhydride	–	80	*(5)*		51.5–52.5	100
(3)	Maleic anhydride	–	50	*(6)*		88–89	37
(2a)	Dimethyl maleate	Dimethyl fumarate	140	*(9a)*		110.5–111.5	89
(2a)	Maleic anhydride	Dimethyl fumarate	150	*(9b)*		240(decomp.)	100
(9a)	Ozone	Hydrogen	–70[b]	*(10)*		>160 (decomp.)	31
(4a)	Ozone	Hydrogen	–70[b]	*(7)*		99–100	77
(2a) + *(2b)*	Dimethyl acetylenedicarboxylate	–	85	*(11a)* + *(11b)* [c]	58–60/10^{-4}	(1.4955)	94
(11a) + *(11b)*	*p*-Chloranil	–	140	*(12)*		125	58
(2a) + *(2b)*	Dimethyl acetylenedicarboxylate	Dimethyl acetylenedicarboxylate	150	*(13a)* + *(13b)* [c]	180/10^{-4}	highly viscous	92
(13a) + *(13b)*	*p*-Chloranil	–	140	*(14)*		243–244	56

[a] A mixture of *(2a)* and *(2b)* was used, only *(2a)* actually reacting under the conditions given.

[b] Temperature of ozonolysis.

[c] Ratio a:b = 78:22 according to the ^{1}H-NMR spectrum.

and working-up losses amounted to 6.3 g = 2.9%. [Yields calculated with respect to reacted *(1)*.] The reaction products were fractionated in a 2-m packed column. *(2a)* + *(2b)* (≈ 1:1), b.p. 74–74.5 °C/80 torr, $n_D^{20} = 1.4898$. *(2a)* + *(2b)* still contained 4% of *cis,cis*-1,3-cyclooctadiene. This additional compound can be detected gas chromatographically only after hydrogenation. *(3)*, b.p. 67 °C/100 torr, $n_D^{20} = 1.4801$.

Received: January 2, 1969 [Z 930 IE]
German version: Angew. Chem. *81*, 186 (1969)

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Synthesis of *trans/syn-* and *trans/anti*-Dimeric Uracil[1]

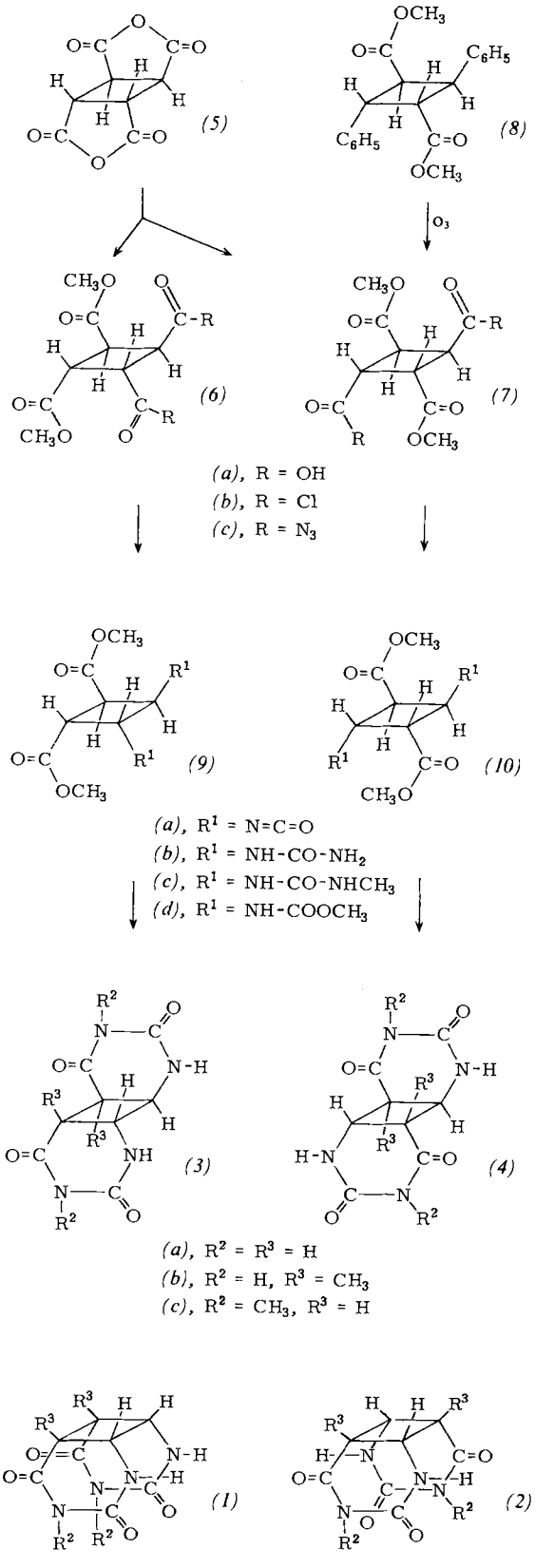
By *P. Richter* and *E. Fahr* [*]

The action of UV radiation on nucleic acids leads to, *inter alia*, dimers of thymine, cytosine, and uracil. These are considered as key compounds for biological damage by UV radiation[2]. In principle, the isomers *(1)*–*(4)* can be formed in such a dimerization. The four isomers of dimeric thymine *(1b)*–*(4b)* have been prepared by UV dimerization of thymine, thymidine, and thymidyl(3′,5′)thymidine[3]; but only the isomers *(1a)* and *(2a)* of dimeric uracil have been known to date[4]. Attempts to prepare *(3a)* and *(4a)* did not lead to products of certain structure[5]; however, these isomers have now been prepared by the following route:

When the dianhydride *(5)*, whose structure is certain[6], is boiled for 2 h with an excess of anhydrous methanol, a mixture is formed of the half-esters *(6a)* and *(7a)*, which can be separated by fractional crystallization from ethyl acetate/*n*-hexane [*(6a)*, yield 39%, m.p. 110–112 °C; *(7a)*, yield 49%, m.p. 189–190 °C]. *(7a)* is also obtained by ozonolysis of dimethyl α-truxillate *(8)*: ozone (*ca.* 17 g) is led into a solution of *(8)* (6.5 mmoles) in ethyl acetate/acetic acid (200 ml) at room temperature, 30% aqueous H_2O_2 (20 ml) is added and the mixture is left for 48 h at room temperature; the solvent is then removed in a vacuum, and the residual oil is rubbed with ethyl acetate/*n*-hexane [yield of *(7a)*, 30%].

The half-esters *(6a)* and *(7a)* are converted separately by thionyl chloride into the acid chlorides *(6b)* and *(7b)* [*(6b)*, yield 85%, m.p. 56–58 °C; *(7b)*, yield 81%, m.p. 80–82 °C], which on treatment with NaN_3 in $CHCl_3$ solution afford the unstable azides *(6c)* and *(7c)*. These azides are not isolated; when heated for an hour under nitrogen they rearrange with loss of N_2 into the isocyanates *(9a)* and *(10a)*[7], which, when gaseous NH_3 is led into their solutions in $CHCl_3$ at room temperature, give the diureido compounds *(9b)* and *(10b)* [*(9b)*, yield 76% calc. on *(6b)*, m.p. 238–239 °C; *(10b)*, yield 81% calc. on *(7b)*, m.p. 198–200 °C; isolated by filtration of the crude product that separates during the reaction and recrystallization from methanol]. When treated separately with 2 N HCl at 70 °C for 2 h, *(9b)* and *(10b)* afford the dimers *(3a)* and *(4a)* [*(3a)*, yield 90%, m.p. from 320 °C (dec.); *(4a)*, yield 75%, m.p. from 300 °C (dec.); the product that separates during the reaction is purified by washing with water]. *(4a)* is less stable thermally than *(3a)*; when boiled with 2 N HCl it is cleaved to uracil.

IR spectroscopic comparison of *(3a)* and *(4a)* with a product considered[5] to be a mixture of *(3a)* and *(4a)* showed that product was *(3a)* and not a mixture thereof with *(4a)*; a mixture is first formed, but *(4a)* decomposes under the reaction conditions.



The above method of synthesis also permits preparation of substituted dimers. For instance, *(9a)* and *(10a)* with methylamine afford, respectively, *(9c)* and *(10c)* [*(9c)*, yield 74% calc. on *(6b)*, m.p. 230–231 °C; *(10c)*, yield 79% calc. on *(7b)*, m.p. 212–214 °C], which when warmed for several hours with 2 N HCl at 70 °C pass into the dimethylated dimers *(3c)* and *(4c)* [*(3c)*, yield 54%, m.p. from 300 °C (dec.); *(4c)*, yield 32%, m.p. 226–228 °C].

Received: January 2, 1969 [Z 931 IE]
German version: Angew. Chem. *81*, 188 (1969)

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[1] Part 16 of: The Action of Radiation on Nucleic Acid Components. – Part 15: ref. [4].

[2] See the review by *E. Fahr*, Biophysik *5*, 2 (1968).

[3] *D. Weinblum* and *H. E. Johns*, Biochim. biophysica Acta *114*, 450 (1966).

[4] *E. Fahr*, *G. Fürst*, and *R. Pastille*, Z. Naturforsch. *23b*, 1387 (1968).

[5] *G. Dörhöfer* and *E. Fahr*, Tetrahedron Letters *1966*, 4511.

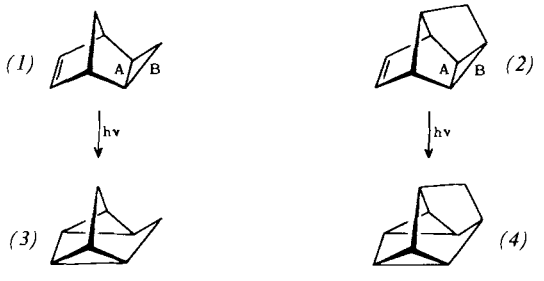
[6] *R. Criegee* and *H. Höver*, Chem. Ber. *93*, 2521 (1960); *G. W. Griffin*, *A. F. Vellturo*, and *K. Furukawa*, J. Amer. chem. Soc. *83*, 2725 (1961).

[7] When boiled for 2 h with methanol, *(9a)* and *(10a)* give, respectively *(9d)* (yield 82%, m.p. 173–174 °C) and *(10d)* (yield 70%, m.p. 164–166 °C).

Photoisomerization of Derivatives of 5-Methylenetetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene[1]

By *H. Prinzbach* and *W. Auge*[*]

The rates and selectivities of photorearrangement differ for compounds of types *(1)* and *(2)*, but generally [2π + 2σ]-cycloaddition between a C=C bond and the internal cyclopropane bond A is favored, this giving compounds *(3)* and *(4)*, respectively[2,3].

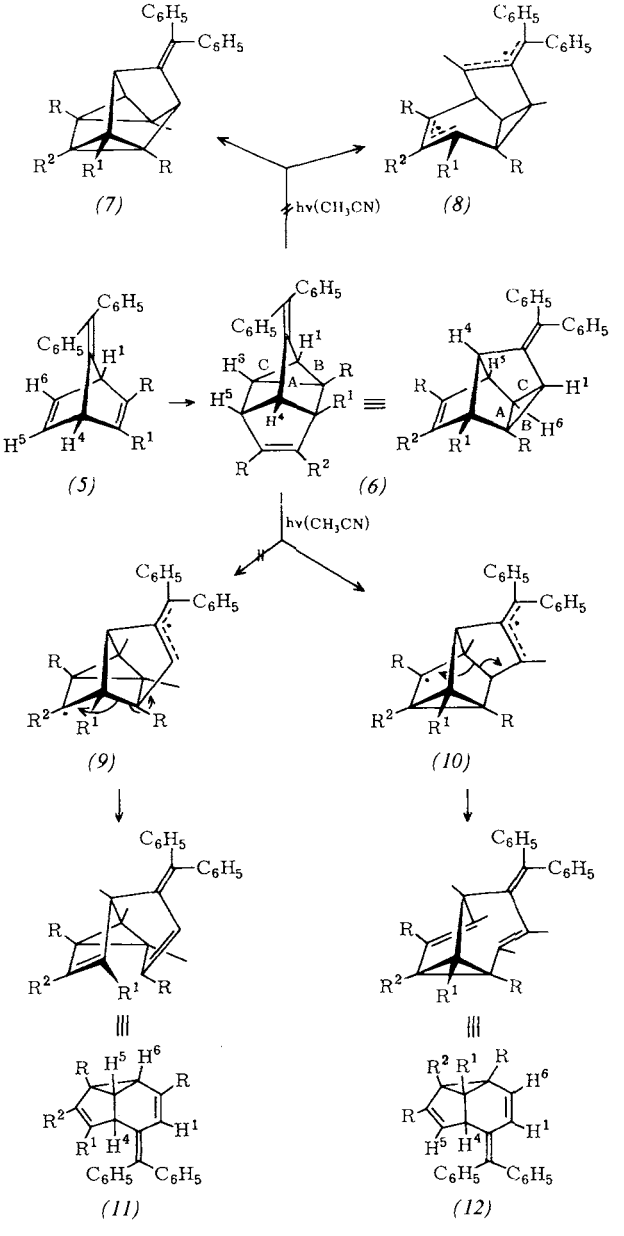


The additional activation[4] of the cyclopropane bonds B and C in methylenetetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene derivatives *(6a)–(6c)*[5] leaves no detectable opportunity for [2π + 2σ]-valence isomerization to afford *(7a)–(7c)*. Thus their direct activation affords the novel 5-methylenetricyclo-[4.3.0.0^{2,9}]nonadiene compounds *(12a)–(12c)* in good to very good yields[7].

In a typical experiment a degassed solution of *(6a)* (*ca.* 450 mg) in acetonitrile (250 ml) is irradiated at −20 °C for *ca.* 180 min with a Hanau Q 81 high-pressure lamp and a Vycor glass filter. The isomerization was followed by qualitative kinetic measurements (UV) which disclosed two isosbestic points, namely, at 228 and 271 nm; in spite of its high self-absorption, the product *(12a)* is largely stable under the conditions of the photolysis: brief over-irradiation decreases the yields only slightly. *(12a)* forms colorless, small crystals from methanol.

The structures of the new compounds *(6)* and *(12)*[8] are proved by their physical data (see Table)[9] and by chemical transformations[10]. As expected, the UV maxima[11] for compounds *(12a)–(12c)* are scarcely influenced by the various substitutions, and the NMR results agree well with those for model substances. The alternative structures *(11a)* to *(11c)* are excluded, as are those of products that can be derived by *a priori* very plausible isomerizations of the 1,5-diene system to bisallyl radicals such as *(8)*[14].

The excited substrates *(6a)–(6c)* become stabilized selectively by fission of the cyclopropane bond B that is activated by the ester group, which, at least for *(6b)* and *(6c)*, results in the diradicals *(10b)* and *(10c)* which are more stable than *(9b)* and *(9c)*[15]. There are previous examples[17] of a similar directing influence of methoxycarbonyl groups on the course of photochemical reactions.



(a), R^1 = H, R = R^2 = CO_2CH_3
(b), R = R^1 = CO_2CH_3, R^2 = H
(c), R^1 = R^2 = H, R = CO_2CH_3
(d), R = R^1 = R^2 = CO_2CH_3

(For ease of comparison the numbering of the protons is kept the same in all the formulas.)

Compound M.p. (°C)	UV [a] λ_{max} (nm) (ε)	NMR [b] (τ)								Molecular ion at *m/e*	Yield [c] (%)
		H^1	R^1 (H^3)	R^2 (H^7)	H^4	H^5	H^6	CO_2CH_3	C_6H_5		
(5a) (142)	218 (S, 20400) 225 (S, 18800) 250 (19500) 305 (S, 1600)	5.42 (M)	2.15 (dD) $J^{3,4} = 3.5$ $J^{1,3} = 1.1$	—	5.70 (M)	2.35–3.00 (M)		6.20 (S)	2.35–3.00 (M)	—	50
(5b) (137–138)	215 (S, 19700) 223 (S, 17900) 249 (18400) 307 (S, 760)	5.59 (T) $J = 2.1$	6.29 (S)	—	5.59 (T) $J = 2.1$	2.70–3.10 (M)		6.29 (S)	2.70–3.10 (M)	—	92
(6a) (119–120)	231 (19600) 276 (15100)	6.94 (dD) $J^{1,6} = 5.3$ $J^{1,4} = 1.5$	6.62 (M)	6.21–6.36	7.00 (M)	6.40 (M)	7.25–7.42 (M)	6.36 (S) 6.21 (S, S)	2.50–3.03 (M)	456	51
(6b) (151–152)	230 (20300) 275 (15400)	6.87 (dD) $J^{1,6} = 5.3$ $J^{1,4} = 1.5$	6.18–6.44	2.60–3.15 (M)	7.03 (M)	6.54 (M)	7.32–7.50 (M)	6.18–6.44 (S, S, S)	2.60–3.15 (M)	—	18
(6c) (190)	230 (18400) 275 (16000)	6.92 (dD) $J^{1,6} = 5.3$ $J^{1,4} = 1.5$	6.64 (M)	2.50–2.90 (M)	7.12 (M)	6.54 (M)	7.34–7.51 (M)	6.20 (S) 6.28 (S)	2.50–2.90 (M)	—	60
(12a) (168–169)	230 (S, 16200) 295 (18300)	4.00 (D) $J^{1,6} = 10$	6.97 (D) $J^{3,4} = 7.5$	6.13–6.50	5.82 (dD) $J^{3,4} = 7.5$ $J^{4,5} = 2.1$	3.37 (M)	3.70 (D) $J^{1,6} = 10$	6.13–6.50 (S, S, S)	2.52–3.10 (M)	—	96
(12b) (108–109)	231 (S, 15100) 289 (18400)	4.26 (D) $J^{1,6} = 10$	6.20–6.50	6.20–6.50	5.75 (D) $J^{4,5} = 2.1$	3.45 (M)	3.56 (D) $J^{1,6} = 10$	6.20–6.50 (S, S, S)	2.60–3.22 (M)	—	80
(12c) (166–167)	231 (S, 17800) 291 (19400)	4.03 (D) $J^{1,6} = 10$	7.42 (T) $J^{3,7} = 7$ $J^{3,4} = 7$	6.89 (D) $J^{3,7} = 7$	5.96 (dD) $J^{4,3} = 7$ $J^{4,5} = 2.5$	3.40 (M)	3.67 (D) $J^{1,6} = 10$	6.20–6.40 (S, S)	2.56–3.07 (M)	398	95

[a] In ethanol; S denotes shoulder. [b] In CCl_4. [c] Not optimized.

Received: January 2, 1969 [Z 932 IE]
German version: Angew. Chem. *81*, 222 (1969)

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[1] Part 26 of Photochemical Rearrangements. – Part 25: *G. Kaupp* and *H. Prinzbach*, Liebigs Ann. Chem., in press.

[2] *H. Prinzbach*, *W. Eberbach*, and *G. v. Veh*, Angew. Chem. *77*, 454 (1965); Angew. Chem. internat. Edit. *4*, 436 (1965); *P. K. Freeman*, *D. G. Kuper*, and *V. N. M. Rao*, Tetrahedron Letters *1965*, 3301; *H. Prinzbach* and *W. Eberbach*, Chem. Ber. *101*, 4083 (1968); cf. also *H. Prinzbach* and *H.-D. Martin*, Helv. chim. Acta *51*, 438 (1968).

[3] *H. Prinzbach* and *D. Hunkler*, Angew. Chem. *79*, 232 (1967); Angew. Chem. internat. Edit. *6*, 247 (1967); *C. F. Huebner et al.*, Chem. Commun. *1966*, 419; *M. Takahashi et al.*, Tetrahedron Letters *1968*, 3387; *R. M. Coates* and *J. L. Kirkpatrick*, J. Amer. chem. Soc. *90*, 4162 (1968); *P. v. R. Schleyer* and *R. E. Leone*, *ibid. 90*, 4164 (1968).

[4] *K. W. Egger*, *D. M. Golden*, and *S. W. Benson*, J. Amer. chem. Soc. *86*, 5420 (1964); *J. A. Berson* and *E. J. Walsh* jr., *ibid. 90*, 4730 (1968).

[5] The substrates *(6a)–(6c)* can be obtained in useful yields from the methylenenorbornadiene derivatives *(5)* [6] and dimethyl acetylenedicarboxylate (ADM) or methyl propiolate. In these additions, vicinal introduction of two ester groups is always avoided; correspondingly, only a 2–5% yield of *(6d)* – insufficient for preparative purposes – is obtained by reaction of *(5b)* with ADM.

[6] *H. Prinzbach* and *J. Rivier*, Tetrahedron Letters *1967*, 3713.

[7] Quantum yield for *(6c)* → *(12c)* at 300 nm (CH_3CN) is $\Phi = 0.20$ (*G. Kaupp* and *H. Prinzbach*, unpublished work).

[8] Elemental analyses are available.

[9] We thank Dr. *H. Achenbach* for determination of the mass spectra and their discussion.

[10] *M. Basbudak*, Diplomarbeit, Universität Freiburg (Germany).

[11] 1,1-Diphenylbutadiene: λ_{max} (cyclohexane) = 297 nm (ε = 18200), 236 (S, 5100) [12]. Dimethylbicyclo[3.1.0]hex-2-ene-3,5-dicarboxylate: λ_{max} (ethanol) = 237 nm (ε = 6440) [13].

[12] *J. J. Eisch* and *G. R. Husk*, J. org. Chemistry *31*, 589 (1966).

[13] *H. Prinzbach*, *H. Hagemann*, *J. H. Hartenstein*, and *R. Kitzing*, Chem. Ber. *98*, 2201 (1965).

[14] See, *e.g.*, *W. Eberbach* and *H. Prinzbach*, Helv. chim. Acta *50*, 2490 (1967). Photolysis of dienes analogous to *(6)* but with a blue-shifted *exo*-methylene chromophore (dimethylmethylene) afforded products that can be formally derived from *(8)*, in yields comparable with those of the compounds *(12)* that were also obtained (*H. Prinzbach* and *W. Auge*, unpublished work).

[15] There are as yet no exact views as to the extent of the stabilization of an alkyl radical by a neighboring methoxycarbonyl group. The currently accepted RE values range from 4 to 9 kcal/mole [16].

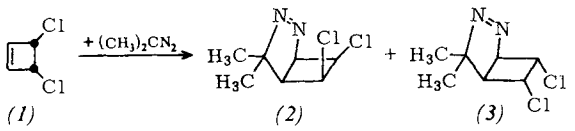
[16] *B. C. Roquitte* and *W. D. Walters*, J. Amer. chem. Soc. *84*, 4049 (1962); J. physic. Chem. *68*, 1906 (1964); *S. W. Benson*, *K. W. Egger*, and *D. M. Golden*, J. Amer. chem. Soc. *87*, 468 (1965); *H. M. Frey*, Advances in Physical Organic Chemistry *4*, 176 (1966); *D. J. Trecker* and *R. S. Foote*, J. org. Chemistry *33*, 3527 (1968); *H. Prinzbach* and *H.-D. Martin*, Chimia *23*, 37 (1969).

[17] *H. Prinzbach* and *E. Druckrey*, Tetrahedron Letters *1965*, 2959; *E. Ciganek*, J. Amer. chem. Soc. *88*, 2882 (1966).

Influence of Chlorine as Substituent on the Course of 1,3-Dipolar Cycloadditions of Diazoalkanes

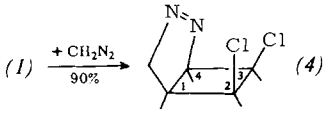
By *M. Franck-Neumann* [*]

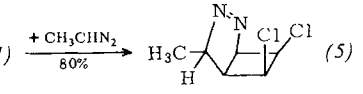
1,3-Dipolar additions of diazoalkanes represent a well known class of reactions [1] that proceed stereospecifically [2] according to a synchronous mechanism [3]. Whereas the electronic effect of substituents attached to the double or triple bond on the rate of reaction has been investigated by *Huisgen et al.* [3], little is known about the effect of substituents not attached to the double bond. As we found in earlier investigations, the highly reactive but sterically demanding compound 2-diazopropane reacts quantitatively with *cis*-3,4-dichlorocyclobutene *(1)* to form the isomeric pyrazolines *(2)* and *(3)* (ratio 1:2.5) [4].



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

If this reaction is carried out with diazomethane or diazoethane, then only one pyrazoline [*(4)* or *(5)*, respectively] is formed in each case.

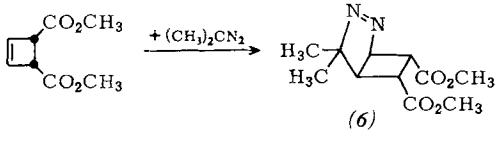




The IR and UV spectra of the adducts *(4)* and *(5)* contain the characteristic absorption bands of the azo group: $\nu(N=N)$ = 1540 cm^{-1}; λ_{max} *(4)* = 322 nm[5]; λ_{max} *(5)* = 325.5 nm; ε = 300. The NMR spectra resemble that of pyrazoline *(2)*: the situation differs from that of the pyrazoline *(3)*, the chemical shifts of the protons H-2, H-3, and H-4 in *(2)* all lying in the same region. Like *(2)*, the adducts *(4)* and *(5)* are much more strongly polar than *(3)* (behavior on thin-layer chromatography, solubility).

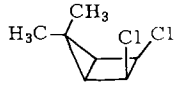
These results can only be explained if the pyrazolines *(2)*, *(4)*, and *(5)* are assumed to be in the *cisoid* form.

In contrast, *cis*-dimethyl 1,2-cyclobutenedicarboxylate[6] does not react with an excess of diazomethane; the sole product of its reaction with 2-diazopropane is the adduct *(6)* [$\nu(N=N)$ = 1540 cm^{-1}, λ_{max} = 328 nm (ε = 218), yield 85%], which has been shown to have a *transoid* structure by NMR spectrometry.

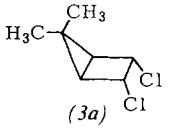


(6)

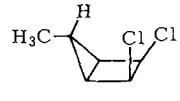
Confirmation of the stereochemistry of the pyrazolines *(2)*, *(3)*, *(5)*, and *(6)*[5] is also provided by their sensitized photolysis[4] to the bicyclo[2.1.0]pentane derivatives *(2a)*, *(3a)*, *(5a)*, and *(6a)* (IR spectrum shows no double bonds; only end absorption is observed in the UV spectrum).



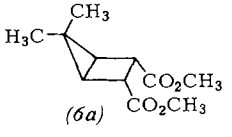
(2a)



(3a)



(5a)



(6a)

The two methyl singlets in the spectrum of *(3a)* and of *(6a)* appear close to each other and have almost the same values of δ (0.96 and 1.27, and 0.98 and 1.21 ppm, respectively), whereas a large difference is observed in the case of *(2a)* (0.92 and 1.62 ppm). It must therefore be concluded from the observed δ value of 1.02 ppm (doublet with J = 6 Hz) that the methyl group in *(5a)* is in the *exo* position. The signal due to H-2 and H-3 also shows that *(2a)* and *(5a)*, and also *(3a)* and *(6a)*, have the same stereochemistry[7].

(2a), δ = 4.72 ppm (T), J = 2 and 2.5 Hz;

(5a), δ = 4.74 ppm (T), J = 1.8 and 2.4 Hz;

(3a), δ = 4.13 ppm (slightly split singlet), J = 0.8 and 0.8 Hz;

(6a), δ = 2.86 ppm (broad singlet), $J \leq 0.8$ Hz.

From these observations it must be assumed that in the transition state the chlorine atoms of *cis*-3,4-dichlorocyclobutene interact with the nitrogen atoms of the diazoalkanes, thereby causing orientation of the molecule and acceleration of the addition.

Received: January 7, 1969 [Z 934 IE]
German version: Angew. Chem. *81*, 189 (1969)

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[1] *R. Huisgen*, Angew. Chem. *67*, 439 (1955).

[2] *T. V. van Auken* and *K. L. Rinehart Jr.*, J. Amer. chem. Soc. *84*, 3736 (1962).

[3] *R. Huisgen, H. Stangl, H. J. Sturm*, and *H. Wagenhofer*, Angew. Chem. *73*, 170 (1961).

[4] *M. Franck-Neumann*, Tetrahedron Letters *1968*, 2979.

[5] The pyrazoline *(4)* decomposes even at room temperature with decrepitation. Its NMR spectrum was therefore recorded at a temperature below 0 °C; it is also impossible to give an exact value for the extinction in the UV. All attempts to photolyze *(4)* to the bicyclo[2.1.0]pentane system were unsuccessful.

[6] *E. Vogel*, Liebigs Ann. Chem. *615*, 14 (1958); *G. Koltzenburg, P. G. Fuss*, and *J. Leitich*, Tetrahedron Letters *1966*, 3409.

[7] The NMR spectra were evaluated as first order spectra; the values of J given are therefore not the true but the apparent coupling constants.

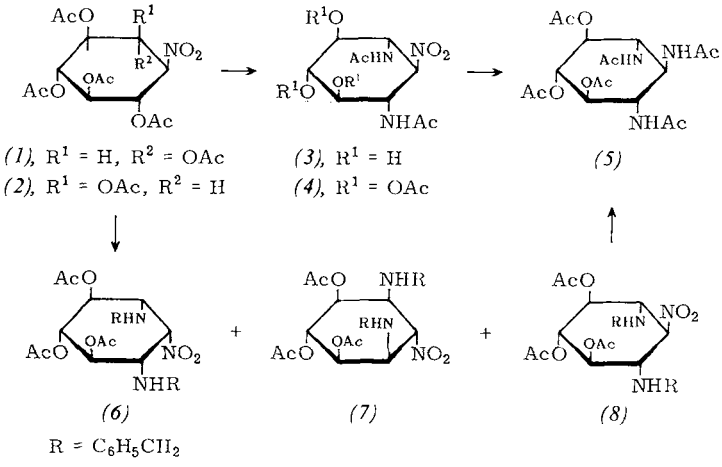
A New Route to Inosatriamines and Triamino Sugars

By *F. W. Lichtenthaler, P. Voss*, and *N. Majer*[*]

Numerous synthetic routes have been devised[2] to the inosamines, inosadiamines, and mono- and di-amino sugars that occur in Nature[1], yet there has so far been no systematic investigation of inositols or sugars containing three amino groups although two 1,3,5-inosatriamines[3,4] and two triamino sugars[5,6] have been prepared. Continuation of our work on the diamination of cyclic nitro diols[6,7] has now led to a new and satisfactory synthetic route to this class of compounds.

2-Nitroalkyl acetates can be converted into nitro amines in one stage by amines or ammonia[8] and this reaction can be applied to cyclic nitro di- and oligo-acetates of types *(1)*, *(2)*, *(9)*, and *(14)* which yield vicinal triamino compounds on hydrogenation of the primary products.

In this way penta-*O*-acetyl-1-deoxy-1-nitroinositol with the *scyllo*- *(1)* or *myo*-configuration *(2)*[9] gives, in both cases, di-*N*-acetyl-2-deoxy-2-nitro-*scyllo*-1,3-inosadiamine *(3)*, decomp. 296–298 °C, in 50–60% yield[10] on treatment with concentrated aqueous ammonia-dioxane (1:1) for 10 h at 25 °C and subsequent *N*-acetylation by acetic anhydride in methanol. Further acetylation by acetic anhydride converts *(3)* into the pentaacetate *(4)*, decomp. 295–298 °C, with CH_3CO resonances at τ = 8.09 (9H) and 8.26 (6H) in [D_6]-DMSO. Hydrogenation of *(3)* over 10% palladium-charcoal and subsequent acetylation affords, smoothly, hexaacetyl-*scyllo*-1,2,3-inosatriamine *(5)*, m.p. 296–298 °C (decomp.)[11] whose acetyl resonances (9H, S, at both τ = 8.09 and 8.28 in [D_6]-DMSO, τ = 7.96 and 8.07 in D_2O) unambiguously prove the presence of three acetoxy and three acetamido groups, all in the equatorial orientation[12].

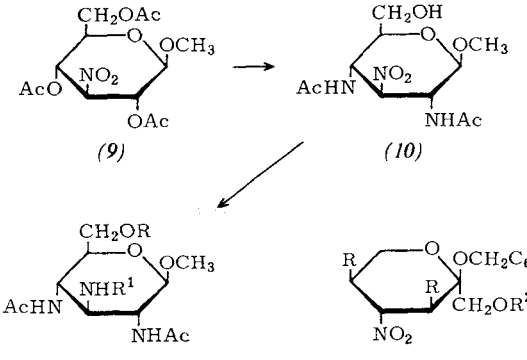


(1), R^1 = H, R^2 = OAc
(2), R^1 = OAc, R^2 = H
(3), R^1 = H
(4), R^1 = OAc
(5)
(6)
(7)
(8)
R = $C_6H_5CH_2$

The results of treating *(1)* or *(2)* (1 mole) with benzylamine (3 moles) in dioxane at 25 °C for 12 h are sterically less homogeneous, for a crystalline mixture of three nitro diamines (70% yield) results, from which the *myo*-isomer *(6)*, rhombs, m.p. 153–154 °C, can be isolated in 7% yield by fractional crystallization, whereafter thin-layer chromatography of the mother-liquor[13] affords the *scyllo*- [*(8)*, needles, m.p. 142 to 143 °C] and the *muco*-compound [*(7)*, needles, m.p. 144 to 145 °C] in 5 and 18% yield, respectively. The configurations of *(6)*–*(8)* were assigned unambiguously from the splitting patterns for the ring-protons in the 100 MHz spectra[14] and in the case of *(8)* by hydrogenation and acetylation to *(5)*.

Methyl tri-*O*-acetyl-3-deoxy-3-nitro-β-D-glucopyranoside *(9)*[15] affords analogously methyl 2,4-bis(acetylamino)-2,3,4-trideoxy-3-nitro-β-D-glucopyranoside *(10)* [(53% yield), dec. at ~ 280 °C, $[\alpha]_D^{22} = -9.3°$ (c = 0.4 in CH_3OH)] when treated with ammonia in methanol and then *N*-acetylated. Hydrogenation of *(10)* over 10% palladium-charcoal in 10:1 methanol-glacial acetic acid gives the acetate salt *(11)* [decomp. from 240 °C, $[\alpha]_D^{22} = -14.2°$ (c = 1 in H_2O), in 85% yield], and appropriate acetylation then yields the tetraacetate *(12)* [m.p. 324–326 °C (decomp.), $[\alpha]_D^{22} = -13.5°$ (c = 0.3 in H_2O)] or the tri-*N*-acetate *(13)* [decomp. 315 °C, $[\alpha]_D^{22} = -11.8°$ (c = 0.5 in CH_3OH)].

The *gluco*-configuration of these compounds follows from the NMR spectra (in [D_6]-DMSO): the proton on C-3 in *(10)* was shown at τ = 4.88 as a 10-Hz triplet, which proves the axial orientation of H-2, H-3, and H-4; and these assignments are confirmed[16] by the positions of the *N*-acetyl resonances of *(10)* (6 H, S, at τ = 8.22) and the acetyl resonances of *(12)* [8.00 (3H), 8.26 (6H), 8.28 (3H)].



(9)
(10)
(11), R = H; R^1 = H • HOAc
(12), R = R^1 = Ac
(13), R = H; R^1 = Ac
(14), R = OAc, R^2 = Ac
(15), R = NHAc, R^2 = Ac
(16), R = NHAc, R^2 = H

Under the same conditions as for *(9)*, the triacetylnitrosorboside *(14)*[17] is diaminated to yield benzyl 3,5-bis(acetylamino)-3,5,4-trideoxy-4-nitro-α-L-glucopyranoside *(16)* [m.p. 260–261 °C (decomp.), $[\alpha]_D^{23} = -97°$ (c = 0.4 in CH_3OH)] and two further, as yet unidentified products. The configuration was deduced from the NMR data for *(15)* [m.p. 224–225 °C, $[\alpha]_D^{23} = -63°$ (c = 0.5 in CH_3OH)]: after elimination of the 3,NH coupling by double resonance for H-3 and H-4, a characteristic AB system appeared for which J_{34} = 9 Hz can be calculated.

Triaminopentoses and triamino-6-deoxyhexoses may also become readily accessible by applying the reaction sequence diamination → *N*-acetylation → hydrogenation to other nitro sugar acetates[18]. Synthesis of dinitroinosatriamines[14] and triamino sugar nucleosides[19] has already been realized.

Received: December 21, 1968; revised: January 27, 1969 [Z 933 IE]
German version: Angew. Chem. *81*, 221 (1969)

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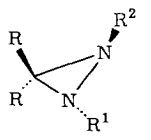
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Separation of Invertomers (Diastereoisomers) of Diaziridines. Slow Inversion at Tervalent Nitrogen Atoms[1]

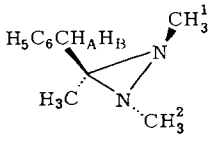
By *A. Mannschreck* and *W. Seitz*[*]

At temperatures up to 100 °C diaziridines *(1)* with different substituents R^1 and R^2 on the nitrogen atoms give ^{1}H–NMR spectra showing two resonances for the groups R on the ring

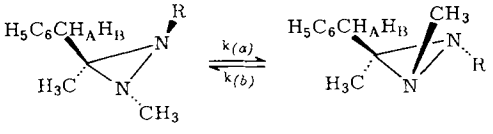
carbon atom[2]. It is thence concluded that inversion of at least one nitrogen atom is a relatively slow process; lower limiting values of 21 kcal/mole can be calculated for the free enthalpies of activation $\Delta G_c^{\ddagger}$. It was therefore predicted[2] that it should be possible to separate the 'invertomers' (diastereoisomers) of suitably substituted diaziridines and similarly also of oxaziridines. *Brois*[3] and *Felix* and *Eschenmoser*[4] have isolated the isomers of 1-chloroaziridines; the presence of optically active oxaziridines[5] has been recently proved[**]; but stable invertomers of diaziridines have not previously become known.



(1), R = H or CH_3



(2)



(3a), R = $CH_2C_6H_5$
(4a), R = H

(3b), R = $CH_2C_6H_5$
(4b), R = H

A limiting value for $\Delta G_c^{\ddagger}$ can also be obtained for *(2)* having equal substituents on the nitrogen atoms but different groups on the ring carbon atom. Compound *(2)* was prepared with m.p. 24–26.5 °C from benzyl methyl ketone, methylamine, and *N*-methylhydroxylamine-*O*-sulfonic acid by a procedure analogous to that described by *Schmitz*[6]. The *N*-methyl signals, of equal intensity, at τ = 7.43 and 7.59 (in diphenyl ether at 28 °C) are not broadened at 159 °C, whence a lower limit of 22 kcal/mole is obtained for $\Delta G_c^{\ddagger}$. Furthermore the spectrum contains, besides the multiplet for the phenyl protons, only the *C*-methyl singlet at τ = 8.92 and the AB absorption of the methylene group at 7.17 and 7.35 (J = 13.9 Hz). These findings can be accommodated only by the *trans*-structure *(2)*.

We have realized the predicted separation in the case of *(3a)* and *(3b)*. The mixture obtained in the synthesis from benzyl methyl ketone, benzylamine, and *N*-methylhydroxylamine-*O*-sulfonic acid gave two non-crystalline products *(3a)* and *(3b)* when twice subjected to preparative thin-layer chromatography at 20 °C on silica gel (Merck's HF_{254}) with 9:1 benzene/ethanol as eluant:

	R_F	$n_D^{19.8}$	τ (N–CH_3)	τ (N–CH_2)	τ (C–CH_3)	τ (C–CH_AH_B)
(3a)	0.6	1.5545	7.64	6.20	8.88	7.06; 7.29 (J = 13.9 Hz)
(3b)	0.5	1.5572	7.46	6.43	8.81	7.15; 7.28 (J = 13.9 Hz)

The τ values (in CCl_4 at 28 °C) agree with those of known diaziridines[2]. The *(3a)* obtained showed no signals of the other isomer, but the experimental samples of *(3b)* still contained 6% of *(3a)*. Elemental analyses and molecular weights accorded with expectation; so did the IR spectra, which differed only slightly, namely, in the region 1080 to 1130 cm^{-1}; both products exhibited the oxidizing power characteristic of diaziridines An equilibrium containing 49.8 ± 0.4% of *(3a)* was established with a half-life of 431 min in C_2Cl_4 solutions at 70.0 °C, whether *(3a)* or *(3b)* was the starting material. Thence the rate constant $k_{(3a)} = k_{(3b)} = 1.34 \times 10^{-5}$ sec^{-1} and $\Delta G^{\ddagger}_{(3a)} = \Delta G^{\ddagger}_{(3b)} = 27.3 \pm 0.2$ kcal/mole were calculated[7].

Compounds *(4a)* and *(4b)* behaved analogously: pure *(4a)*, m.p. 27–28 °C, crystallized from a solution of their mixture[8] in pentane at −10 °C. Repeated removal of *(4a)* by crystallization and thin-layer chromatography afforded 90%-pure *(4b)* with m.p. < 5 °C. Under the experimental conditions used for *(3a)* and *(3b)* the values $R_{F(4a)} = 0.4$, $R_{F(4b)} = 0.3$, $\Delta G^{\ddagger}_{(4a)} = 27.1$, and $\Delta G^{\ddagger}_{(4b)} = 26.3$ kcal/mole were obtained[9]; thus one isomer preponderates (75.3%) in the equilibrium mixture and we attribute the structure *(4a)* to it for steric reasons. The assignments of *(3a)* and *(3b)* could only be made on the basis of this finding.

Since no sign of by-products appeared during any of the equilibrations carried out, we assign a low probability to mechanisms in which the three-membered ring is opened; it is more likely that the isomers are interconverted by consecutive inversions at the nitrogen atoms[10].

Received: January 13, 1969 [Z 935 IE]
German version: Angew. Chem. *81*, 224 (1969)

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[**] *Note added in proof* (Feb. 17, 1969): Very recently we have concentrated the two invertomers (diastereoisomers) of 2,3-dimethyl-3-benzyloxaziridine. At 75 °C no sign of equilibration was observed over a period of 3.5 days, *i.e.* $\Delta G^{\ddagger} > 30$ kcal/mole. *A. Mannschreck* and *J. Linss*, unpublished results.

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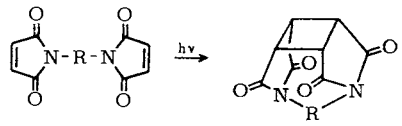
Intramolecular Photocycloaddition of *N,N'*-Alkylenedimaleimides [**]

By *F. C. De Schryver, I. Bhardwaj*, and *J. Put* [*]

Maleic anhydride and maleimide derivatives can undergo photoaddition reactions with other double or triple bonds or with themselves[1,2]. A large number of intramolecular photocycloadditions of this kind are known[3] but, as stated by *Eaton*[4], "the proximity of the condensing systems in these examples might have special significance in the ease of the cycloaddition reaction".

In most hitherto known intramolecular photodimerizations, C_4 cycloaddition[2] results in formation of a five- or six-membered ring. We wish to report the photocyclomerization of dimaleimides *(1)*, in which the reacting double bonds are separated by an alkyl chain, to the tetracyclic compounds *(2)*.

The reaction is carried out in CH_3CN or CH_2Cl_2. The structure of the product is confirmed by the IR and NMR spectral data, and especially by the mass spectra (see Table). The absorption characteristics of the –CH=CH– system in *(1)* are no longer present in *(2)*, but have been replaced by bands that can be attributed to a cyclobutane ring. The ultraviolet spectra of the products *(2)* show no absorption due to a –CH=CH–CO system at about 300 nm.



(1) (2)

	R	(1) M.p. (°C)	(1) IR (ν, cm⁻¹) [a]	(1) NMR (δ) [b]	(2) Yield (%)	(2) M.p. (°C)	(2) IR (ν, cm⁻¹) [a]	(2) NMR (δ) [b]	(2) M⁺	M.W. [c]
a	$(CH_2)_3$	174.5	3085, 680, 840	6.73	100	350	3040	—	234	
b	$(CH_2)_4$	206	3094, 690, 840	6.89	85	350	3020	3.80	248	
c	$(CH_2)_5$	107	3080, 695, 835	6.75 ∞	98	349	3010	3.80	262	264
d	$(CH_2)_6$	144 [d]	3090, 695, 835	6.74	95	291	3000	3.80	276	280
e	$(CH_2)_7$	85.5	3080, 690, 860	6.76	80	269	2980	3.80	290	
f	CH_2OCH_2	129.5 [e]	3100, 698, 840	6.81	100	320 (decomp.)	3040	—	236	

[a] In KBr. [b] Resonance signals of the four cyclobutane protons, all signals are singlets. All spectra recorded in $CDCl_3$ except for *(1b)* and *(2b)* which were recorded in [D_6]-DMSO; *(2a)* and *(2f)* are not sufficiently soluble. [c] Molecular weight measured with a Mechrolab 301 A vapor pressure osmometer in $CHCl_3$. [d] 136–141 °C [5]. [e] 128–132 ° [6].

Long-range intramolecular cyclomerizations of this kind also seem to occur during UV irradiation of dinucleotides containing pyrimidine bases[7].

As expected, when the two maleimide moieties are joined by a rigid phenyl ring, as in *m*-phenylenedimaleimide, no intramolecular cyclization occurs but a polymeric material is formed.

The cyclodimerization of *N,N'*-hexamethylenedimaleimide *(1d)* to 5,12-diazatetracyclo[10.2.1.1^{2,5}.0^{3,14}]hexadecane-4, 13,15,16-tetraone *(2d)* was studied in more detail. A tenfold increase of the concentration of *(1d)* (5×10^{-3} mol l^{-1} to 5×10^{-2} mol l^{-1}) resulted in a small decrease in the yield from 95% to 85%, the remainder being polymeric material. Addition of benzophenone as photosensitizer also decreased the yield to 80%, while the presence of oxygen in no way inhibited the reaction. Most surprising is the ease and speed of the reaction. Under the same conditions and in the absence of a sensitizer, *N*-butylmaleimide yields only 15% of the expected dimer.

Received: January 29, 1969 [Z 936 IE]
German version: Angew. Chem. *81*, 224 (1969)

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[**] The authors are indebted to the Center of High Polymer Research and Gevaert-Agfa for supporting this research and to the National Science Foundation for a fellowship (J.P.).

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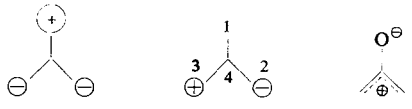
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Formal Diradicals Which Should Have Singlet Ground States[1]

By *R. Gleiter* and *Roald Hoffmann*[*]

Molecules whose every classical valence structure is at best a diradical one generally emerge theoretically and experimentally as triplet ground states. We have for some time been interested in the problem of stabilizing the singlet states of such formal diradicals[2]. Two novel procedures for accomplishing this task are reported in this communication.

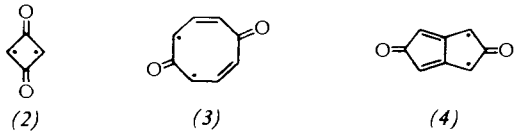
Consider trimethylenemethane, a typical carbon diradical, which in a D_{3h} geometry possesses a degenerate pair of nonbonding π orbitals. These are to be occupied by a pair of electrons, and theoretically[3] and experimentally[4] the ground state of the system appears to be a triplet. Of the two nonbonding orbitals A and B, A has density at C_1, whereas orbital B by symmetry does not[5].



A B *(1)*

Substitution in trimethylenemethane of an oxygen atom for CH_2 at the C_1 position would be anticipated to break the degeneracy of A and B by stabilizing A and leaving B unaffected. The resulting species is oxyallyl *(1)*, the ring-opened zwitterionic form of cyclopropanone. A previous calculation which we carried out on this molecule[2b] showed that the lowest singlet was considerably stabilized, but that a triplet remained the ground state of the molecule by 0.1 eV. In order to obtain diradicals with singlet ground states we scrutinized the molecular orbitals of a large number of carbon diradicals, keeping an eye out for those molecules in which one nonbonding molecular orbital possessed electron density at one or more carbon atoms which did not appear in the other nonbonding orbital. After substituting the appropriate number of oxygens in these differentiated positions we carried out Pariser-Parr-Pople calculations with extensive configuration interaction[6].

We discovered three species, *(2)–(4)*, which were definitely singlet ground states, and a number of other borderline cases. The position relative to the ground state of the first two excited states of *(2)–(4)* is listed below the corresponding formula.

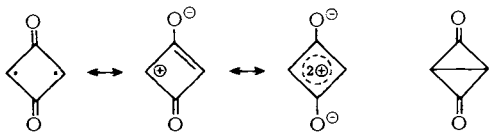


(2) *(3)* *(4)*

$^1B_{2u}$	2.03	$^1B_{2u}$	1.71	$^1B_{2u}$	2.15
$^3B_{2u}$	0.99	$^3B_{2u}$	0.34	$^3B_{2u}$	0.88
^1A_g	(0)	^1A_g	(0)	^1A_g	(0)

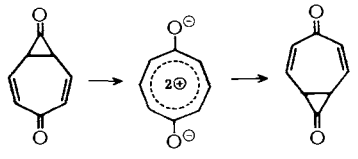
We have drawn diradical valence structures for *(2)–(4)*, but the calculations in each case showed final charge distributions characteristic of the expected polar resonance structures, such as *(2a)* and *(2b)*.

Each of these molecules would be expected to be highly colored. Substituted derivatives of *(2)* are known[7,8], and are strong chromophores.



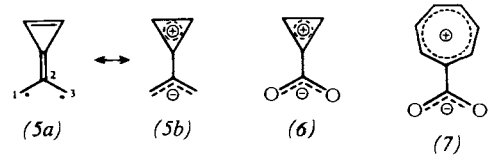
(2) (2a) (2b) (2c)

A remaining unanswered question is whether these planar molecules are in fact more stable than the nonplanar bicyclic isomers [*e.g.* *(2)* → *(2c)*]. Some extended Hückel calculations indicate that *(2)* is more stable than *(2c)*, but we do not consider the result very reliable in this instance. The stabilization of *(3)* is of great interest, since it suggests the possibility of achieving a Cope rearrangement with negative activation energy.



(3a) (3b) (3c)

A related class of molecules is exemplified by *(5)*. The classical valence structure *(5a)* implies a diradical; however, the resonance structure *(5b)* clearly suggests a closed shell, and



(5a) (5b) (6) (7)

the simple Hückel calculation gives a gap of 0.704 β between occupied and unoccupied levels[9]. Nevertheless, according to our SCF calculations the ground state of *(5)* is a triplet, some 1.1 eV below the lowest singlet – the energy gap is thus not large enough for stabilization of the singlet state.

We noticed, however, that the highest occupied MO of *(5)* was an essentially localized nonbonding allyl orbital at C-1 and C-3, whereas the lowest unoccupied MO was localized in the three-membered ring. Replacement of the methylene groups at C-1 and C-3 by oxygens produced the necessary selective stabilization of the highest occupied MO.

The ground state of the cyclopropenylium carboxylate *(6)* is a singlet, with a $^3B_2$ state 0.97 eV above it. Similarly we find a singlet ground state for the cycloheptatrienylium carboxylate *(7)*, with a $^3B_2$ state 0.97 eV above it.

Received: January 27, 1969 [Z 937 IE]
German version: Angew. Chem. *81*, 225 (1969)

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[1] The SCF–CI program we used was written by *A. Imamura*. We are grateful to the National Science Foundation, the National Institutes of Health, and the Chevron Research Corporation for financial support of this work.

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[5] A convenient basis, symmetry adapted for reduction of symmetry from D_{3h} to C_{2v}, is chosen for the degenerate orbital.

[6] The details of our particular variant are given in reference [2a]. We always included all singly and doubly excited configurations, and many higher excited configurations as well. The final results for the species *(3)*, for example, are for the 70 most significantly contributing configurations selected from a total of some 800 examined. Pariser-Parr-Pople calculations are normally quite reliable for π-electron spectra; however we have no calibration points for these diradicals, and we consider the results only qualitatively informative.

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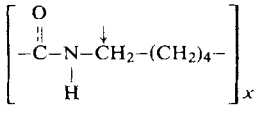
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The Thermal Oxidation of *N*-Vicinal Methylene Groups in Polyamides, a Reaction Dependent on Conformation

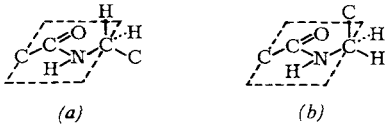
By *H. Krüssmann*, *G. Valk*, *G. Heidemann*, and *S. Dugal*[*]

In the thermal oxidation of polycaprolactam *(1)*, as in the thermal oxidation of low-molecular weight alkyl amides, the *N*-vicinal methylene group (arrowed) is the preferred site of attack[1,2].



(1)

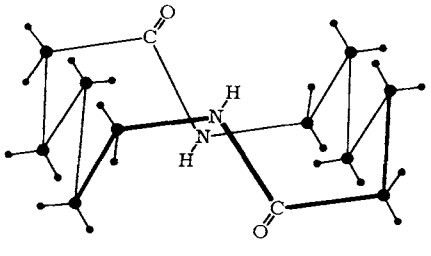
This group is distinguished by an interaction (hyperconjugation) which takes place between its protons and the 4π electrons of the carboxamide group[3]; an interaction which should be particularly intensive if the *N*-vicinal methylene group is in the *trans*-conformation to the amide group (Fig. 1).



(a) (b)

Fig. 1. *trans* (a) and *gauche* (b) conformations of the *N*-vicinal CH_2 group. The dotted parallelogram indicates the plane of the amide group.

Proof of this hypothesis was afforded by thermally oxidizing compounds *(1)* and 1,8-diazacyclotetradecane-2,9-dione [cyclo-bis(ε-aminocaproyl)] *(2)* at 200–220 °C. *(1)* and *(2)* consist of the same fundamental units; in contrast to *(1)*, compound *(2)* contains α-methylene groups in the *gauche* position only[4,5].



(2)

Under the reaction conditions the rotations of the α-methylene groups of *(1)* are no longer frozen in, so that a statistical distribution of *gauche*- and *trans*-conformations of the α-methylene groups occurs in the ordered as well as in the disordered region, whilst the conformation of *(2)*, which melts at 348 °C, remains stable[6]. Oxidation and subsequent hydrolysis leads to the formation, among other degradation products, of an homologous series of aliphatic mono- and dicarboxylic acids, aldehydes, amines, and ω-amino acids[1,2]. In order to eliminate the influence of possible different degrees of oxidation the ratio of adipic acid to *n*-butylamine was chosen as a measure of the reactivity of the *N*-vicinal methylene groups. *n*-Butylamine is not a secondary product of *N*-vicinal oxidation; it is bound as amide and occurs exclusively by way of chain cleavage as a result of loss of the α-carbon atom of the fundamental unit.

The adipic acid and *n*-butylamine were each determined gas chromatographically, the former as the dimethyl ester after ether extraction of the hydrolyzate and the latter as trifluoroacetamide after steam distillation of the hydrolyzate.

The ratio of adipic acid to butylamine in the hydrolyzate of thermally oxidized *(1)* is substantially greater than that in the hydrolyzate of thermally oxidized *(2)* (Table 1).

Table 1. Amounts of adipic acid and butylamine obtained as degradation products in the thermal- and photooxidation of polycaprolactam.

	Thermal oxidation		Photooxidation
	(1)	*(2)*	*(1)*
Adipic acid (c_1) (μmole/113 g)	12000	3000	5000
n-Butylamine (c_2) (μmole/113 g)	10	160	300
c_1/c_2	1200	19	17

A further indication of the dependence of the reactivity of *N*-vicinal groups on the conformation can be gained from the photooxidation of *(1)*[7]. The ratio of adipic acid to butylamine in the hydrolyzate of photooxidized *(1)* is of the same order of magnitude as that in the hydrolyzate of thermally oxidized *(2)*. In the photooxidation, in which the secondary reactions proceed *via* the same mechanism as the thermal oxidation[8], a constant ratio of *trans* and *gauche* *N*-vicinal methylene groups is obtained since under the reaction conditions the rotations of the methylene groups are frozen in. The disordered regions, in which the *N*-vicinal methylene groups are predominantly in the *gauche* conformation, are the only regions vulnerable to attack by oxygen.

The investigations show that the *N*-vicinal methylene groups in the *trans* conformation to the amide group are about 60 times more reactive than the *N*-vicinal methylene groups in the *gauche* position.

Received: January 9, 1969 [Z 938 IE]
German version: Angew. Chem. *81*, 226 (1969)

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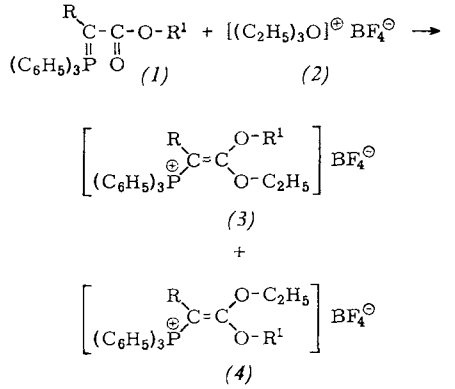
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O-Alkylation of Alkoxycarbonylalkylidenetriphenylphosphoranes

By *H. J. Bestmann*, *R. Saalfrank*, and *J. P. Snyder*[*]

Alkoxycarbonylalkylidenetriphenylphosphoranes *(1)* undergo *C*-alkylation on treatment with alkyl halides[1]. We have now found that *O*-alkylation occurs when *(1)* is treated with triethyloxonium tetrafluoroborate *(2)* to give the hitherto unknown 1-substituted 2-ethoxy-2-alkoxyvinyltriphenylphosphonium tetrafluoroborates *(3)* and *(4)*.



(1) *(2)*

(3)

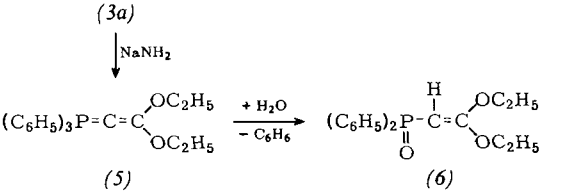
+

(4)

	R	R^1	*(3)* m.p. (°C)	yield (%)
(a)	H	C_2H_5	105	68
(b)	$C_6H_5-CH_2$	C_2H_5	178	97
(c)	C_6H_5	C_2H_5	182	99
(d)	$H_3CO_2C-CH_2$	C_2H_5	151	98
(e)	$H_5C_2O_2C$	C_2H_5	107	95
(f)	Br	C_2H_5	178 (decomp.)	98

If $R^1 \neq C_2H_5$ then a mixture of the geometric isomers *(3)* and *(4)* is formed, as suggested by our NMR-spectroscopic investigations[2]. Reaction of *(1)* with R = H and $R^1 = CH_3$ affords, for example, a mixture of 67% *(3)* [^{1}H–NMR: τ = 5.93 ($O-CH_3$), S] and 33% *(4)* [^{1}H–NMR: τ = 6.50 ($O-CH_3$), S]. In all the examples investigated, we found that protons of the O–R group *cis* to the triphenylphosphine group are shielded by the phenyl rings and appear at higher τ values than the corresponding protons of the *trans* O–R group.

Compound *(3a)* can be converted by sodium amide into the pale yellow crystalline ylid *(5)* [m.p. 83 °C, ^{1}H–NMR: τ = 8.95 (6 H ~ CH_3), T; 5.63 (4 H ~ CH_2), Q; 2.85, M; 2.00 (aromatic protons, total 15 H), M], which loses benzene on reaction with water to give the phosphine oxide *(6)* (m.p. 164 °C).



(3a) *(5)* *(6)*

General procedure for the preparation of (3), $R^1 = C_2H_5$

A solution of *(1)* (0.1 mole) in anhydrous dichloromethane is added to a well-cooled solution of *(2)* (0.1 mole) in the same solvent under nitrogen. After 30 min the reaction mixture is evaporated to dryness under vacuum and the residue is recrystallized from dichloromethane/ethyl acetate.

Received: January 17, 1969; revised: February 14, 1969 [Z 939 IE]
German version: Angew. Chem. *81*, 227 (1969)

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Temperature Dependence of the NMR Spectrum of a Soluble Ziegler-Natta Catalyst

By *K. H. Reichert* and *M. Mallmann*[*]

Biscyclopentadienylmethyltitanium(IV) chloride and trimethylaluminum react extremely rapidly with each other to form a titanium-aluminum complex. Formation of the complex is followed by very slow loss of methane[1]. The NMR signals of the methyl protons of $(C_5H_5)_2TiClCH_3$ (a) and of $Al(CH_3)_3$ (b) are shown in Figure 1.

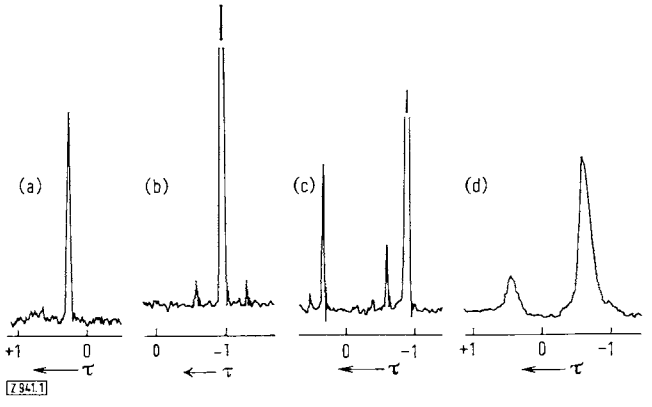
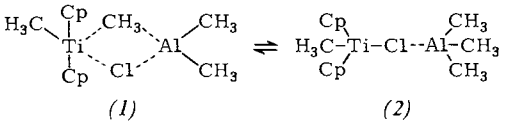


Fig. 1. ^1H—NMR spectrum a) of a 0.5 M solution of $Cp_2TiClCH_3$ in benzene at 33 °C; b) of a 0.5 M solution of $Al(CH_3)_3$ in benzene at 33 °C; c) immediately after mixing solutions of both compounds in toluene at 33 °C, $[Cp_2TiClCH_3] = 0.38$ mole/l, $[Al(CH_3)_3] = 0.5$ mole/l; d) after cooling the reaction solution to −60 °C. TMS was used as external standard.

Immediately after the mixing of the above components, three resonance signals (c) appear in the ratio 1:0.47:3.8. The two outer signals appear at almost the same position as do those of the starting compounds. The intensity of the middle signal is very much dependent on temperature. It decreases when the temperature is lowered and completely disappears at −40 °C. The ratio of the intensities of the remaining signals (d) is about 1:4. On increasing the temperature the middle signal reappears. At the starting temperature the original signals are once again obtained; the ratio of the three intensities, however, changes somewhat (1:0.37:4). The process is reversible. These findings can be best explained by assuming an equilibrium to be present between the two different structures *(1)* and *(2)* of the primary titanium-aluminum complex.

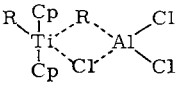


(1) *(2)*

Cp = Cyclopentadienyl

At low temperatures, the titanium-aluminum complexes ought to have a tetrahedral structure *(2)* in agreement with the proton resonance signals occurring in the ratio 1:4. (excess of alkylaluminum). With increasing temperature the equilibrium is displaced in favor of the octahedral complex *(1)*; an additional signal, that of the bridge methyl group, is then to be observed. The very slow decomposition taking place after complex formation and during the time of measurement can be disregarded at the concentration ratios given. Only after several hours is a slight change of the original spectrum to be observed.

If the interpretation of this finding is valid then the respective structural parts of the complex formed are also to be considered when the question of these catalytic systems is discussed from the standpoint of polymerization active species. An octahedral structure[2] is generally assigned to the active species. Our results[3] suggest that the complex *(3)* should initiate polymerization.



(3)

R = Alkyl

Received: November 28, 1968; revised: January 30, 1969 [Z 941 IE]
German version: Angew. Chem. *81*, 228 (1969)

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CONFERENCE REPORTS

Fluorinated Inorganic Radicals

By *H. J. Emeléus*[*]

In recent years the chemistry of fluorine-containing radicals such as BF, CF_3, SiF_2, NF_2, $N(CF_3)_2$, SO_3F, and $(CF_3)_2NO$ has been widely studied and substantial advances in preparative inorganic chemistry have resulted.

The radicals BF and SiF_2 are typical of those formed in high temperature reactions at a low pressure between the element and its fluoride (BF_3 or SiF_4). Under these conditions *Margrave* and his co-workers have shown that the SiF_2 radical reacts, for example, with ethylene to form the cyclic compounds $(CH_2)_2(SiF_2)_2$ and $(CH_2)_4(SiF_2)_2$. Higher boron and silicon fluorides such as B_3F_5 and Si_4F_{10} have also been described, as well as mixed boron-silicon fluorides ($SiF_3SiF_2BF_2$ and $SiF_3(SiF_2)_2BF_2$).

The NF_2 radical, which *Colburn* showed to be formed in the reversible dissociation of N_2F_4, combines with other free radicals. With NO it forms NF_2NO and with SF_5, formed *inter alia* by the thermal dissociation of S_2F_{10}, it yields SF_5NF_2. It may also be added to olefins and will abstract

hydrogen from compounds such as thiols to give NF_2H. The bistrifluoromethylamino radical, though less reactive, has yielded many new derivatives, though not directly. These include $Hg[N(CF_3)_2]_2$, $[(CF_3)_2N]_2S$, $[(CF_3)_2N]_2S_2$, $[(CF_3)_2N]_2Se$, and $(CF_3)_2NSeCl$. Addition of $(CF_3)_2NCl$ to PF_3 or PF_2Cl gives phosphorus(v) derivatives and with $P(CF_3)_3$ and $(CF_3)_2NCl$ it is possible, by stepwise elimination of CF_3Cl, to form $P[N(CF_3)_2]_3$.

The radical FSO_2O, formed in the reversible thermal dissociation of bis(fluorosulfonyl)peroxide, FSO_2OOSO_2F, has been shown, largely by *Cady* and his co-workers, to undergo a number of typical addition reactions. Thus with C_2F_4 it forms $FSO_2O(CF_2)_2OSO_2F$ and, with SF_4, $FSO_2OSF_4OSO_2F$. It also reacts directly with halogens to give fluorosulfonates (*e.g.* $ClSO_3F$, $I(SO_3F)_3$).

The bistrifluoromethyl nitroxide radical, first isolated by *Blackley* and *Reinhard*, forms a violet gas with much the same stability as nitric oxide. It is formed by the oxidation of $(CF_3)_2NOH$ and has now been shown to react at room temperature with mercury to form crystalline $Hg[ON(CF_3)_2]_2$, from which the radical may be recovered quantitatively at 85 °C. The radical reacts with PF_3 to give $PF_3[ON(CF_3)_2]_2$. The mercurial is also a useful reagent for the transfer of the $(CF_3)_2NO$ group, $POCl_3$ and $PSCl_3$ forming $PO[ON(CF_3)_2]_3$ and $PS[ON(CF_3)_2]_3$, respectively, while BCl_3 gives $B[ON(CF_3)_2]_3$.

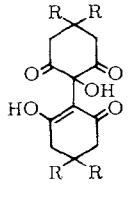
Lecture at Göttingen on July 4, 1968 [VB 179 IE]
German version: Angew. Chem. *81*, 190 (1969)

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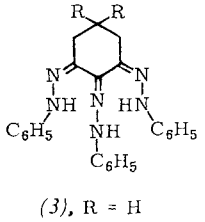
Potassium Nitrosobissulfate as Specific Oxidizing Agent in Organic Chemistry

By *H.-J. Teuber* [*]

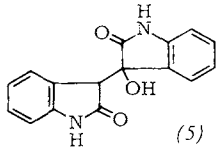
Enols, like phenols, are oxidized by potassium nitrosobissulfate (Fremy's salt), $ON(SO_3K)_2$. Dihydroresorcinol and dimedone are converted into the tertiary alcohols *(1)* and *(2)*, respectively; the former product can also be synthesized from its components, 1,2,3-cyclohexanetrione and dihydroresorcinol. *(1)* and *(2)* are cleaved by phenylhydrazine to the tris(phenylhydrazones) *(3)* and *(4)* and are



(1), R = H
(2), R = CH_3

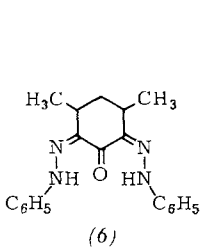


(3), R = H
(4), R = CH_3

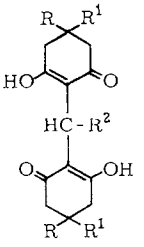


(5)

cyclized to furan derivatives by acids or by catalytically excited hydrogen. Oxindole is analogously oxidized to the compound *(5)*, which affords isoindigo by dehydration. In the case of 4,6-dimethyl-1,3-cyclohexanedione the formation of a dimer (aldol reaction) does not occur, but the oxidation product formed (as in the reaction with selenium dioxide) can be isolated as bisphenylhydrazone *(6)*.



(6)



(7a), R = R^2 = H, R^1 = C_6H_5
(7b), R = H, R^1 = C_6H_5, R^2 = CH_3
(8), -R-R^1- = -$(CH_2)_5$-, R^2 = H

A competing reaction that is also observed with *(1)* and *(2)* preponderates when 5-phenyl-1,3-cyclohexanedione and spiro[4.5]decane-7,9-dione are oxidized in aqueous-alcoholic solution: the starting ketone condenses with the aldehydes formed from the methanol (or ethanol), giving *(7a)* [or *(7b)*] or *(8)*. It is thus proved that under these conditions alcohols are dehydrogenated to aldehydes. In the case of 2-methyl-1,3-cyclohexanedione the ring is cleaved; this occurs also with 1,2-cyclohexanedione, which is converted into adipic acid (*J. Hohn*).

In acid solution benzhydrazide affords N_2 and benzoic acid, but in alkaline solution gives benzaldehyde and benzoylbenzylidenehydrazine (*G. Köhler*).

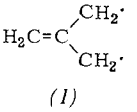
Lectures at Kiel (Germany) on November 21, 1968,
and at Stuttgart (Germany) on December 5, 1968
German version: Angew. Chem. *81*, 190 (1969) [VB 180 IE]

[*] Prof. Dr. H.-J. Teuber
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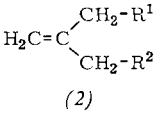
Trimethylenemethane, a Theoretically and Synthetically Valuable Allylic Structure

By *F. Weiss* [*]

Trimethylenemethane, in the form of the diradical 2-methylene-1,3-propanediyl *(1)*, is an interesting allylic species containing the skeleton of α,α'-disubstituted isobutenes *(2)*.



(1)



(2)

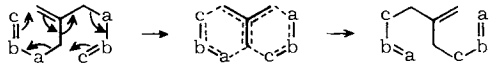
The theoretically predicted triplet ground state of *(1)* has recently been confirmed by EPR studies of the diradical produced by low-temperature photolysis of 4-methylene-1-1-pyrazoline and of 3-methylenecyclobutanone. This reactive 1,3-diradical can, like the cyclobutadienes, be isolated as its stable tricarbonyliron complex.

The properties of the 1,3-diradical as intermediate can be explained on the basis of its triplet structure. For instance, it affords practically no methylenecyclopropane, but instead 1,4-dimethylenecyclohexane, *i.e.*, a coupling product, when α,α'-dihaloisobutenes react with potassium vapor, when 6-methylene-1,4-dioxepane-2,3-dione is pyrolyzed, when the above-mentioned photolysis reactions are carried out, and when trimethylenemethane-tricarbonyliron is photolyzed in pentane. If other triplet radicals are also formed in the first step, then *(1)* can react partly with them, *e.g.*, with triplet methylene produced from diiodomethane. Cycloaddition of *(1)* to olefins such as butadiene, cyclopentene, and cyclopentadiene has been achieved only in the photochemical reactions mentioned above.

Trimethylenemethane intermediates produced under nonradical conditions also behave unusually. Reaction of α,α'-

dichloroisobutene with tetracarbonylnickel leads to 1,4,7-trimethylenecyclononane in good yield, and this reaction with magnesium gives a series of macrocyclic and open-chain oligomers as well as methylenecyclopropane and 1,4-dimethylenecyclohexane.

The symmetrical structure of α,α'-disubstituted isobutenes permits a double allylic rearrangement in accord with the general scheme *(3)* → *(4)* → *(5)*. These reactions have been



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

specially studied in connection with the Claisen rearrangement; examples are rearrangement of isobutenylenedicarboxylic esters by NaH to γ-methylenepimelic acids and of aryl ethers of isobutenediol at 200 °C to bisphenols. Further, interesting thermal rearrangements can be effected with cyclic ethers of isobutenediol: At 450 °C 5-methylene-1,3-dioxanes give the isomeric methylallyl ester and, if C-2 carries a vinyl group, also the isomeric glutaraldehydes. At 200 °C 3,4-dihydro-3-methylene-2*H*-[1,5]benzodioxepin gives a 2,4-cyclohexadienone by a (presumably stepwise) Claisen rearrangement, and at 450 °C this is further converted into isomeric products consisting mainly of a furylcyclopentenone.

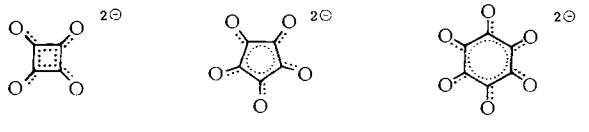
Lecture at Mülheim/Ruhr on November 21, 1968
German version: Angew. Chem. *81*, 191 (1969) [VB 181 IE]

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Ugine Kuhlmann, Centre de Recherches de Lyon
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New Aromatic Systems

By *R. West* [*]

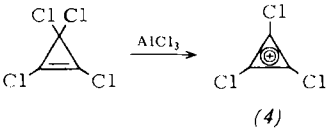
It has recently been recognized that the cyclic anions $C_nO_n^{2-}$ of squaric acid *(1)*, croconic acid *(2)*, and rhodizonic acid *(3)* form a homologous series of aromatic compounds.



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

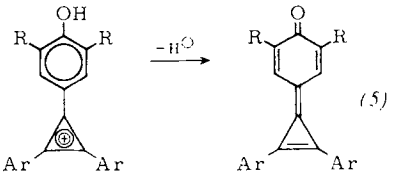
Structural studies show that these anions have symmetric, planar structures with considerable π-bonding contributions from the C–C bonds. The properties of the substances are, in general, in good agreement with predictions of the Hückel-LCAO–MO theory.

Reaction of tetrachlorocyclopropene with $AlCl_3$ leads to the trichlorocyclopropenylium ion *(4)*, which is an aromatic system where the C–C bonds are even stronger than in benzene. One, two, or three of the chlorine atoms can be replaced by aryl groups when $C_3Cl_3^+$ is treated with aromatic hydrocarbons.



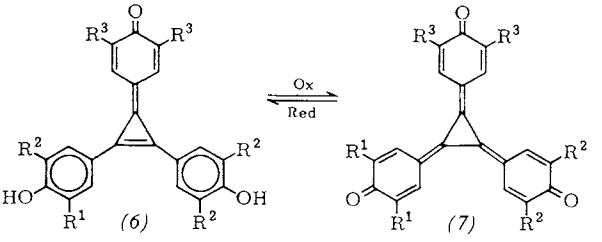
(4)

If one of the aromatic rings carries a *para*-hydroxy group, the triarylcyclopropenylium ion is readily deprotonated to a quinonoid system *(5)*.



(5)

If all three aromatic rings carry hydroxyl groups, compounds *(6)* are obtained which can be oxidized to triquinonoid cyclopropanes *(7)*. Compounds *(7)* are stable, dark purple solids with a quite new electronic structure.



(6) *(7)*

In the redox processes *(6)* ⇄ *(7)*, anion radicals and monoradicals can be shown by ESR spectroscopy to occur as intermediates and they can be characterized.

Lecture at Giessen (Germany) on December 17, 1968, and at Braunschweig (Germany) on November 4, 1968 [VB 183 IE]
German version: Angew. Chem. *81*, 229 (1969)

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Studies on the Mechanism of Mixed Function Oxygenations

By *V. Ullrich* [*]

Mixed function oxygenations occur according to the equation:

$$RH + DH_2 + O_2 \rightarrow ROH + D + H_2O$$

where RH is an organic substrate and DH_2 is a reduced hydrogen-donor. The very complicated course of these enzymatic reactions can be considered according to three points of view:

1. How is the oxygen molecule activated? 2. How are the electrons transferred to the oxygen? 3. How is the electron transport coupled with the hydroxylation of the substrate?

To obtain an insight into the activation of the oxygen molecule the model systems described previously [1] have been developed further. Reduction of oxygen by the iron(II)-thiosalicylic acid complex leads to an electrophilic oxenoid complex [**] which hydroxylates aliphatic and aromatic compounds and compounds containing isolated double bonds in the same way as enzymically activated oxygen does. A decisive role in this system is played by sulfur as ligand, which in combination with the Fe^{2+} ion makes two-electron reduction of the oxygen molecule possible.

In many mixed-function oxygenases cytochrome P 450 participates in the activation of oxygen. A reaction velocity $t_{1/2}$ of about 300 msec and 1:1 stoichiometry have been established for its reaction with oxygen. The unusual spectral and chemical properties of cytochrome P 450 can be explained on the basis of its function as a two-electron donor.

Participation of cytochrome P 450 in activation of oxygen has been shown in the case of hydroxylation of cyclohexane by the microsomal fraction of liver by the photochemical action spectrum of the CO-complex.

As observed with other substrates of microsomal mixed function oxygenase systems[2] cyclohexane causes a change in the spectrum of oxidized cytochrome. The extent of the spectral shift is directly correlated with the enzyme activity. This confirms the assumption[2] that the change in the spectrum is caused by formation of an enzyme-substrate complex. Only about 12% of the cytochrome present in rat-liver microsomes can form this enzyme-substrate complex, although this level is increased to 32% by pretreatment of the animals with phenobarbital.

It can be deduced from studies on the rate of reduction of the cytochrome that the enzyme-substrate complex is reduced appreciably faster than substrate-free cytochrome, thus indicating a coupling of electron transport with hydroxylation.

Lecture at the Max-Planck-Institut für Ernährungsphysiologie, Dortmund, on November 11, 1968
German version: Angew. Chem. *81*, 229 (1969) [VB 184 IE]

[*] Dr. V. Ullrich
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[**] An 'oxenoid' complex is defined by its ability to transfer an oxygen atom with six electrons.

[1] *V. Ullrich* and *Hj. Staudinger* in *B. Hess* and *Hj. Staudinger:* Biochemie des Sauerstoffs. Springer Verlag, Berlin 1968, p. 229.

[2] *J. B. Schenkman, H. Remmer,* and *R. W. Estabrook,* Molecular Pharmacol. *3*, 113 (1967).

Simultaneous Transport of Mass and Heat with Wall Reactions (Hydrogenation of Ethylene on a Platinum Catalyst in an Annulus)

By *G. Jeromin* and *F. Fetting* [*]

During heterogeneous exothermal reactions on catalytically active walls temperature gradients are set up under adiabatic conditions between the surface and the gas stream in flow reactors. If the reaction rate is so high that it is determined only by the rate of mass transport, an analogy can be assumed between the removal of heat from the hot wall and transport of mass to the catalytically active wall; in such cases it is relatively easy to calculate the wall temperatures that are achieved in the stationary state. The temperature plateau depends on the adiabatic excess temperature and thus on the reaction enthalpy as well as on the concentrations of the reacting components.

These relations have been treated theoretically for several years past, but experimental material is available only rarely and for 'local' conditions (on a thin wire). In the present work the temperatures achieved were studied in connection with their dependence on the size of the influences for integral conditions.

Hydrogenation of ethylene (reaction enthalpy $\Delta H_R = -32$ kcal/mole) was used as model reaction. The gas mixture throughout contained 5 vol-% of ethylene with various amounts of hydrogen, nitrogen, or argon. The reaction took place on a 5- or 25-cm long platinum film prepared on a longer glass tube (outer diameter 18.1 mm) which formed the inner tube of an annular-space reactor. The temperature along the catalyst wall was measured in a simple manner by means of a thermoelement that could be moved along the internal wall of the inner tube.

The measurements showed the steep rise in temperature of about 100–200 °C where the gases first reach the catalyst. Since the Lewis number was more than unity the temperature increased in all cases along the catalyst layer. The temperature finally reached depended on the conversion that had resulted and only indirectly, by way of this quantity, on the flow rate. Transition to turbulent flow increased the wall temperatures slightly in spite of the drop in conversion. Increasing the length of the reactor in front of the catalyst to permit development of the flow-rate profile did not yield any unequivocal result. Such investigations can give practical indications of the temperature distribution at different positions, *e.g.* in platinum gauze, as in combustion of ammonia to nitrous oxide and in preparation of hydrocyanic acid by *Andrussov*'s method. They provide a clear example of the application of the analogy between heat and mass transport coupled with a heterogeneous chemical reaction.

Lecture at Erlangen (Germany) on December 13, 1968
German version: Angew. Chem. *81*, 230 (1969) [VB 185 IE]

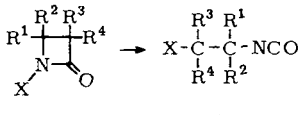
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SELECTED ABSTRACTS

A new rearrangement of β-lactams has been observed by *K.-D. Kampe*. *N*-Bromo- and *N*-chloro-2-azetidinone *(1)* rearrange in the presence of C–C unsaturated compounds, *e.g.* allyl chloride, vinyl chloride, and vinyl ether, and catalytic



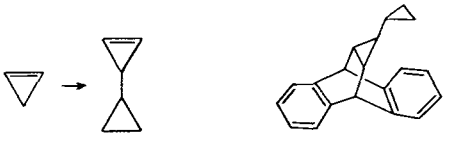
(1) *(2)*

X = Br, Cl

quantities of radical-formers to give β-bromo- and β-chloroalkyl isocyanates *(2)*. The groups R^1–R^4 are inert substituents. / Tetrahedron Letters *1969*, 117 / –Ma.

[Rd 968 IE]

The thermal dimerization of cyclopropene, one of the most reactive of the olefins, has been investigated by *P. Dowd* and *A. Gold*. Whereas extremely vigorous polymerization occurs at room temperature, the dimer *(1)* is obtained at –25 °C in CH_2Cl_2 or *n*-pentane solutions. The dimerization proceeds



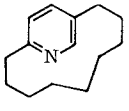
(1) *(2)*

possibly by the "ene" mechanism. *(1)* can be isolated by gas chromatography at room temperature, but owing to its extreme instability it must be stored at –78 °C. At 10 °C it is converted by anthracene in $CHCl_3$ into the adduct *(2)*, m.p. 117–117.5 °C. / Tetrahedron Letters *1969*, 85 / –Ma. [Rd 969 IE]

The anodic oxidation of Ag_2O to AgO in KOH solutions was investigated by *M. Fleischmann, D. J. Lax,* and *H. R. Thirsk.* Ag/Ag_2O electrodes were oxidized at a controlled potential which was varied in 20-mV steps over a range of 300 mV and the voltage-time graphs were recorded. Ag^+ ions in the Ag_2O react with adsorbed OH radicals in the rate-determining step to give AgO and H^+. Once formed, AgO nuclei continue to grow in three dimensions at the Ag_2O/electrolyte interface. At low electrode potentials, because of the preceding OH^- discharge equilibrium, it is found that the reaction is first order with respect to OH^-; at high electrode potentials the areas on which the AgO grows are completely covered, and the reaction becomes independent of the potential and the OH^- concentration. / Trans. Faraday Soc. *64*, 3137 (1968) / –Hz. [Rd 958 IE]

The kinetics of the evaporation of sodium chloride from the (100) faces of single crystals has been investigated between 450 and 650 °C by *J. E. Lester* and *G. A. Somorjai* using a vacuum microbalance. For crystals the steady rate of evaporation depends on the dislocation density at the surface, and increases if the latter is increased by means of mechanical pressure. The relative rates of evaporation of NaCl and Na_2Cl_2 were measured by mass spectrometry; with non-stressed crystals the activation energies for the evaporation are 53 ± 1 kcal/mole for the monomer and 62 ± 1 kcal/mole for the dimer. In the temperature range investigated, between 30 and 5% of the vapor was found to be the dimer, irrespective of the surface dislocation density. Addition of Ca^{2+} greatly reduces the rate of evaporation, and Br^-, OH^-, and O_2^- have no measurable effect. / J. chem. Physics *49*, 2940 (1968) / –Hz. [Rd 959 IE]

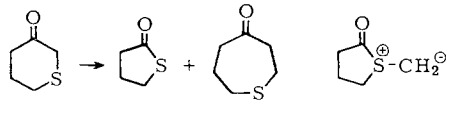
[*n*]-(2,5)-Pyridinophanes have been synthesized by *H. Gerlach* by acid-catalyzed ring closure of bis(β-aminovinyl) diketones to give [*n*]-(2,5)-pyridinophan-*n*-ones and subsequent Wolff-Kishner reduction of the latter. The NMR spectra of the new *ansa*-compounds show a strong upfield shift of the signals due to the methylene protons, which is particularly pronounced for bridges having $n < 12$, as well as restricted rotation of the pyridine nucleus; it therefore proved possible to isolate



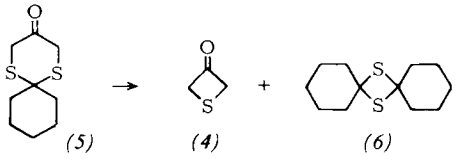
(1)

diastereoisomeric [*n*]-(2,5)-pyridinophanols. [9]-(2,5)-Pyridinophane *(1)* was resolved into the thermally highly stable enantiomers. / Chimia *22*, 493 (1968) / –Ma. [Rd 971 IE]

The photochemistry of thiacycloalkan-3-ones has been investigated by *K. K. Maheshwari* and *G. A. Berchtold.* Irradiation of thiacyclohexan-3-one with a 450-W lamp in *tert*-butanol (19 h, 78% conversion) afforded thiacyclohexan-3-ol (16%)



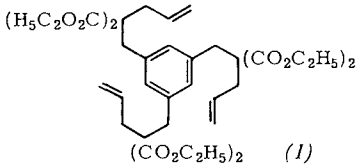
(1) *(2)* *(3)*



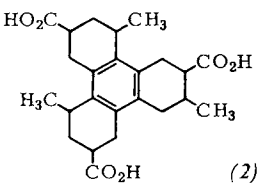
(5) *(4)* *(6)*

and *tert*-butyl 4-methylthiobutyrate (14%), whereas in 1,1,2-trichloro-1,2,2-trifluoroethane (Freon-113) (8h, 90–95% conversion) tetrahydrothiophen-2-one *(1)* and thiacycloheptan-4-one *(2)* are each formed in 6–8% yield. The ylid *(3)* may possible be responsible for insertion of the CH_2 group during the formation of *(2)*. Ring expansion and contraction in this manner has not been observed with other compounds of this kind. Irradiation of 1,3-dithiacyclohexan-5-one in acetonitrile gave thietan-3-one *(4)* (21%), and compound *(5)* in Freon-113 yielded *(4)* and *(6)*. / Chem. Commun, *1969*, 13 / –Ma. [Rd 972 IE]

A synthesis of symmetrically substituted triphenylenes by triple ring closure of tris(4-pentenyl)benzenes has been described by *P. Canonne* and *A. Regnault.* Compound *(1)*, obtained from tris(bromomethyl)benzene and an excess of sodioallylmalonic ester, is hydrolyzed, decarboxylated, and cyclized to compound *(2)* by heating for 7 hours with $AlCl_3$.



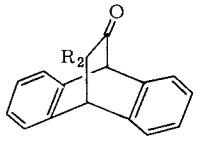
(1)



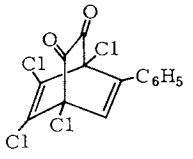
(2)

Reduction with $LiAlH_4$ and aromatization with Pd/C at 250 °C yields 1,3,5,7,9,11-hexamethyltriphenylene (m.p. 97 °C), whereas treatment with Pd/C at 320 °C affords 1,3,6,8,10-pentamethylcyclopenta[*def*]triphenylene (m.p. 192 °C). / Tetrahedron Letters *1969*, 243 / –Kr. [Rd 976 IE]

"Bis(carbon monoxide)", C_2O_2, is probably formed on photolytic decomposition of cyclic compounds such as *(1)* and *(2)* having a dioxoethylene bridge in benzene[1], according to *J. Strating, B. Zwanenburg, A. Wagenaar,* and *A. C. Udding.* Compound *(1)* affords anthracene and CO (by decomposition of C_2O_2) in 100% yield, and compound *(2)* gives tetrachlorobiphenyl (97%) and CO. The mass spectrum of *(1)* shows, *inter alia*, a strong peak at M – 2 CO, a peak at



(1), R_2 = O
(2), R_2 = 2 H



(2)

m/e 56 ($C_2O_2^+$), and a negligible peak at M – CO. The photolysis of compound *(3)* to anthracene, dianthracene, and ketene (60% yield after 1 h) lends support to the concept that the bridge is removed as a whole. Pyrolysis of compounds such as *(1)* and *(2)*, which requires high temperatures, also leads to CO. / Tetrahedron Letters *1969*, 125 / –Kr. [Rd 977 IE]

[1] Cf. *D. Bryce-Smith* and *A. Gilbert*, Chem. Commun. *1968*, 1319.

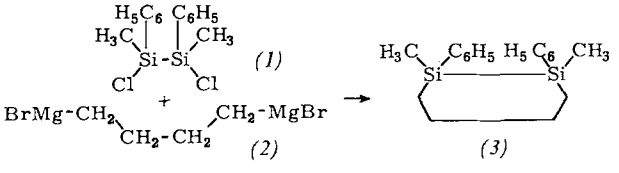
The regularity of the electronic work function for metal electrodes in electrolyte solutions on irradiation with UV light ($\lambda = 365$ nm) has been investigated by *Y. V. Pleskov* and *Z. A. Rotenberg*. In concentrated solutions of electrolyte, the photocurrent I is related to the electrode potential φ over a wide range according to the equation

$$I = A\,(\varphi_0 - \varphi)^{5/2} \qquad (1)$$

where A is a constant. The threshold potential φ_0 amounts to -0.31 ± 0.03 V measured against the saturated calomel electrode, a value that is independent of the nature of the electrode metal (Hg, Pb, Tl/Hg, In/Hg were investigated). The electronic work function for mercury (at zero charge potential) in the electrolytes is 3.26 eV. In dilute electrolyte solutions, in which the potential drop from the electrode to the bulk of the solution extends over a fairly large distance, a current-voltage curve analogous to eq. (1) is obtained if φ is replaced by $\varphi - \psi_1$; ψ_1 denotes the potential at a distance of one ionic radius from the electrode surface, which can be determined by a model calculation. Measurement of the photocurrent and evaluation according to eq. (1) permits determination of the zero charge of metals in electrolyte solutions. / J. electroanalyt. Chem. Interfacial Electrochem. *20*, 1 (1969) / –Hz. [Rd 978 IE]

Reactions of *N,N*-bis(trifluoromethyl)hydroxylamine *(1)* with sulfur and nitrogen halides in the presence of CsF have been examined by *J. A. Lott, D. P. Babb, K. E. Pullen,* and *J. M. Shreeve*. New compounds of the type $(CF_3)_2NOX$, which are stable at 20 °C, were isolated and characterized by their IR, NMR, and mass spectra. $[(CF_3)_2NO]_2SO_2$ and $(CF_3)_2NOSO_2F$ are formed from *(1)* and SO_2F_2 in the molar ratio 2:1 and 1:1 respectively, $[(CF_3)_2NO]_2SO$ and $(CF_3)_2NOS(O)F$ from *(1)* and SOF_2 in the molar ratio 7:3 and 3:5 respectively, and $[(CF_3)_2NO]_2S$ and $[(CF_3)_2NO]_2S_2$ from *(1)* and SCl_2 and S_2Cl_2 respectively. The unstable compound $(CF_3)_2NONF_2$ is formed in the corresponding reaction of *(1)* with NF_2Cl. / Inorg. Chem. *7*, 2593 (1968) / –Bl. [Rd 979 IE]

1,2-Dimethyl-1,2-diphenyl-1,2-disilacyclohexane has been prepared by *K. Tamao, M. Ishikawa,* and *M. Kumada* from compound *(1)* and the Grignard reagent *(2)* (yield 75%); the same authors resolved the compound into its stereoisomers by fractional distillation or preparative gas chromatography. They also succeeded in synthesizing the analogous 1,2-bis-(*p*-chlorophenyl) compound, the isomer having the shorter



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

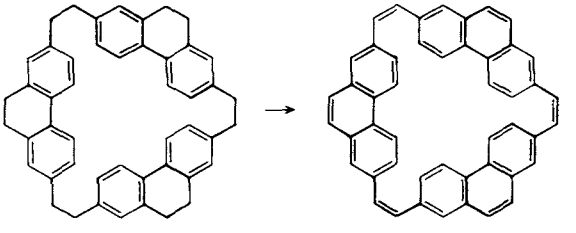
retention time and the greater dipole moment being recognized as the *cis* form. *cis-* and *trans-(3)* can be oxidized stereospecifically with perbenzoic acid to *cis-* and *trans*-2,7-dimethyl-2,7-diphenyl-1-oxa-2,7-disilacycloheptane, respectively. – 1,2-Difluoro-1,2-dimethyl-1,2-disilacyclohexane, which is formed with NH_4HF_2 from *cis,trans-(3)*, *cis-(3)*, or *trans-(3)* in concentrated sulfuric acid, is always obtained in the *cis-trans* ratio of 1: ≈ 1.9. Addition of ethanol to solutions of the fluoro compounds in hexane or benzene can also give rise to *cis-trans* isomerization, which is reported to proceed *via* a compound containing pentacoordinated silicon. / Chem. Commun. *1969*, 73 / –Kr. [Rd 981 IE]

Potassium 2-germaacetate *(1)* has been obtained by *P. M. Kuznesof* and *W. L. Jolly* on reaction of germylpotassium with carbon dioxide in melting 1,2-dimethoxyethane as a white salt-like substance that is relatively stable in aqueous solution at room temperature. The structure of its anion is deduced to be analogous to that of acetate from the IR and UV spectra of *(1)* and from the course of its hydrolysis (water, 2 days at 85 °C), according to

$$GeH_3CO_2^- + H_2O \rightarrow GeH_4 + HCO_3^-$$

Acidification of an aqueous solution of *(1)* affords a solution of 2-germaacetic acid ($pK = 3.5$), which decomposes with a half-reaction time of *ca.* 30 min at pH = 2 to CO as well as non-stoichiometric amounts of GeH_4 and an insoluble orange solid containing Ge and H. / Inorg. Chem. *7*, 2574 (1968) / –Bl. [Rd 980 IE]

[2.2.2](2,7)Phenanthrenophanetriene *(2)* has been synthesized by *W. Jenny* and *R. Paioni* from hexahydrophenanthrenophane *(1)* and *N*-bromosuccinimide; the reaction first affords a hexabromo derivative that is subsequently debrominated with zinc. The deep yellow compound *(2)*, which is very



(1) *(2)*

difficultly soluble in nearly all the common solvents, does not melt below 500 °C, and turns red above 300 °C. Its structure was proved by the mass spectrum [molecular ion at *m/e* 606 (390 °C)] and the NMR spectrum (in $AsCl_3$). On further heating a peak appears in the mass spectrum at *m/e* 600, which could indicate dehydrogenation to [12]coronaphthene. / Chimia *23*, 41 (1969) / –Kr. [Rd 982 IE]

BOOK REVIEWS

Reallexikon der Medizin und ihrer Grenzgebiete (Encyclopedia of Medicine and Related Fields) Vol. II: Cargile Membrane to E-cell. Edited by *G. Thiele* and *H. Walter*. Urban & Schwarzenberg, Munich 1968, 1st Edit., 805 pp., loose-leaf binding with plastic covers, DM 140.–.

The second volume of this encyclopedia has appeared surprisingly soon after the first[1], and it too makes an excellent impression. The most important terminology found in medical and related literature have been compiled and interpreted with great expertise and certainly with great industry. The illustrations aid in understanding the text, in particular those of the more complicated chemical structures. If one may form a conclusion about the entire work on the basis of the chemical, biochemical, and physicochemical entries,

[1] Angew. Chem. *81*, 43 (1968); Angew. Chem. internat. Edit. *8*, 87 (1969).

the verdict is very favorable. Few inaccuracies of expression are found, and the editors seem to have succeeded in avoiding obvious errors to the extent that thorough random sampling did not reveal any mistakes. It is a pity that in the case of chemical terms antiquated spelling (z and k instead of c) and nomenclature more common in pharmacy has been included, instead of adhering strictly to the style used in the standard works of the German chemical literature. However, it must be emphasized that this is an encyclopedia for students of medicine though chemists active in the areas bordering the medical sciences will find much useful information, not available elsewhere in such a precise and handy form.

H. Grünewald [NB 773 IE]

Das Fischer Lexikon Chemie (The Fischer Encyclopedia – Chemistry) A–Z. Edited by *H. Kelker, F. Klages, R. Schwarz,* and *U. Wannagat.* S. Fischer-Verlag, Frankfurt 1968. New edition, 400 pp., 46 figures, bound. DM 4.80.

The "Chemistry" volume of the Fischer Encyclopedia, which first appeared in 1961 and of which 125000 copies have since been sold, has now been published in a new edition. Many of the entries have been brought up to date, others have been revised or included for the first time, and nearly everywhere it has been necessary to include recent developments. The editors have done this thoroughly and skilfully and the new edition deserves if anything even greater success than the first.

Comparatively few key-words are given (42 altogether), but each represents an article covering several pages and imparting the relevant information in textbook-like manner. The attraction of the volume lies in the fact that the alphabetical arrangement of the entries gives rise to an unconventional structure, differing from the usual textbook; it allows related material to be kept together, and frequently leads to unfamiliar aspects.

A point worth making is that the index should also have been seen and corrected by the authors. This procedure was evidently not followed in the case of the present volume, as is shown by the numerous misprints which have no place in a book of this kind.

Anyone who likes to have his chemistry near him to read on the train, in the waiting room, or at his desk, will be delighted with this volume.

H. Grünewald [NB 774 IE]

ABC Biologie (The ABC of Biology). Edited by *G. Dietrich* and *F. W. Stöcker.* Verlag Harri Deutsch, Frankfurt-Zürich. No date given. 920 pp. 14 color plates. Plastic binding, DM 49.80.

This volume is welcome, even if one does not agree that biology is daily "penetrating deeper into social life" (foreword). It attempts to provide something like a synthesis of biology, physiology, botany, and zoology, and in this it is eminently successful. For a biochemist in particular, the concepts of biology that derive from the observation of the entire organism are not always completely clear, and accurate definitions of the terms are often needed. The encyclopedia covers about 6000 entries. The numerous illustrations in the text and longer articles containing comprehensive and comparative explanations of particularly important entries are of special value.

The information is in general reliable, but it does not always reflect the latest developments in the field (*e.g.* insulin), either in style or in content. There are occasional errors (*e.g.* $h\nu$ = Planck's constant), and the "germanized" spelling, which makes looking up references unnecessarily difficult, is regrettable. All this does not, however, detract from the value of this volume. The chemist who wants to check up on the meaning of biological concepts would be well advised to have this work in his private library.

H. Grünewald [NB 775 IE]

Appretur der Textilien. Mechanische und chemische Technologie der Ausrüstung (Textile finishing. Mechanical and chemical finishing technology) by *W. Bernard.* Springer-Verlag, Berlin-Heidelberg-New York, 1967. 2nd revised Edit., viii, 406 pp., 403 figures, DM 78.–.

In the eight years that have elapsed since the publication of the first edition, there have been many changes in textile finishing. Not only have new cotton finishing processes (particularly for high-grade finishing) been introduced, but processes have also been developed in the synthetics field, such as antistatic treatment, hydrophilic treatment, and the fixing of synthetic or mixed fibers. It was also necessary to consider technical innovations in connection with finishing aids into account.

The first chapter of the book describes mechanical finishing operations, dealing on the one hand with new methods and on the other with new machinery. The second part is concerned with chemical finishing. In addition to the usual stiffening, weighting, and filling processes, the chemicals required in their execution are also discussed. This is followed by modern finishes such as antistatic treatment, chemical finishing for wool textiles, oil-repellent and dirt-repellent finishing, and high-grade finishing. In describing the processes the author emphasizes the practical application, and spends no more time on chemical aspects than is necessary.

The book is well arranged and contains excellent illustrations, so that it is fairly easy for the reader to gain a picture of the range of finishing processes and machinery.

At the end of the book there is a very useful list of suppliers of finishing machinery and finishing agents and a comprehensive subject index. The book is a valuable aid not only for the practical textile worker but also for all those whose professional training requires a knowledge of textile finishing.

H. Rath [NB 781 IE]

Lehrbuch der Pharmakognosie. Auf phytochemischer Grundlage (Textbook of pharmacognosy. On a phytochemical basis). By *E. Steinegger* and *R. Hänsel.* Springer-Verlag, Berlin-Heidelberg-New York 1968. 2nd Edit., xii, 531 pp., numerous figures and tables, DM 78.–.

This book, which first appeared five years ago as "Lehrbuch der allgemeinen Pharmakognosie", is a "comparative, descriptive plant biochemistry" in which attention is centered on medicinal plants, their active principles, and their use. The main part of the book, which deals with the various drugs, is accordingly arranged largely on a phytochemical basis. This is particularly true of the following chapters: "Plant acids as main active principles" (5 pp.), "Carbohydrate drugs" (43 pp.), "Glycoside drugs" (104 pp.), "Tannin drugs" (10 pp.), "Proteins and enzymes" (17 pp.), and with certain limitations also "Fats, oils, and other lipids" (22 pp.). Occasionally, when it seems more appropriate to the authors for didactic reasons, an alternative classification system is used. Thus the chapter on "Alkaloid drugs" (93 pp.) is arranged more in accordance with botanical principles, while the chapters on "Ethereal oils, resins, and balsams" (79 pp.) and on drugs whose active principles are unknown (49 pp.) are arranged in accordance with therapeutic principles. A special chapter is devoted to "Drugs from microorganisms" (32 pp.). This layout is largely retained from the first edition, though the various sections have been very carefully revised and updated almost throughout.

Each chapter is preceded by a survey of the group of substances in question. The botanical origins and extraction of the various drugs, their contents, and their special properties, physiological action, and therapeutic importance are discussed in detail.

The reduction of the number of pages from 595 to 531 is mainly due to trimming in the general section, in which special chapters devoted to drug morphology and to systematic, genetic, and physiological problems of pharmacobotany in the first edition have been omitted from the

second edition. On the other hand, the chapter entitled "Introduction to the phytochemical principles of pharmacognosy", which also belongs to this section, has been expanded (55 pp.) and brought into line with current knowledge. Probably the most striking change is the complete rearrangement of the formulas, which has resulted in a considerable improvement.

This book, which is intended primarily for pharmacy students and for practising druggists, contains a wealth of information for anyone concerned with drug research and phytochemistry, and can therefore be strongly recommended.

E. Sprecher [NB 780 IE]

Einführung in die Naturphilosophie, Band I: Naturerkenntnis und Wirklichkeit. Band II: Die Erkenntnis des Lebendigen. (Introduction to Natural Philosophy. Vol. I: The understanding of nature and reality. Vol. II: The understanding of Life) by *H. Sachsse*. Verlag Friedr. Vieweg und Sohn, Braunschweig 1968. 1st Edit., Vol. I: 232 pp., 7 figures, DM 17.50; Vol. II: 289 pp., 35 figures, 23 tables, DM 22.80.

In these two works the author does not adopt the normal approach of fusing together the results of natural scientific studies and philosophical apriorisms. Instead, he reflects – starting from the basis of scientific theory – on classical and modern problems of the science of experience and philosophy (Part I includes natural law, probability, space measurement, formulation of theories, and the concept of substance; Part II embraces causality and finality, regulation and control, data processing, deliberation, and spontaneity) to come closer to an understanding of man, using human behavior as an example.

By a skilful choice of material, supported by numerous examples, diagrams, and sketches, the author succeeds in presenting a readable, interesting work. The book guides the reader rather than throwing about terms and serving up the results. The objectivity and stimulating presentation of this important contribution to the metatheory of natural science – with its aim of serving the interdisciplinary exchange of information – merits wide distribution.

A. F. Kremmeter [NB 783 IE]

Chemie in nichtwäßrigen ionisierenden Lösungsmitteln, Bd. III: Chemie in flüssigem Distickstofftetroxid und Schwefeldioxid (Chemistry in non-aqueous ionizing solvents, Vol. III: Chemistry in liquid dinitrogen tetroxide and sulfur dioxide). Edited by *C. C. Addison, W. Karcher,* and *H. Hecht*. Friedr. Vieweg und Sohn, Braunschweig 1967, Pergamon Press, Oxford. 1st Edit., xiv, 206 pp., 27 figures, 35 tables, DM 68.–.

In the first part of this book[1] *C. C. Addison,* who (as a glance at the literature list shows) has himself worked mainly in this field, discusses dinitrogen tetroxide as a solvent. The second part, dealing with chemistry in liquid sulfur dioxide, was written by *W. Karcher* and by *H. Hecht,* a co-worker for many years of *G. Jander,* who himself worked in this field. Both parts are thus written by experts who are very familiar with the subjects discussed.

The physical and chemical properties of the pure solvents are first described, and the solubilities of many substances and solvate formation are then reported, organic substances also being included in the case of dinitrogen tetroxide. Solvolysis reactions and the reverse "neutralization-like" processes are described in terms of heterolytic dissociation of the solvent

$$N_2O_4 \rightarrow NO^+ + NO_3^- \quad \text{and} \quad 2\,SO_2 \rightarrow SO^{2+} + SO_3^{2-}$$

though it should be said that this is only a working hypothesis in the case of sulfur dioxide.

[1] Cf. Angew. Chem. *79*, 731 (1967); Angew. Chem. internat. Edit. *6*, 719 (1967).

The very different character of the two solvents is made very clear: one is a substance having a predominantly fast oxidizing action, whereas oxidations and reductions are strongly inhibited in the other. (This naturally affects the ranges of application of the solvents.) Both parts of the book show very impressively the numerous preparative possibilities offered by the two solvents. The well printed book is also well worth reading by those who are interested in theoretical aspects of inorganic chemistry. *F. Seel* [NB 779 IE]

Production of the Boranes and Related Research. Chief editor: *R. T. Holzmann,* edited by *R. L. Hughes, I. C. Smith,* and *E. W. Lawless*. Academic Press, New York-London, 1967. 1st Edit., x, 533 pp., numerous figures and tables, $22.00.

Between 1950 and 1965, many new discoveries have been made by scientists working for various companies in the USA in the borane field and a number of problems have been thoroughly investigated in connection with the high-energy fuel development program. Since only provisional or partial reports on the results of "Project Hermes", "Project Zip", and "Project HEF" have been published, though the projects were suspended in 1959, this first compilation in book form is very welcome.

The book is divided into a section on starting materials for the preparation of boron hydrides and one on their preparation. Further chapters are devoted to alkylboranes and carboranes. Separation, purification, and analysis methods are described. However, a short chapter on boron-nitrogen chemistry is not properly tied in. Extensive chapters on toxicology, IR spectra, molecular structures, and physical properties of boranes and carboranes are also included. The text is supplemented by tables covering several pages.

The 1673 references, some of which (pp. 490–504) are not related to the text, include several hundred articles that are difficult to obtain. This is the particular value of the book. On the other hand, the results obtained by many other research groups are not all included.

The book should find a place in every library because of its abundant tabular material and the source data. It provides those who work in the field of boron compounds with a very good compilation of the literature on boron hydrides.

R. Köster [NB 784 IE]

The Chemistry of Boron and its Compounds. Edited by *E. L. Muetterties*. John Wiley & Sons, London-New York 1967. 1st Edit., xiv, 700 pp., 200 figures, 220 s.

Numerous monographs on boron chemistry have been published in recent years. A book is now available which, in one volume, contains a complete and up to date account of boron chemistry. The editor has engaged the services of a number of well known research workers for the treatment of the individual subgroups so that a competent review approaching the frontiers of research is ensured.

After an introduction to the properties of the element that are dependent on the structure of the boron atom (structural properties, multicenter bonds, polyhedral structures, acceptor properties, problems of multiple bonds), *J. C. Hoard* and *R. C. Hughes,* discuss the element and compounds having a high boron content (130 pp.). They give a very instructive report on the modifications of boron as well as of metal borides and the significance of the structures in the light of the multicenter bond theory. One chapter is devoted to a discussion of "The Structural Chemistry of Borates" (54 pp.) by *J. O. Edwards* and *V. I. Ross*; here the main emphasis is placed on a clear system of classification based on structural principles. In the reviewer's opinion the work of *Lehmann* has been somewhat neglected. Mechanistic aspects considerably enhance the topical character of the chapter entitled "The Structure and Acidity of Boric Acid and its Relation

to Reaction Mechanisms" (*R. P. Bell, J. O. Edwards,* and *R. B. Jones,* 14 pp.).

M. F. Hawthorne gives an exemplary discussion of the boranes (102 pp., including a wealth of experimental material). The main stress is on decaborane chemistry, polyhedral borane ions, and the carboranes; the chemistry of diborane and tetrahydridoborates are considered in an undeservedly brief manner. An excellent critical review of boron halides is given in a short space by *G. May* (52 pp.). 66 pages are devoted to the boron-nitrogen compounds. The layout of the section written by *K. Niedenzu* and *J. W. Dawson* resembles that of their book; however, more recent results are considered. *M. F. Lappert* arranges the boron-carbon compounds (174 pp.) according to their reactivity and to general considerations, which leads to a useful comparative account. The classes of compounds discussed by *G. W. Parshall* and *E. L. Muetterties* demonstrate how relatively small our knowledge is of boron-phosphorus (30 pp.), boron-sulfur, and boron-selenium compounds. Particularly in this field a certain lack of reliable information becomes apparent.

Unfortunately the index of the book is not very attractive, containing as it does too many wrong page numbers. On the other hand, the number of printing errors in the text is small. All in all, the book gives a good review of a still highly topical and ever-fascinating field of chemistry, its variety and peculiarities that stem from multicenter bonding and the related bond theory problems. The reader quickly recognizes a certain independence of this element in the periodic system, and the fact that despite the enormous developments made in the last 15 years many parts of boron chemistry still represent unknown territory and even the well explored fields still conceal problems. This book can be recommended to anyone wishing to gain an overall picture of the chemistry of boron.

H. Nöth [NB 747 IE]

Reviews in Macromolecular Chemistry. Edited by *G. B. Butler* and *K. F. O'Driscoll.* Marcel Dekker, Inc., New York 1967. 1st Edit., Vol. I, vii, 449 pp., numerous illustrations and formulas, $16.50; Vol. II, viii, 380 pp., numerous illustrations, $16.50.

The constantly increasing number of scientific publications makes it difficult or impossible for the individual to keep abreast of advances in all fields of interest; reviews are therefore becoming increasingly important for the fast and comprehensive dissemination of knowledge. The advantage of reviews over handbooks is that they are up to date and can deal with very specialized topics.

The present series of books edited by *Butler* and *O'Driscoll* provides a brief survey of current topics in macromolecular chemistry. Though there are several such series of publications in this field, this new arrival must be welcomed for its breadth of subject. However, it remains to be seen whether the coordination and arrangement of the topics is such as to avoid duplication of effort. Volume 1 of this series contains seven articles, which give some idea of the wide outlook of the book.

K. O'Driscoll and *T. Yonezawa* present a critical review of the application of molecular orbital theory to the polymerization of vinyl compounds. Though the authors distinctly state that MO theory has so far enjoyed only limited success in the calculation of polymerization processes, the review shows that considerable progress has been made in the field of free-radical polymerization.

A. Gurgiolo contributes an excellent report on developments in polyalkylene oxides in 1963 and 1964. The initiators and polymerization mechanisms are compared; in addition to a detailed description of the physical properties of the polymers, the use of crosslinked polyalkylene oxides in the elastomer field is discussed. Though this comprehensive article (150 pp., 352 references) deals with applied aspects mainly by reference to the literature it still provides a good review.

The article by *D. Lyman* on "Polyurethanes" is intended mainly for chemists working with synthetic polymers; in contrast to the book of the same title by *Vieweg/Höchtlen,* which appeared at about the same time, this author deliberately ignores the technological side of polyurethane chemistry. This is a very readable report, which provides a rapid survey of the polyurethane field. However, the fact that the discussion is mainly concerned with linear polyurethanes should be indicated in the title.

L. Reich and *S. Stirala* describe the uncatalyzed, uninhibited thermal oxidation of saturated olefins. The literature is covered up to and including 1964, and the extensive experimental data are well arranged.

Thermally stable polymers are discussed in an article by *W. de Winter.* Although the article is written very concisely, it is easily readable (24 pp., 161 references) and gives a good survey of the state of development up to 1965.

D. Lyman presents a review of biochemical polymers. The clearly written article deals mainly with the use of polymers as organ substitutes. The influence of the chemical structure, shaping, and the surface state on the tissue compatibility and the polymer-blood reaction are discussed; however, little information is given on the use of hydrophilic polymers.

Advances in gel permeation chromatography are described by *J. Johnson, R. Porter,* and *M. Cantow.* The article covers the literature up to 1966, and deals mainly with separations in organic solvents. The literature data on the influence of experimental parameters on the form of the maxima are critically compared.

Volume 2 of this series also contains seven articles. Polymers containing phosphorus in the main and side chains are discussed in two contributions by *M. Sander* and *A. Steininger.* The comprehensive article (178 pp.) presents a good survey of the rapid development that has taken place during the past ten years in the chemistry of organophosphorus polymers.

The theory of polyester formation is discussed by *D. Salomon,* with special reference to the alkyd resins. Microgel formation and its influence on the polymer structure are dealt with in particular detail.

General symmetry considerations for stereoregular polymers are discussed in a short article by *A. Liquori.*

After a general survey of polymerizability and the polymerization mechanism of cyclic compounds, *R. Patsiga* describes the few known cases of successful copolymerization of vinyl compounds with cyclic compounds.

The other contributions also deal with interesting topics in macromolecular chemistry. *K. Ramey* and *W. Brey* report on the use of high-resolution NMR spectroscopy to establish the structures of polymers; *D. Blackadder* reviews the field of polymer single crystals, and an article by *G. Cameron* and *J. MacCallum* deals with the thermal degradation of polystyrene.

These reviews, which appear as separate items in the Journal of Macromolecular Science, will be widely read; the choice of subjects guarantees an excellent survey of current topics in macromolecular chemistry.

W. Heitz [NB 782 IE]

Molecular Orbital Theories of Bonding in Organic Molecules. By *R. L. Flurry, jr.,* Marcel Dekker, Inc., New York 1968, 1st Edit., x, 334 pp., numerous figures and tables, $17.75.

As is mentioned in the Introduction of the book, the author wrote it with two objects in mind. Firstly, he wished to provide an understanding of chemical bonding on the basis of the MO theory, and secondly he wished to offer accurate procedures for those who would like to carry out semi-empirical MO calculations for themselves. The second aim has been largely achieved. The eighth chapter provides a very good summary of the formalism of the Pariser-Parr-Pople (PPP) method and its variants. The brief survey (in

Chapter 9) of the current calculation methods for σ electrons is a welcome inclusion.

In the first two thirds of the book, the author follows the principle of proceeding from formally simple to formally difficult methods (this does not mean from conceptually simple to conceptually difficult), with the result that the reader understands nothing correctly, since the basis for understanding or the definitions already used usually appear about fifty pages later. For example, the elegant Longuet-Higgins method for the determination of certain molecular orbitals is given at a point where its relation to the actual HMO theory and its importance for molecules containing heteroatoms are not yet clear. The author also fails to take the opportunity of showing the relation between this method and the qualitative resonance theory.

In the discussion of the spectra of polyenes on the basis of the electron gas model, no reference is made to the importance of bond alternation. In spite of its unfortunate arrangement and the presence of a number of chapters that appear superfluous to the reviewer (*e.g.* on calculation tricks to simplify the Hückel equations), the book is more precise and more correct in many details than other comparable discussions. Little is said on the topic mentioned in the title, *i.e.* the MO theory of chemical bonding in organic molecules. The book would be better named "Procedures for Semiempirical MO Calculations".

W. Kutzelnigg [NB 785 IE]

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 4 50 75, Telex 46 1855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 4
APRIL 1969
PAGES 227–294

Lysozymes: A Chapter of Molecular Biology

By P. Jollès[*]

Hen egg-white lysozyme was the first enzyme whose tertiary structure could be elucidated. The peptide chain of this enzyme is arranged in two sections, of approximately equal size, that are separated by a deep cleft. Substrates (and inhibitors) are bound in this cleft via hydrogen bonds and are hydrolyzed under the action of Glu 35 and Asp 52, which form the active site of the enzyme. Although the lysozymes, which occur in many species of animals and plants, exhibit differences in their chemical behavior, they have the same qualitative biological activity; quantitatively important differences have been noted which also concern the specificity. Infection of E. coli with bacteriophages gives rise to a lysozyme whose formation is controlled by the phage DNA. The fact that mutated lysozymes are produced when the phages are treated with mutagens opens new fields of research in molecular biology.

1. Introduction

Hen egg-white lysozyme (EC 3.2.1.17) is one of the most extensively studied enzymes: its primary structure, the disposition of its disulfide bonds, its spatial behavior (first three-dimensional structure of an enzyme molecule), its active center, specificity, and mode of action have all been investigated in detail.

Lysozymes are not only found in hen and other bird egg-whites but are widespread enzymes, occurring in many human tissues and secretions, and in various other vertebrates and invertebrates; their presence has also been established in bacteria, phages, and plants. For these reasons, many fruitful comparative studies have been carried out, concerning mainly the relationship between their chemical structure and their biological activity. The purpose of the present review is not to summarize the research done since 1963 [1], but rather to draw the attention of the reader to some particular points and developments that are of interest for the study not only of the lysozymes but also of other enzymes.

2. Hen Egg-White Lysozyme

2.1. Primary Structure and Disulfide Bonds

The sequence of hen egg-white lysozyme was determined by *Jollès et al.* [2,3] and by *Canfield* [4]; it is a protein containing 129 amino-acid residues which

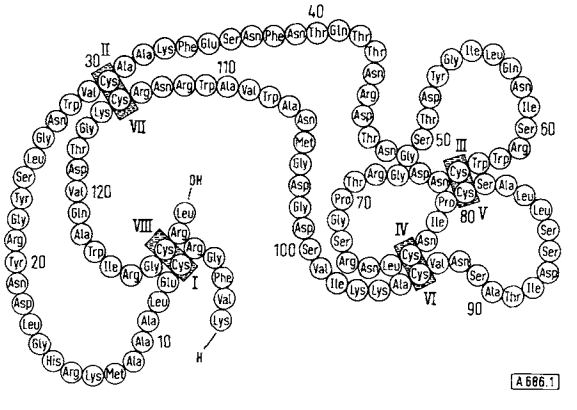


Fig. 1. Primary structure and disulfide bonds of hen egg-white lysozyme.

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[1] *P. Jollès*, Angew. Chem. *76*, 20 (1964); Angew. Chem. internat. Edit. *3*, 28 (1964).

[2] *J. Jollès* and *P. Jollès*, C. R. hebd. Séances Acad. Sci. *253*, 2773 (1961).

[3] *J. Jollès, J. Jauregui-Adell, I. Bernier*, and *P. Jollès*, Biochim. biophysica Acta *78*, 668 (1963).

[4] *R. E. Canfield*, J. biol. Chemistry *238*, 2698 (1963).

form a single polypeptide chain cross-linked at four places by disulfide (–S–S–) bonds [5–7] (Fig. 1).

2.2. Three-Dimensional Structure

The conformation of lysozyme has been determined by X-ray analysis [8]. The method depends on the preparation and study of a series of protein crystals into which additional heavy atoms, such as uranium atoms, have been introduced without otherwise affecting the crystal structure. The first successful applications of this method were in the study of sperm-whale myoglobin by *Kendrew* and of horse hemoglobin by *Perutz*. Comparison of the electron density distribution at 2 Å resolution with the primary structure revealed the spatial arrangement of each of the 129 amino acid residues of hen egg-white lysozyme and permitted the positions of some 95% of the atoms to be located to within about 0.3 Å.

The molecule may be considered in two parts. The first 40 residues form a right-hand wing in which the peptide chain is coiled twice around a core of non-polar residues in a stable-looking conformation (α-helix structure). Residues 41–95 branch out to form a left-hand wing which appears to have a less rigid conformation and contains a high proportion of polar residues. The remainder of the chain partially closes the gap between the two wings and wraps around the outside of the right-hand wing leaving a pronounced cleft between the two parts of the molecule [9].

In contrast to the myoglobin molecule, which consists of long stretches of α-helix linked by generally short non-helical corners, the α-helix content of lysozyme is only about 40%; there is evidence that nearly all of the helices are distorted to some extent from the standard structure, usually without affecting the number of residues per turn of helix [10]. There are three runs of helix, each about 10 residues long (5 to 15, 24 to 34, 88 to 96) for which the axial translation per residue and number of residues per turn fall close to the α-helix values of 1.5 Å and 3.6, respectively, given by *Pauling* and *Corey* (Table 1). There is a further shorter length of helix (80 to 85) which appears to be quite close to the 3.0_{10} type of hydrogen bond arrangement and an isolated turn (119 to 122) of 3.0_{10} helix (Figure 2).

Table 1. Parameters of helical regions of hen egg-white lysozyme [10].

Residues	Unit rise (Å)	Unit rotation (°)	Units per turn
5–15	1.51	100.2	3.59
24–34	1.48_5	98.3	3.66
80–85	1.66	106.6	3.38
88–96	1.45_5	96.7	3.72

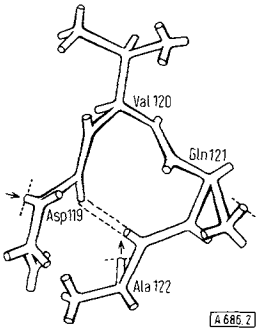


Fig. 2. A single turn of 3.0_{10} helix, showing also the conformation of Val 120 [10]. The hydrogen bonds are represented by dashed lines.

Another interesting but non-helical region [10] is formed by residues 41 to 54 where the chain doubles back on itself to form two strands arranged in the manner of an antiparallel pleated sheet (*Pauling* and *Corey* [11]) such as is thought to be the basic structure of silk fibroin [12] (Fig. 3).

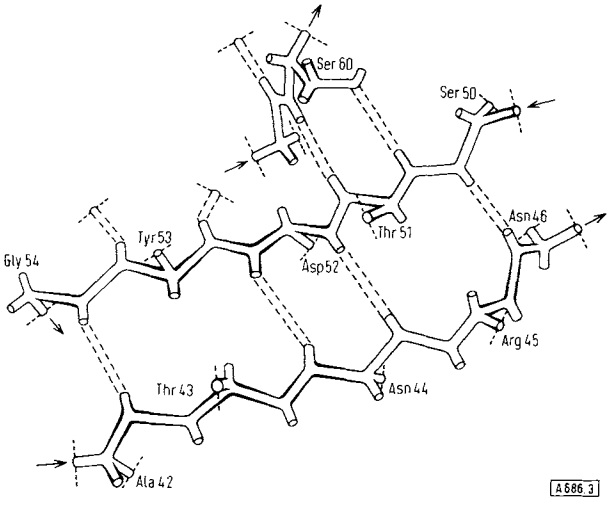


Fig. 3. Region between Ala 42 and Gly 54 where the main chain folds back on itself to form an antiparallel pleated sheet arrangement [10]. The hydrogen bonds are represented by dashed lines.

The acidic (Asp and Glu) and basic (Lys, Arg, and His) side chains and the terminal groups are all distributed over the surface of the molecule; this is also true of the remaining polar side chains, with two exceptions (Glu 57; Ser 91). In contrast, the great majority of the non-polar or hydrophobic side chains are in the interior of the molecule [10], where they are by no means distributed uniformly throughout the length of the chain. There is none between residues 38 and 55 and the deep cleft in the molecule seems to divide it into two parts of markedly different character (right-hand and left-hand wings, see above). In fact, lysozyme, like myoglobin, is quite well described as an oil drop with a polar coat [13].

[5] *P. Jollès, J. Jauregui-Adell*, and *J. Jollès*, C. R. hebd. Séances Acad. Sci. *258*, 3926 (1964).

[6] *J. R. Brown*, Biochem. J. *92*, 13 P (1964).

[7] *R. E. Canfield* and *A. K. Liu*, J. biol. Chemistry *240*, 1997 (1965).

[8] *C. C. F. Blake, D. F. Koenig, G. A. Mair, A. C. T. North, D. C. Phillips*, and *V. R. Sarma*, Nature (London) *206*, 757 (1965).

[9] *L. N. Johnson*, Exposés annu. Biochim. méd. *27*, 31 (1966).

[10] *C. C. F. Blake, G. A. Mair, A. C. T. North, D. C. Phillips*, and *V. R. Sarma*, Proc. Roy. Soc. (London), Ser. B *167*, 365 (1967).

[11] *L. Pauling* and *R. B. Corey*, Proc. nat. Acad. Sci. USA *37*, 729 (1951).

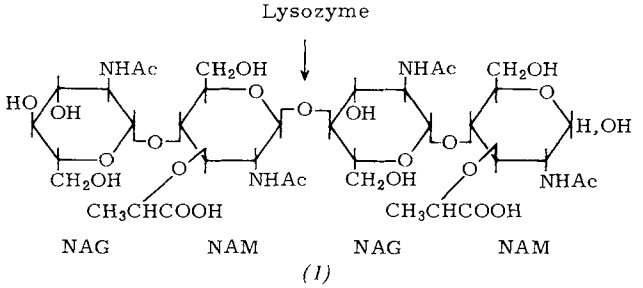
[12] *R. E. Marsh, R. B. Corey*, and *L. Pauling*, Acta crystallogr. *8*, 62 (1955).

[13] *D. C. Phillips*, Sci. American *215*, 78 (1966).

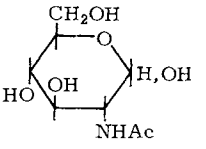
2.3. The Activity of Lysozyme

Simultaneously with his discovery of lysozyme, *Fleming*[14] discovered a gram-positive species of bacteria, *Micrococcus lysodeikticus*, which is particularly susceptible to the action of the enzyme. It was many years later when *Salton*[15] demonstrated that the substrate is located entirely within the bacterial cell wall. An indication of the type of linkage attacked by lysozyme was first established when *Berger* and *Weiser*[16] showed that lysozyme also degrades chitin, the linear polymer of *N*-acetylglucosamine (NAG). They concluded that the enzyme possesses β (1→4) glucosaminidase activity.

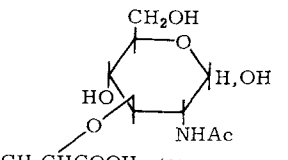
Salton and *Ghuysen*[17] subsequently isolated a tetrasaccharide containing equimolar amounts of NAG and *N*-acetylmuramic acid (NAM) from lysozyme digests of *M. lysodeikticus* cell walls. On incubation with lysozyme, this tetrasaccharide yielded a disaccharide containing NAG and NAM. It was deduced that the tetrasaccharide is a dimer of this disaccharide in which the two units are joined by the lysozyme-sensitive β (1→4) linkage. Its complete structure was established only in 1963 by *Jeanloz et al.*[18] as *N*-acetylglucosaminyl-β-(1→4)-*N*-acetylmuraminyl-β-(1→4)-*N*-acetylglucosaminyl-β-(1→4)-*N*-acetylmuramic acid *(1)*.



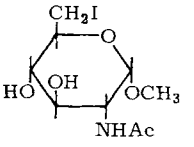
(1)



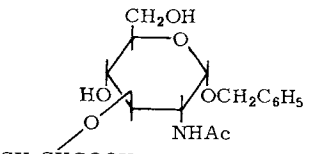
(2)



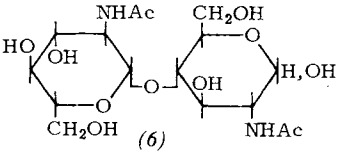
(3)



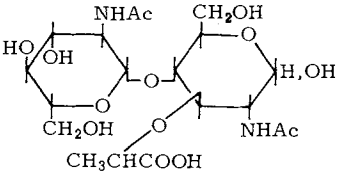
(4)



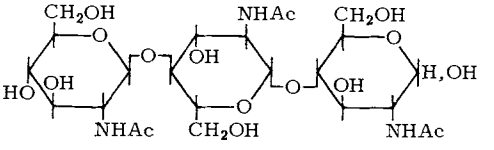
(5)



(6)



(7)



(8)

The proposed structure of the cell-wall mucopolysaccharide, containing alternate units of NAG and NAM residues joined by β (1→4) linkages, is very similar to the structure of chitin, the only difference being the inclusion of NAM residues in the former; it is therefore probable that the effects of lysozyme upon chitin and upon the bacterial cell walls are very closely related. In fact, a large proportion of the recent work on the activity of lysozyme has been concerned with its properties as a chitinase, especially during its interaction with relatively short oligomers of NAG. NAG *(2)* and other simple amino-sugar molecules *(3)–(7)*, including trimeric NAG *(8)*, act as competitive inhibitors of the activity of lysozyme by binding to the enzyme in the same way as a part of the large substrate molecule. Experiments at low resolution with low molecular weight inhibitors related either to the bacterial cell wall substrate or to the poly-NAG substrate have shown that the sugars bind the lysozyme at a number of different places in the cleft between the right-hand and left-hand wings of the lysozyme molecule[9,19,20].

Trimeric NAG *(8)* fills the top half of the cleft and is bound to the enzyme by a number of interactions; six strong hydrogen bonds have been identified, two of them connecting an NAG residue to the side chains of the tryptophan residues 62 and 63. Among the more important nonpolar interactions are those between the NAM residue and the ring system of Trp 62: these deserve special mention because they are affected by small changes in the conformation of the enzyme molecule that occur on reaction with the trisaccharide *(8)*[13].

Insofar as the complex formed by tri-NAG and the enzyme is stable, it differs from the enzyme-substrate complex involved in catalysis. Furthermore, it is known that at low concentrations, tri-NAG is rather an inhibitor than a substrate that is broken down. As tri-NAG fills only half of the cleft, the presence of more sugar residues, filling the remainder, would appear

[14] *A. Fleming*, Proc. Roy. Soc. (London), Ser. B *93*, 306 (1922).

[15] *M. R. J. Salton*, Nature (London) *170*, 746 (1952).

[16] *L. R. Berger* and *R. S. Weiser*, Biochim. biophysica Acta *26*, 517 (1957).

[17] *M. R. J. Salton* and *J. M. Ghuysen*, Biochim. biophysica Acta *36*, 552 (1959); *45*, 355 (1960).

[18] *R. W. Jeanloz*, *N. Sharon*, and *H. M. Flowers*, Biochem. biophys. Res. Commun. *13*, 20 (1963).

[19] *L. N. Johnson* and *D. C. Phillips*, Nature (London) *206*, 761 (1965).

[20] *C. C. F. Blake*, *L. N. Johnson*, *G. A. Mair*, *A. C. T. North*, *D. C. Phillips*, and *V. R. Sarma*, Proc. Roy. Soc. (London), Ser. B *167*, 378 (1967).

necessary for the formation of a reactive enzyme-substrate complex. In fact, another three sugar residues can be added to the tri-NAG in such a way that satisfactory interactions can take place between the atoms of the substrate and those of the enzyme [13]. However, the forth sugar residue must be distorted a little out of its most stable "chair" conformation into a conformation in which its carbon atoms 1, 2, and 5 and the oxygen atom attached to C-5 all lie in a plane [13]. The distortion assists in breaking the substrate below the fourth sugar. This observation and many other results indicate that the linkage which is broken is the one between the fourth and the fifth sugar residue (between C-1 and the oxygen in the glycosidic linkage). The most reactive groups in the vicinity of this bond are the side chains of Asp 52 and Glu 35.

According to observations by *Phillips* [13], *Blake et al.* [20], and *Vernon* [21], the events leading to the rupture of the bacterial cell wall probably take the following course:

1) The substrate becomes attached to the enzyme and is held in position by hydrogen bonds and by other forces; in the process the ring of the fourth sugar residue becomes distorted and takes up a conformation favoring formation of a carbonium ion.

2) A proton is transferred to the glycosidic oxygen atom from the side chain of Glu 35.

3) Heterolysis of the C_1 carbon-oxygen bond gives a carbonium ion which is stabilized by interaction with the negative charge of the side chain of Asp 52.

4) The disaccharide obtained from the hexasaccharide diffuses away and a water molecule attacks the carbonium ion, thus completing hydrolysis (Fig. 4).

It is apparent that three factors are responsible for the catalytic effect: general acid-catalysis; activation of the substrate by distortion; and electrostatic interaction.

At this stage, it is fitting to quote a remark made by *Perutz* [22]: "For the first time we have been able to interpret the catalytic activity of an enzyme in stereochemical terms. It seems rash to generalize from the structure of one enzyme, but we may broaden our base by elevating myoglobin and haemoglobin to the rank of honorary enzymes, as *Monod* has suggested, and call the heme groups their active sites. What these three proteins have in common is the distribution of polar and non-polar side chains; the interior of the lysozyme as well as that of the globin chains is made up largely of hydrocarbons, providing a medium of low dielectric constant. In each case the active center lies in a pocket formed by this non-polar medium, and the pocket contains some polar residues which are essential for activity."

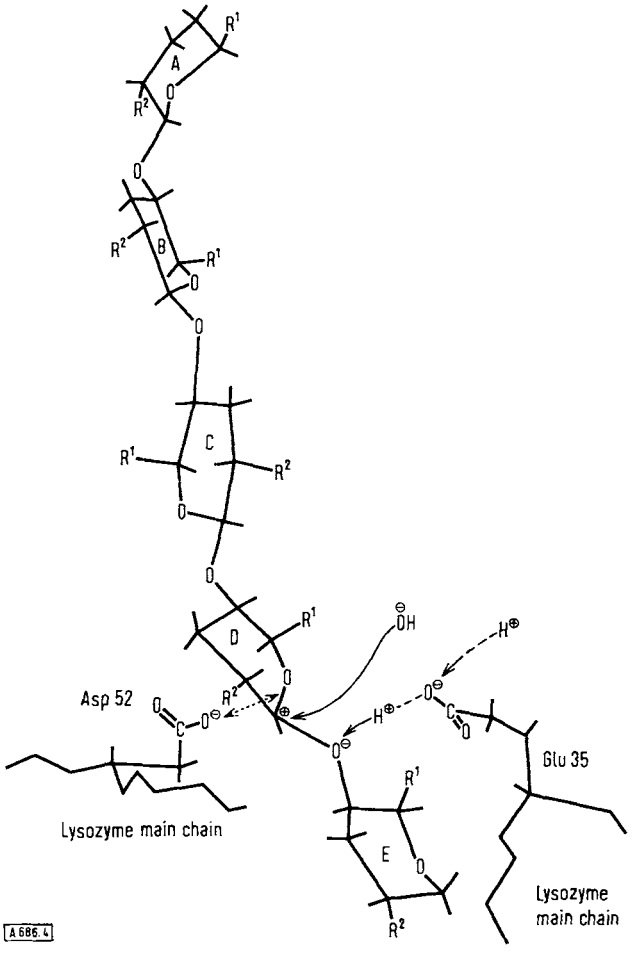


Fig. 4. Splitting of substrate by lysozyme is believed to involve the proximity and activity of two side chains, Glu 35 and Asp 52. A proton probably becomes detached from the OH group of residue 35 and attaches itself to the oxygen atom that joins rings D and E, thus breaking the bond between the two rings [13].

[21] *C. A. Vernon*, Proc. Roy. Soc. (London), Ser. B *167*, 389 (1967).

2.4. Biosynthesis of Lysozyme

The incubation of minced hen oviduct with ^{3}H-leucine was undertaken by *Canfield* and *Anfinsen* [23], and led to the formation of radioactive lysozyme. The distribution of radioactivity in the leucine residues along the polypeptide chain of the reduced, carboxymethylated protein was established by isolation of leucine-containing peptides produced by trypsin digestion. The peptides were then hydrolyzed and the specific radioactivities of the leucine residues were determined. Samples of radioactive lysozyme isolated from oviduct minces that had been incubated for 3 and 5 minutes, showed unequal labeling of leucine residues, and the relative specific radioactivities were found to increase from the NH_2-terminal to the COOH-terminal end of the chain.

These observations [23] are consistent with the model of amino acid assembly in which the polypeptide chain grows unidirectionally, initiation occurring at the NH_2-terminal end and termination at the COOH-terminal end. It seems reasonable to assume [13] that the folding of the protein chain to its native conformation begins at the amino end even before synthesis is complete. Parts of the polypeptide chain, particularly those near the terminal amino end, may fold into stable conformations that can still be recognized in the finished molecule and that act as "internal templates", or centers around which the rest of the chain is

[22] *M. F. Perutz*, Proc. Roy. Soc. (London), Ser. B *167*, 448 (1967).

[23] *R. E. Canfield* and *C. B. Anfinsen*, Biochemistry *2*, 1073 (1963).

folded [13]. The three-dimensional model provides support for these ideas, especially as the first residues at the terminal amino end form a compact structure.

2.5. Relationship between Structure and Activity

2.5.1. The NH_2- and COOH-Terminal Sequences

The NH_2- and COOH-terminal sequences are split off by aminopeptidase and carboxypeptidase respectively. The shortened enzymes, des-lysylvaline-lysozyme [24] and des-arginylleucine-lysozyme [25] are always active. At low ionic strength the des-arginylleucine-lysozyme is even slightly more active than the native molecule, whereas at high ionic strength it proves to be significantly less active.

2.5.2. Role of the Tryptophan Residues

Hen lysozyme contains six tryptophan residues per molecule. Recent X-ray studies at a 2 Å resolution demonstrated the importance of some of these residues for the biological activity [8, 19]. Other studies in this field were made by chemical and physical methods [19, 26, 27] (see Table 2).

According to recent investigations by *Kronman et al.* [37] *N*-bromosuccinimide shows no specificity in its reaction with the tryptophan groups of lysozyme. Caution must therefore be exercised in the use of this reagent for determining the extent of "exposure" of side chains of native proteins.

2.5.3. Role of the Histidine Residue

Numerous investigations on lysozymes whose molecules contain only one histidine residue have shown that this amino acid is not involved in the active site. Fully active lysozymes containing no histidine have, in fact, been isolated from duck egg-white [38].

2.5.4. Role of the Cystine Residues

Hen egg-white lysozyme contains four disulfide bridges. With the discovery of lysozymes containing three [39], two [40], or no [41] cystine bonds per molecule, it appeared that these latter are not essential for biological activity. However, *Jollès et al.* [42] showed that the presence of disulfide bridges is important for the heat stability of the enzymes. Lysozymes with four cystine bonds are relatively stable in acidic or neutral solution when heated for 0.5 or 1 min at 100 °C. Human lysozymes (three cystine residues) are a little more heat sensitive; when the cystine content drops to only two residues, as in goose lysozyme, the heat stability is almost lost.

Table 2. Relationship between the chemical modification of tryptophan residues and the biological activity of hen egg-white lysozyme.

Reagent	Number of modified tryptophan residues		Conversion product	Amino acid (no.)	Ref.
	for complete deactivation	without loss of activity			
N-bromosuccinimide	2				[28]
N-bromosuccinimide	4		oxindole	[a]	[29]
iodine	1.1		probably oxindole	[a]	[30]
hydrogen peroxide	1.4		[a]	[a]	[31]
2-hydroxy-5-nitro-benzyl bromide		2	[a]	[a]	[32]
N-bromosuccinimide	1			62	[33]
5 mole iodine	1			108	[34]
1 mole iodine	2			108, 62	
iodine	1			108	[35]
ozone		2	*N'*-formyl-kynurenine	108 111	[36]

[a] Not examined

[24] *J. Jollès* and *P. Jollès*, Biochem. biophysic. Res. Commun. *22*, 22 (1966).

[25] *W. T. Morgan* and *J. P. Riehm*, Biochem. biophysic. Res. Commun. *30*, 50 (1968).

[26] *K. Hayashi*, *T. Imoto*, and *M. Funatsu*, J. Biochemistry [Tokyo] *55*, 516 (1964).

[27] *S. S. Lehrer* and *G. D. Fasman*, Biochem. biophysic. Res. Commun. *23*, 133 (1966).

[28] *I. Bernier* and *P. Jollès*, C. R. hebd. Séances Acad. Sci. *253*, 745 (1961).

[29] *G. J. S. Rao* and *L. K. Ramachandran*, Biochim. biophysica Acta *59*, 507 (1962).

[30] *F. J. Hartdegen* and *J. A. Rupley*, Biochim. biophysica Acta *92*, 625 (1964).

[31] *Y. Hachimori*, *H. Horinishi*, *K. Kurihara*, and *K. Shibata*, Biochim. biophysica Acta *93*, 346 (1964).

[32] *T. Bewley* and *C. H. Li*, Nature (London) *206*, 624 (1965).

[33] *K. Hayachi*, *T. Imoto*, *G. Funatsu*, and *M. Funatsu*, J. Biochemistry (Tokyo) *58*, 227 (1965).

[34] *C. C. F. Blake*, Proc. Roy. Soc. (London), Ser. B. *167*, 435 (1967).

[35] *J. A. Rupley*, Proc. Roy. Soc. (London), Ser. B *167*, 416 (1967).

[36] *A. Previero*, *M.-A. Coletti-Previero*, and *P. Jollès*, J. molecular Biol. *24*, 261 (1967).

[37] *M. J. Kronman*, *F. M. Robbins*, and *R. E. Andreotti*, Biochim. biophysica Acta *143*, 462 (1967).

[38] *J. Jollès*, *G. Spotorno*, and *P. Jollès*, Nature (London) *208*, 1204 (1965).

[39] *P. Jollès*, *D. Charlemagne*, *J.-F. Petit*, *A.-C. Maire*, and *J. Jollès*, Bull. Soc. chim. biol. *47*, 2241 (1965).

[40] *A.-C. Dianoux* and *P. Jollès*, Biochim. biophysica Acta *133*, 472 (1967).

[41] *A. Tsugita* and *M. Inouye*, J. molecular Biol. *37*, 201 (1968).

[42] *J. Jollès*, *A.-C. Dianoux*, *J. Hermann*, *B. Niemann*, and *P. Jollès*, Biochim. biophysica Acta *128*, 568 (1966).

It has also been established that the lysozyme with the smallest cystine content has the highest specific activity [42]. If the specific activity of hen egg-white lysozyme is set at unity, then a value of the same order is found for the duck enzymes, and 3 ± 0.5 for the human lysozymes and 5 ± 0.5 for the goose enzyme. Interaction between the substrate and the active center of the goose enzyme probably occurs more easily because this enzyme exhibits a lower degree of folding.

2.5.5. Reactivation of Reduced Lysozyme

Lysozyme fully reduced with β-mercaptoethanol in 8 M urea can be reactivated by enzymic and non-enzymic procedures. Enzymic reactivation [43, 44] occurs, without any induction period, by disulfide interchange [45]. Non-enzymic reactivation proceeds by oxidation of the reduced protein in buffered solutions containing small amounts of β-mercaptoethanol. The reoxidized lysozyme has the same tertiary structure as the native enzyme [46, 47]. Active lysozyme can also be regenerated from the mixed disulfide of hen lysozyme and cystine [48].

2.5.6. Cross-linking of Lysozyme

The cross-linking of lysozyme has been effected by reaction with phenol-2,4-disulfonyl chloride. The cross-linked protein retains its enzymic activity, has approximately the same molecular weight as native lysozyme, and, according to optical rotatory dispersion analysis [49], has essentially the same conformation.

2.5.7. Irradiation of Lysozyme

Crystallized lysozyme has been irradiated with doses of X-rays between 1 and 100 millirads and with γ-rays from ^{60}Co [51]. Doses of a few millirads have no measurable effect on activity or on the amino acid composition of lysozyme. However, increased doses convert the original protein into a large number of modified proteins showing an increased or reduced lysozyme activity. Only X-ray doses of the order of magnitude of 100 mrads produce changes in the amino acids which can be determined with an Autoanalyzer. These changes involve mainly the sulfur-containing, the aromatic, and the long chain aliphatic amino acids [50].

2.5.8. Conclusion

The importance of residues 35 (Glu) and 52 (Asp) and of some Trp residues for the biological activity led to a number of synthetic assays. Thus the synthesis of polypeptides having carboxyl functions in hydrophobic as well as in hydrophilic regions (Phe/Glu = 1/0.3; mean molecular weight 63650) has been reported [52]; it was claimed that they are able to degrade the cell walls of *M. lysodeikticus*. The syntheses of short sequences of hen lysozyme were reported by *Morley* [53] and *Jollès* [54].

2.6. Application of Physico-Chemical Methods to the Study of Lysozyme

On interaction with either a substrate or an inhibitor lysozyme displays a red shift in its ultraviolet spectrum and it was implied from model studies that tryptophan was involved in this shift [55, 56].

In the presence of *N*-acetylglucosamine, the circular dichroism of lysozyme increases in the aromatic range, a phenomenon that is also attributed to participation of tryptophan [57].

Significant changes in the tryptophan fluorescence can occur on binding of appropriate inhibitors [58, 59]. Large changes in the tryptophan fluorescence of lysozyme and of the lysozyme-tri-*N*-acetyl-D-glucosamine complex are observed with changing pH and are associated with changes in the ionization of certain groups of the enzyme [58, 60, 61]. These fluorescence changes occur over a pH range in which the gross conformation is thought to be invariant. The selective quenching of tryptophan fluorescence in lysozyme by iodide ions is also observed [62]. Fluorescence changes in ultraviolet-irradiated lysozyme were studied by *Churchich* [63].

The optical rotatory dispersion of aqueous solutions of lysozyme has been measured over a wavelength range of 195–600 nm [64]. By this technique, questions regarding the conformation of the enzyme under different conditions have been investigated [64–67].

[43] *R. F. Goldberger, C. J. Epstein,* and *C. B. Anfinsen,* J. biol. Chemistry *239,* 628, 1406 (1964).

[44] *P. Venetianer* and *F. B. Straub,* Biochim. biophysica Acta *67,* 166 (1963).

[45] *D. Givol, R. F. Goldberger,* and *C. B. Anfinsen,* J. biol. Chemistry *239,* PC 3115 (1964).

[46] *C. J. Epstein* and *R. F. Goldberger,* J. biol. Chemistry *238,* 1380 (1963).

[47] *R. F. Goldberger* and *C. J. Epstein,* J. biol. Chemistry *238,* 2988 (1963).

[48] *L. Kanarek, R. A. Bradshaw,* and *R. L. Hill,* J. biol. Chemistry *240,* PC 2756 (1965).

[49] *G. L. Moore* and *R. A. Day,* Science (Washington) *159,* 210 (1968).

[50] *K. Dose, S. Risi,* and *H. Rauchfuss,* Biophysik *3,* 202 (1966).

[51] *A. M. Desai* and *K. S. Korgaonkar,* Radiat. Res. *21,* 61 (1964).

[52] *V. K. Naithani* and *M. M. Dhar,* Biochem. biophysic. Res. Commun. *29,* 368 (1967).

[53] *J. S. Morley,* unpublished.

[54] *P. Jollès* and *J. Jollès,* Helv. chim. Acta *51,* 980 (1968).

[55] *K. T. Hayashi, G. Imoto,* and *M. Funatsu,* J. Biochemistry (Tokyo) *54,* 381 (1963); *55,* 516 (1964).

[56] *F. W. Dahlquist, L. Jao,* and *M. Raftery,* Proc. nat. Acad. Sci. USA *56,* 26 (1966).

[57] *A. N. Glazer* and *N. S. Simmons,* J. Amer. chem. Soc. *88,* 2335 (1966).

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Recent progress in the application of NMR to problems of protein structure and function has made it possible to obtain more detailed information on the behavior of enzymes in solution [68]. Partial assignments in the low field (aromatic) region of the lysozyme spectrum, a comparison of several denatured conformations, and spectral changes resulting from inhibitor binding were reported [68].

The elucidation of the tertiary structure of lysozyme has stimulated various attempts to find stereochemical rules relating the primary to the tertiary structure [69]; this approach might be complemented by a statistical analysis of the amino acid sequences [70]. A method of recognizing α-helical segments in the polypeptide chains with known primary structure is currently being investigated [71].

Sophianopoulos [72] and *Antonini* [73] found that the enzyme polymerizes reversibly with increasing pH at 20 °C; between pH 5 and 9, the dimer predominates.

Before concluding this section, mention should be made of the studies by *Hamaguchi* [65] concerning the effect of different reagents, of pH, and of temperature on the stability and conformation of lysozyme.

2.7. Mechanism of Action of Lysozyme

Lysozyme has been used extensively in degrading bacterial walls (see Section 2.3.) [17, 18]. The influence of various chemical modifications of the walls on lysozyme sensitivity were recently studied by *Salton* [74] (Table 3) and *Hara* [75]. The isolation of a disaccharide

Table 3. The influence of chemical substitution of cell walls on lysozyme sensitivity [74].

Modification	Effect
O-Acetylation (OH)	Complete inhibition
Esterification (COOH)	Partial inhibition
Diethylammonium salt formation (COOH)	Partial inhibition
Deacetylation at nitrogen	Inhibition
N-Succinylation ($-NH_2$)	Stimulation
Reaction with 1-fluoro-2,4-dinitrobenzene ($-NH_2$)	No effect
Reaction with 5-dimethylamino-1-naphthalene-sulfonyl chloride (DANS) ($-NH_2$)	No effect

(NAG–NAM), of two disaccharide peptides, and the corresponding tetrasaccharides from lysozyme digests of *Micrococcus lysodeikticus* cell walls was described in detail by *Sharon* [76, 77]. These compounds have been used for the study of the enzymic activity of lysozyme. The synthesis of derivatives of muramic acid made possible further investigations on the specificity of the enzyme [78]. Once it had been shown that lysozyme acts on colloidal chitin [16], there followed a number of reports on the purification of soluble *N*-acetylglucosamine oligosaccharides of varying chain lengths [79, 80] and of the action of the enzyme on these compounds [81] ("chitinase activity" EC 3.2.1.14, of lysozyme).

One of the low-molecular-weight substances that have been investigated in detail as a substrate for lysozyme is the tetrasaccharide NAG–NAM–NAG–NAM. Digestion of this compound into disaccharide has been followed by *Sharon* [76] by paper chromatography, colorimetry, and polarimetry. Together with the disaccharide, numerous oligosaccharides were characterized.

In addition to hydrolysis, lysozyme also catalyzes transglycosylation [76, 82]; it is feasible that hydrolysis of the tetrasaccharide does not proceed by direct cleavage but by a transfer mechanism (Scheme 1). Transglycosylation reactions were also reported with short-chain chitin oligosaccharides [83–86].

2 tetraose (D–D) → Hexaose (D–D–D) + Disaccharide (D)
D–D–D + D–D → D–D–D–D + D
2 D–D–D → D–D–D–D–D + D
2 D–D–D → D–D–D–D + D–D

Scheme 1. Course of the transglycosylation reaction induced by lysozyme [82].

"D" stands for the cell-wall disaccharide isolated from *M. lysodeikticus* (NAG–NAM).

Lysozyme can also act as a transferase; thus *Sharon* [87] observed that the enzyme is able to transfer NAG-NAM residues to a variety of mono- and disaccharide acceptors (NAG, D-glucose, D-glucosides, *etc.*) and to form and cleave β(1→2) glycosidic bonds. *N*-acetylglucosamine, and closely related oligosaccharides strongly inhibit the enzymic activity of lysozyme [88], as also do derivatives of D-glucosamine [89]. Fluorescence studies show that these inhibitors interact with the tryptophan residues in the active site of the enzyme (Table 4).

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Table 4. Changes in the position of the emission maximum (λ_{max}) and in the height of the emission maximum (Q) of lysozyme on addition of an inhibitory sugar [88].

Sugar [a]	Conc. for 50% inhibition (mM)	$\Delta\lambda_{max}$ (nm) [b]	ΔQ (%) [c]
Tetra-NAG	~1	−10	+40
Di-NAG	0.6	−10	+25
Di-NAG–NAM	3	−10	−12
NAG–NAM pentapeptide	3	−10	+ 7
Gal-NAG	7	−10	+18
NAG	7	0	− 7
NAG–NAM	12	0	−12
NAG–NAM methyl ester	25	0	−12
Cellobiose	>100	0	0

[a] The oligosaccharides are β (1→4) linked.
[b] $\Delta\lambda_{max}$ = shift in the emission maximum.
[c] ΔQ = change of the height of the emission maximum relative to that of the enzyme alone (= 100%).

Further synthetic lysozyme substrates, which can be assayed colorimetrically, have been described by *Lowe* [90] and *Osawa* [91].

2.8. Immunological Studies

Tsugita et al. succeeded in isolating four immunologically active peptides from a peptic digest of lysozyme and in elucidating their chemical structures; these peptides seemed to bear at least one antigenic determinant [92,92a]. A peptide obtained by trypsin degradation, consisting of three peptide sequences Trp 62 → Arg 68, Asn 74 → Leu 83, and Leu 84 → Lys 96 linked by two disulfide bonds Cys 64 → Cys 80 and Cys 76 → Cys 94, was also found to exhibit weak but definite immunological activity. According to *Bonavida et al.* [93], lysozyme treated with cyanogen bromide retains a large proportion of the immunological features of the native enzyme. The proximity of the enzyme active center and an antigenic determinant of lysozyme has also been suggested [94]. Univalent antibodies of low molecular weight (3.5 S) could be purified by gel-filtration and DEAE-cellulose chromatography from lysozyme antisera of rabbits [95]. A selective fractionation of anti-lysozyme antibodies of different determinant specificities and the formation of antibodies with specificity directed against a unique region in native lysozyme have recently been described [95a].

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3. Lysozymes of Different Origins

Lysozymes are widely distributed enzymes; they are found in a great number of organs, tissues, and secretions (spleen, kidney, leucocytes, tears, saliva, milk, serum) of vertebrates. They also occur in invertebrates, bacteria, phages, and plants. Previous studies with hen egg-white lysozyme led us to attribute the following properties to this enzyme [1]: (a) basic protein; (b) low molecular weight (15000); (c) stability at acidic pH at higher temperatures; (d) lability at alkaline pH; (e) lysis of suspensions of *Micrococcus lysodeikticus*; (f) its action on an appropriate substrate liberates compounds that can be detected by reagents for reducing sugars and amino sugars. However, our recent research [96] in this field has shown that this definition of a lysozyme must be at least partly modified. A brief survey of the purification, analysis, structure, and properties of some lysozymes will be undertaken in the second part of this review.

3.1. Purification, Analysis, and Structure

3.1.1. Two Different Lysozymes in the Same Secretion: Duck Egg-White Lysozymes [97]

During ion-exchange chromatography of a duck-lysozyme rich material on Amberlite CG-50, two (sometimes three) enzymes were characterized [97], *i.e.* duck lysozymes I, II, and III (in the order of elution from the column). Two of them (II and III) were always found, even when the enzymes were purified from a single egg of a well defined species; they are devoid of histidine [97–100] (Fig. 5).

Duck II: H-Lys-Val-Tyr-Ser-Arg-Cys-Glu-Leu-Ala-Ala-Ala-Met-Lys-
Hen: H-Lys-Val-Phe-Gly-Arg-Cys-Glu-Leu-Ala-Ala-Ala-Met-Lys-
Duck III: H-Lys-Val-Tyr-Gln-Arg-Cys-Glu-Leu-Ala-Ala-Ala-Met-Lys-
Human milk: H-Lys-Val-Phe-Glu-Arg-Cys-Glu-Leu-Ala-Arg-

Arg-Leu-Gly-Leu-Asp-Asn-Tyr-Arg-Gly-Tyr-Ser-Leu-Gly-Asn-Trp-Val-
Arg-His-Gly-Leu-Asp-Asn-Tyr-Arg-Gly-Tyr-Ser-Leu-Gly-Asn-Trp-Val-
Arg-Leu-Gly-Leu-Asp-Asn-Tyr-Arg-Gly-Tyr-Ser-Leu-Gly-Asn-Trp-Val-

Cys-Ala-Ala-Asn-Tyr-Glu-Ser-Ser-Phe-Asn-Thr-Glu-Ala-Thr-Asn-Arg-
Cys-Ala-Ala-Lys-Phe-Glu-Ser-Asn-Phe-Asn-Thr-Gln-Ala-Thr-Asn-Arg-
Cys-Ala-Ala-Asn-Tyr-Glu-Ser-Gly-Phe-Asn-Thr-Glu-Ala-Thr-Asn-Arg-
-Trp-Glu-Ser-Gly-Tyr-Asn-Thr-Arg-

Asp-Thr-Asn-Gly-Ser-Thr-Asx-Tyr-
Asp-Thr-Asn-Gly-Ser-Thr-Asp-Tyr-
Asp-Thr-Asn-Gly-Ser-Thr-Asx-Tyr-
-Ser-Thr-Asp-Tyr-

Fig. 5. Chemical structures of the N-terminal moities (53 amino acids) of duck egg-white lysozymes II and III. Comparison with hen egg-white lysozyme [100]. N-terminal sequence and peptides in the active site (Glu 35 and Asp 52) of human milk lysozyme [107]. Asx denotes Asp or Asn.

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Thus it was possible, for the first time, to isolate from the *same* secretion *two* lysozymes which not only exhibit different chromatographic behavior but also have slight structural differences [99, 100], which cannot be deduced from a simple comparison of the amino acid compositions. However, these slight differences do give rise to differences in reaction velocities, in the behavior towards a competitive inhibitor such as NAG [101], and in the apparent affinity constants for the bacterial substrate [102] (Table 5).

3.1.2. An Unusual Bird Lysozyme: Goose Egg-White Lysozyme [40]

Only one lysozyme could be isolated from geese of different species and characterized by ion exchange chromatography. Its amino acid composition is quite different from those of other bird egg-white lysozymes [40, 103]. The low cystine (two residues/molecule) and tryptophan (three residues/molecule) contents [104] are of special importance. Goose lysozyme is very labile at higher temperatures, even at acidic pH [101]; its reaction velocity against *M. lysodeikticus* cells [102] and its specificity toward low molecular weight substrates at pH 6.2 are very different from those of other lysozymes [104, 105].

3.1.3. Lysozymes from Normal Human Tissues and Secretions

Jollès et al. [39, 96] obtained a great number of lysozymes from normal human tissues and secretions in a chromatographically pure state by ion exchange chromatography on Amberlite CG-50, *i.e.* lysozymes from milk [106, 107], tears [107], saliva [108], placenta [109], spleen, serum, and leucocytes [110]. All these human enzymes exhibit a very similar behavior on chromatography while differing considerably from bird lysozymes. In this connection it is worth mentioning that two hen lysozymes (egg-white and lung) were found to show widely diverging chromatographic behavior; the same applies to two dog lysozymes (spleen and kidney) [1].

Amino acid analyses of all the human lysozymes yielded comparable results. These data seem to indicate the probable identity of the enzyme in all human tissues and secretions. The analytical results are in agreement with recent observations of *Osserman* and *Lawlor* [111]. However, the data concerning the duck enzymes II and III, which embody structural differences despite very similar analyses, suggest that caution should be exercised in interpreting the results obtained for human lysozymes. A comparison of the tryptic peptides of the reduced carboxymethylated enzymes seems necessary. Detailed chemical structure studies concerning milk lysozyme are already in progress [107].

The peptide maps obtained by electrochromatography from milk and saliva lysozymes seem almost identical [107]. Research designed to clarify possible dissimilarities between other human lysozymes is currently in progress. The human lysozymes isolated by *Jolles et al.* have all approximately three to four times the activity of hen egg-white lysozyme (when titrated with suspensions of *M. lysodeikticus* at equivalent concentrations).

3.1.4. Lysozymes from Leukemia Patients

In the case of some leukemias, large quantities of lysozyme(s) are found in the blood [112] and/or in the urine [111]. *Jollès et al.* [112] determined the serum lysozyme concentration in a group of patients with a variety of diseases of hemopoietic tissues. A correlation was observed between the serum lysozyme level and the granulocyte count; a possible relationship with the monocyte count was also suggested. The lysozymes of serum and leucocytes from patients suffering from chronic myelogenous leukemia were purified and analyzed [110]. Their composition seemed identical with that of the enzymes from normal tissues. However, on ion-exchange chromatography on Amberlite CG-50 the main active peak was always followed by a smaller one; a comparison of the peptide maps of both enzymes will be necessary to ascertain whether they are identical or not.

Osserman and *Lawlor* [111] purified human serum and urinary lysozymes in monocytic and monomyelocytic leukemias and found a close correspondence with the values found for healthy human beings [107]. *Jollès* confirmed, by an automated method [113], that only those leukemia patients suffering from an acute myeloblastic leukemia excrete large quantities of lysozyme; during purification of the enzyme two biologically active peaks were again observed on ion-exchange chromatography [114]. Their specific activities were higher than those from normal human lysozymes.

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3.1.6. Phage Lysozymes: A Contribution to the Study of the Genetic Code. First *in Vitro* Synthesis of an Enzyme

Escherichia coli cells produce a lysozyme after infection with bacteriophage [115]. Since this process is controlled by phage DNA, various mutants of lysozyme can easily be obtained by treating phage with mutagens [116]. Some important problems regarding

H-Met-Asn-Ile-Phe-Glu-Met-Leu-Arg-Ile-Asp-Glu-Gly-Leu-Arg-Leu-Lys-Ile-Tyr-Lys-Asp-Thr-Glu-Gly-Tyr-Tyr-Thr-Ile-Gly-Ile-Gly-His-Leu-Leu-Thr-Lys-Ser-Pro-Ser-Leu-Asn-Ala-Ala-Lys-Ser-Glu-Leu-Asp-Lys-Ala-Ile-Gly-Arg-Asn-Cys-Asn-Gly-Val-Ile-Thr-Lys-Asp-Glu-Ala-Glu-Lys-Leu-Phe-Asn-Gln-Asp-Val-Asp-Ala-Ala-Val-Arg-Gly-Ile-Leu-Arg-Asn-Ala-Lys-Leu-Lys-Pro-Val-Tyr-Asp-Ser-Leu-Asp-Ala-Val-Arg-Arg-Cys-Ala-Leu-Ile-Asn-Met-Val-Phe-Gln-Met-Gly-Glu-Thr-Gly-Val-Ala-Gly-Phe-Thr-Asn-Ser-Leu-Arg-Met-Leu-Gln-Gln-Lys-Arg-Trp-Asp-Glu-Ala-Ala-Val-Asn-Leu-Ala-Lys-Ser-Arg-Trp-Tyr-Asn-Gln-Thr-Pro-Asn-Arg-Ala-Lys-Arg-Val-Ile-Thr-Thr-Phe-Arg-Thr-Gly-Thr-Trp-Asp-Ala-Tyr-Lys-Asn-Leu-OH

Fig. 6. The amino acids equence of T4 phage lysozyme [41]. The sequence of T 2 phage lysozyme is the same with 3 substitutions: Asn (40) → Ser, Ala (41) → Val, Thr (151) → Ala [115a].

the genetic code may well prove solvable by comparing the chemical structure of mutated lysozymes with that of wild type lysozyme. By use of acridines such as proflavine, which is known as a frame-shift mutagen [117], one can determine not only the absolute RNA code words for amino acids *in vivo* but also the direction of reading of lysozyme messenger RNA and its nucleotide sequence. *Tsugita et al.* [118] have already determined 16 absolute code words for eleven amino acids, demonstrated the direction of messenger RNA reading, and elucidated a part of the nucleotide sequence of the messenger RNA of T4 phage lysozyme from a comparative study of the chemical structure of the proteins of wild type and double proflavine-induced mutants.

The complete amino acid sequence of T4 phage lysozyme was also elucidated [41]. The molecular weight was reported to be *ca.* 18000. No common primary structure was found between T4 phage lysozyme and egg-white lysozyme, but the distribution of basic, acidic, and hydrophobic amino acids seems to be similar. T4 phage lysozyme contains no S–S bridge and only two tryptophan residues per molecule. It is less stable than the hen enzyme [119].

Active lysozyme of bacteriophage T4 has been synthesized in a cell free system programmed by RNA from cells infected with the phage. The appearance of this lysozyme in the *in vitro* system has the characteristics of a *de novo* synthesis, which is mRNA specific and is inhibited by chloramphenicol, puromycin, and RNase. The incorporation of amino acids and the appearance of lysozyme activity have similar kinetics and a similar dependence on Mg. RNA from a T4 mutant with an amber mutation in the lysozyme structural gene is unable to stimulate the synthesis of lysozyme, thus showing that the measured activity is that of phage lysozyme [120, 121].

3.1.7. Lysozymes from Invertebrates

Jollès et al. [123, 124] have found traces of lysozyme(s) in many species of invertebrates; annelids, molluscs, and echinoderms contain larger quantities. Of special interest are the observed seasonal variations of the amount of enzyme [125], as well as the fact that these enzymes possess a high chitinase activity. The presence of lysozyme-like substances in insects has been reported by *Mohrig* [125a].

3.1.8. Lysozymes from Plants

The presence of bacteriolytic activity in plant tissues was first reported by *Fleming* [14] in 1922. Later *Meyer et al.* [126] reported lysozyme activity in crude proteolytic enzyme preparations from papaya and fig latex. In 1955, *Smith et al.* [127] prepared a crystalline lysozyme from papaya latex and quite recently *Howard* and *Glazer* [128] studied such a lysozyme in detail. It was found that papaya lysozyme has a molecular weight of about 25000, that glycine is its sole amino-terminal residue, and that the molecule consists of a single polypeptide chain. Papaya lysozyme lyses *M. lysodeikticus* cell walls at a rate one-third of that exhibited by egg-white lysozyme; however, it displays a chitinase activity toward tetra-*N*-acetyl-D-glucosamine 400 times that of hen lysozyme. No involvement of tryptophan residues in the active site of papaya lysozyme could be demonstrated. Similar observations have been made by *Jollès et al.* [122] with a turnip lysozyme.

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3.2. Reaction Velocity, Specificity, and Mode of Action

Lysozymes from different animal species and sometimes also from different organs or secretions of the same animal are chemically different but have qualitatively the same biological activity, *i.e.* they promote lysis of a suspension of dead cells of *Micrococcus lysodeikticus* (basic definition of a lysozyme)[129].

Quantitatively the reaction velocity differs from one enzyme to another; differences in the specificity[96,105], behavior toward inhibitors[101,102], *etc.*, were later observed. In all these experiments, various substrates were employed, *e.g.* dead cells of *M. lysodeikticus*, cell walls from lysozyme sensitive bacteria (*B. megatherium*), cell walls from Mycobacteria[130], soluble substrates from *M. lysodeikticus*, polymers of *N*-acetylglucosamine obtained from chitin (chitotetraose, *etc.*), and cell-wall saccharides such as NAG–NAM–NAG–NAM.

3.2.1. Reaction Velocity. Apparent Affinity Constants

Under the same conditions, bird egg-white lysozymes digest many of the above mentioned substrates more rapidly than do human lysozymes[96,129]. At pH 6.2, duck lysozymes seem to have the most complete and most rapid action on chitotetraose and chitopentaose[105]. Affinity constants of seven different lysozymes for the bacterial substrate are shown in Table 5[102].

Table 5. Apparent affinity constants of lysozymes from different origins for *Micrococcus lysodeikticus* cells [102].

Lysozyme		Apparent affinity constant (mg cells/l)
Human		
	normal leucocytes	90 ± 10
	normal plasma	100 ± 5
	milk	110 ± 10
Avian		
	hen egg-white	115 ± 10
	duck egg-white II	150 ± 10
	duck egg-white III	200 ± 20
	goose egg-white	400 ± 100

3.2.2. Specificity and Mode of Action

The action of hen, duck, and human lysozymes on the substrates mentioned in Section 3.2 leads not to the formation of free sugars or amino acids but, in many cases, to the disaccharide NAG–NAM[96,129]. Like the hen enzyme, duck lysozymes and human-tear lysozyme degrade the tetrasaccharide NAG–NAM–NAG–NAM to the disaccharide NAG–NAM but not to free amino sugars. About 30% of the tetrasaccharide was not hydrolyzed. However, transglycosylation products were observed thus suggesting that the mode of action of these four lysozymes is the same[131]. The four lysozymes mentioned digest tetra-NAG and penta-NAG in a similar manner: the same digestion products are observed including free NAG and transglycosylation products. The quantity of tetra-NAG not digested varies at a given pH from one enzyme to another[105].

However, the goose lysozyme behaves differently: at pH 6.2 *M. lysodeikticus* cells are digested rapidly but the lysis soon stops. Low molecular weight substrates, such as NAG–NAM–NAG–NAM or chitotetraose are gradually attacked only at lower pH[105]. The reaction products obtained from the cells also vary with the pH[104].

3.2.3. The Behavior of Lysozymes in the Presence of an Inhibitor

It has been shown that hen egg-white lysozyme can be inhibited by NAG[19,30]. Under the same experimental conditions, this inhibitory action varies greatly from one enzyme to another[101]. The human lysozymes are more strongly inhibited by NAG than is hen lysozyme. At pH 6.2, the two duck enzymes are inhibited to less than 50% and goose lysozyme is practically uninhibited (Fig. 7). Similar results were

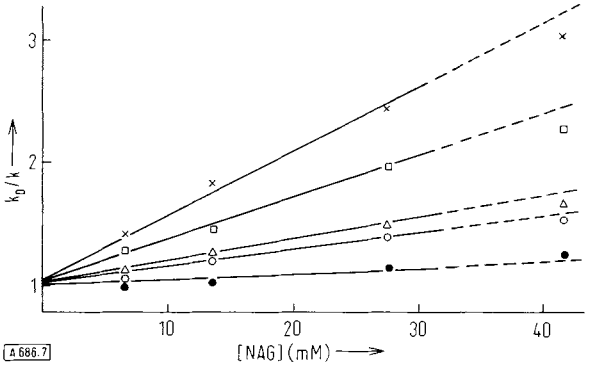


Fig. 7. Inhibition of the action of different lysozymes (0.63×10^{-6} M) on *M. lysodeikticus* cells by NAG (at pH 6.2) [101]. × = human, □ = hen, △ = duck II, ○ = duck III, ● = goose.

obtained with tetra-NAG[101]. Other inhibitors of hen lysozyme, such as histamine or L-histidine methyl ester[88], also inhibit goose lysozyme at concentrations similar to those used for the hen enzyme[101].

3.2.4. Immunological Comparison of Lysozymes

Arnheim and *Wilson*[132] purified lysozyme by Sephadex G-75 chromatography from the egg-whites of 17 species of birds in the order Galliformes and tested

[129] *P. Jollès*, Proc. Roy. Soc. (London) B *167*, 350 (1967).

[130] *H. de Wijs* and *P. Jollès*, Biochim. biophysica Acta *83*, 326 (1964).

[131] *N. Sharon*, *J. Jollès*, and *P. Jollès*, Bull. Soc. Chim. biol. *48*, 731 (1966).

[132] *N. Arnheim* and *A. C. Wilson*, J. biol. Chemistry (1968), in press.

for reactivity with antichicken lysozyme. The chicken and its closest relative, the jungle fowl, have lysozymes that appear to be indistinguishable from each other. The lysozymes of all the other species tested (partridges, quails, pheasants) could be distinguished from the chicken enzyme by quantitative micro-complement fixation. Immunodiffusion failed to detect most of these differences in antigenic structure. A particularly close relationship was observed between the lysozymes of the chicken, partridge, and American quails.

Ossermann and *Lawlor*[111] reported some immunochemical data which suggest the identity of the human lysozymes studied until now. Dissimilarities to bird egg-white enzymes were substantiated by the failure of the antiserum to a human lysozyme to inhibit the activity of the egg enzyme.

4. Concluding Remarks

4.1. Definition and Significance of Lysozymes

The results described in Section 3 necessitate a slight revision[96] of the definition of a lysozyme given in Sections 1 and 2. It is possible to imagine a lysozyme with an isoelectric point lower than 10.5–11 (hen enzyme); the molecular weight can be higher than 15000, as for the phage enzyme (18000)[119]; the stability at higher temperatures is lost when the cystine content of the enzyme becomes too low[42]. A property common to all the enzymes studied so far is the ability to rapidly lyse bacteria such as *M. lysodeikticus* by splitting β (1 → 4) linkages between a NAM and a NAG residue. Behavior towards low molecular weight substrates seems to depend on the pH, at least for some of the enzymes[104].

Only few details are available concerning the role of lysozymes *in vivo*[133]. Hen egg-white lysozyme is the only lysozyme yet to have been used clinically, owing to its basic character (addition to cow milk) and its antibacterial action. The latter can be explained in terms of enzymic action on substrates in the cell walls of gram-positive and gram-negative bacteria, although the substrates are not easily accessible in the gram-negative type. *In vivo* in the presence of substances such as enzymes, complement fractions, immunoglobulins [133a], or nucleic acids [133b], lysozyme seems to have some additional properties that have not yet been studied.

In vivo lysozyme can be included in an artificial structure formed by phospholipids and protein that is, by components common to many biological membranes, capable of masking its catalytic activity[134]. The demonstration of such a phenomenon may offer a new approach in the study of enzyme latency and may be of some importance in the development of a theory of membrane formation.

4.2. The Place of Lysozyme Among the Enzymes Degrading Peptidoglycans

The enzymes degrading peptidoglycans of bacterial cell walls are mainly bacteriolytic endoenzymes. They can be grouped into three classes: carbohydrases, acetylmuramyl-L-alanine amidases, and peptidases[135]. Carbohydrases include endoacetylmuramidases, endoacetylglucosaminidases, and exoacetylglucosaminidases. Lysozymes belong to the group of endoacetylmuramidases, which also include the "32 enzyme" from *Streptomyces albus* G[136], the "F_1 enzyme" from *St. albus* G[137], the "B enzyme" from *Chalaropsis*[138], and Autolysin from *Streptococcus faecalis*[139].

It is worth mentioning that lysozyme and penicillin, which were both discovered by *Fleming*, react with the same peptidoglycan from bacterial cell wall. Lysozyme splits the NAM–NAG linkage and penicillin mainly prevents biosynthesis of the peptide bridges. Furthermore, penicillin inhibits the lytic action of lysozyme, probably because it bears a structural resemblance to a portion of the bacterial cell wall, *N*-acetylmuramic acid[140] (Fig. 8).

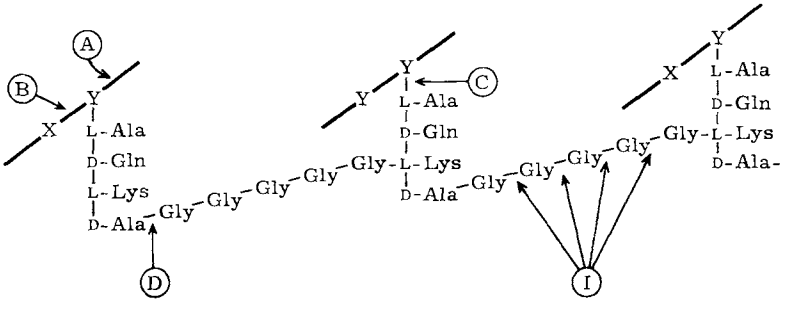


Fig. 8. A fragment of the peptidoglycan of *Staphylococcus aureus* showing point of cleavage by various enzymes [135]. X = NAG; Y = NAM; A = lysozyme; B = endoacetylglucosaminidase; C = acetylmuramyl-L-alanine amidase; D and I = endopeptidases.

4.3. Lysozyme and Evolution

Lactose synthetase (EC 2.4.1.c) catalyzes the following reaction[141]:

UDP-D-galactose + α-D-glucose → lactose + UDP

[133] *P. Jollès*, Revue des Docteurs en Pharmacie (Paris) 1968.

[133a] *M. W. Smith*, *R. Witty*, and *P. Brown*, Nature (London) *220*, 387 (1968).

[133b] *D. Cattan*, *D. Bourgoin*, and *M. Joly*, Bull. Soc. chim. biol. *50*, 409 (1968).

[134] *D. Romeo* and *B. de Bernard*, Nature (London) *212*, 1491 (1966).

[135] *J. L. Strominger* and *J.-M. Ghuysen*, Science (Washington) *156*, 213 (1967).

[136] *J. M. Ghuysen* and *J. L. Strominger*, Biochemistry (Washington) *2*, 1110, 1119 (1963).

[137] *E. Munoz*, *J. M. Ghuysen*, *M. Leyh-Bouille*, *J.-F. Petit*, and *R. Tinelli*, Biochemistry *5*, 3091 (1966).

[138] *D. J. Tipper*, *J L. Strominger*, and *J. M. Ghuysen*, Science (Washington) *146*, 781 (1964).

[139] *M. J. Conover*, *J. S. Thompson*, and *G. D. Shockman*, Biochem. biophysic. Res. Commun. *23*, 713 (1966).

[140] *H. Felsenfeld* and *R. E. Handschumacher*, Molecular Pharmacol. *3*, 153 (1967).

[141] *U. Brodbeck*, *W. L. Denton*, *N. Tanahashi*, and *K. E. Ebner*, J. biol. Chemistry *242*, 1391 (1966).

The soluble enzyme from milk requires the presence of two proteins, A and B, for activity; individually these proteins do not exhibit any catalytic activity. The present view is that A and B proteins are naturally occurring subunits and that enzymic activity is dependent upon the formation of an AB complex. The B protein was crystallized and identified as α-lactalbumin. Its structure was also established (Fig. 9). It

Hen lysozyme: H-Lys-Val-Phe-Gly-Arg-Cys-Glu-Leu-Ala-Ala-
Bovine α-lactalbumin: H-Glu-Glu-Leu-Thr-Lys-Cys-Glu-Val-Phe-Arg-

Ala-Met-Lys-Arg-His-Gly-Leu-Asp-Asn-Tyr-Arg-Gly-Tyr-Ser-Leu-Gly-
Glu-Leu-Lys————Asp-Leu-Lys-Gly-Tyr-Gly-Gly-Val-Ser-Leu-Pro-

Asn-Trp-Val-Cys-Ala-Ala-Lys-Phe-Glu——Ser-Asn-Phe-Asn-Thr-Gln-
Glu-Trp-Val-Cys-Thr-Thr——Phe-His-Thr-Ser-Gly-Tyr-Asp-Thr-Glx-

Ala-Thr-Asn-Arg-Asn-Thr-Asp-Gly-Ser-Thr-Asp-Tyr-Gly-Ile-Leu-Gln,
(Ala,Ile,Val,Glx)-Asx——Asx-(Glx,Ser,Thr,Asx)-Tyr-Gly-Leu-Phe-(Glx-

Ile-Asn-Ser-Arg-Trp-Trp-Cys-Asn-Asp-Gly-Arg-Thr-Pro-Gly-Ser-Arg-
Ile,Asx,Asx)-Lys-Ile-Trp-Cys-Lys-Asx-Asx-Glx-Asx-Pro-His-Ser-Ser-

Asn-Leu-Cys-Asn-Ile-Pro-Cys-Ser-Ala-Leu-Leu-Ser-Ser-Asp-Ile—Thr-
Asx-Ile——Cys-Asn-Ile-Ser-Cys-Asp-Lys-Phe-Leu-Asx-Asx-Asx-Leu-Thr-

Ala-Ser-Val-Asn-Cys-Ala-Lys-Lys-Ile-Val-Ser-Asp-Gly-Asp-Gly-Met-
(Asx,Asx,Ile)-Met-Cys-Val-Lys-Lys-Ile-Leu——Asp-Lys-Val-Gly-Ile-

Asn-Ala-Trp-Val-Ala-Trp-Arg-Asn-Arg-Cys-Lys-Gly-Thr-Asp-Val-Gln-
Asn-Tyr-Trp-Leu-Ala-His-Lys-Ala-Leu-Cys-Ser-Glu-Lys-Leu-Asp-Gln-

Ala-Trp-Ile-Arg-Gly-Cys——Arg-Leu-OH
——Trp-Leu————Cys-Glu-Lys-Leu-OH

Fig. 9. Amino acid sequence of bovine α-lactalbumin compared with the sequence of hen egg-white lysozyme [142]. Asx stands for Asp or Asn; Glx for Glu or Gln.

shows that α-lactalbumin has a close structural similarity to hen egg-white lysozyme. According to *Brew et al.* [142], the wide distribution of lysozyme in the animal kingdom taken in conjunction with the unique occurrence of α-lactalbumin and lactose in milk suggests that the direct evolution of α-lactalbumin from a lysozyme in an ancestor of the mammals was a prime step in the evolution of lactose synthetase and of the mammary gland. α-Lactalbumin also seemed to be involved in reactions leading to the synthesis of β(1→4) linkages whereas lysozyme hydrolyzed such bonds. However, more recently the B protein appeared to act as a substrate modifier, changing the specificity of the A protein (inhibition of Gal-NAG synthesis in favor of Gal-Glc synthesis). Furthermore, a genetic relationship also exists between avidins and lysozymes [143].

Although lysozyme and α-lactalbumin have similar chemical structures [142] the latter has no lytic activity, probably because residue 35 (Glu) of hen lysozyme, which is important for the catalytic activity, is replaced by a hystidine residue.

However, despite the fact that hen egg-white-, phage-, and papaya-latex lysozymes have entirely different chemical structures, they all promote lysis of *M. lysodeikticus* cells. The main function of hen egg-white lysozyme, other bird lysozymes (even the goose enzyme with its quite different behavior), human lysozymes (mol. wt. 15000) [96, 107], *etc.*, which have similar structures and active sites (Fig. 5), seems to be digestion of bacterial cell walls, whereas phage lysozyme (mol. wt. 18000) [119] seems to exhibit a specific affinity for *E. coli* cells. On the other hand, papaya-latex lysozyme (mol. wt. 25000) [128] is much more a chitinase than a lysozyme and the tryptophan residues no longer seem to be involved in the active site. This is also true for turnip lysozyme and lysozymes from invertebrates. The question thus arises whether such enzymes can still be called lysozymes, which should primarily be muramidases (lysozyme = *N*-acetylmuramylhydrolase) with slight chitinase activity. The chitinase activity must be present, since an enzyme obtained from *Chalaropsis* which has only muramidase activity was not called lysozyme [144].

Received: June 19, 1968 [A 686 IE]
German version: Angew. Chem. *81*, 224 (1969)

[142] *K. Brew, T. C. Vanaman*, and *R. L. Hill*, J. biol. Chemistry *242*, 3747 (1967).

[143] *N. M. Green*, Nature (London) *217*, 254 (1968).

[144] *J. H. Hash* and *M. V. Rothlauf*, J. biol. Chemistry *242*, 5586 (1967).

Biosynthesis of Lichen Substances, Products of a Symbiotic Association

K. Mosbach[*]

Lichens are composed of algae and fungi living together in symbiotic association and forming characteristic, often polycyclic lichen substances that are rarely encountered in other organisms. While the cultures of the unassociated individual constituents of the lichens can live for an unlimited time some doubt surrounds their viability in nature; their biosynthetic powers are not additive in the lichens. The results concerning the biosynthesis of the lichens that are discussed in the present article were obtained mainly with ^{14}C-labeled compounds.

1. The Makeup of Lichens

The lichens, about 15000 species of which are now known, are symbiotic forms of life composed of a fungal part (mycobiont) and an algal part (phycobiont). Symbiosis generally represents a close and enduring association of unlike organisms. Lichens are the most advanced form of this symbiotic process, called also mutualism, in which both organisms demonstrably gain from the association.

The properties of a lichen association differ sharply in many respects from those of the individual partners. Firstly, although the fungus and the algae require moisture (hygrophilia), they often occur in dry locations when combined as lichens (xerophilia). Algae are plants that prefer full light (photophytes), while fungi prefer shade (sciophytes); as lichens they thrive both in extremely light and in dark places. Secondly, the lichen association produces a new morphological unit, which is effected chiefly by a differentiation of the fungal component during combination with the algal component. Protective devices against evaporation are formed, as well as supporting structures and reproductive organs foreign to either partner alone. Thirdly, many "lichen substances" are formed in the associated organism, whose aromatic representatives with few exceptions occur solely in lichens.

The morphology of the lichens is characterized by great variety. Three essential forms can be distinguished: Crustose lichens are little differentiated, their thallus grows to only a few millimeters, and they grow in close contact with their substrata. Foliose lichens are more highly organized forms with a deciduous leaf-like thallus structure. Fruticose lichens display highly differentiated forms with stems, small branches, and leaves; they anticipate the differentiation of roots, buds, and leaves that occurs in flowering plants. Some beard lichens (*Usnea*) grow to a length of 5 m[1] (Fig. 1).

The fungal component determines especially the appearance of the lichen. Most lichen fungi belong to the class of sac fungi (*Ascomycetes*) but some lichens are encountered, mainly in the tropics, in which basidia fungi (*Basidomycetes*) occur as lichen formers. Finally, a few cases are known of imperfect fungi (*Deuteromycetes*) forming mycobionts. In the course of evolution the lichen fungi have become so far adapted to the association that they are unable to exist for any length of time without an algal partner. By way of contrast, lichen algae can occur as individual species. 12 genera of the blue-green algae (*Cyanophyceae*) and 21 genera of green algae (*Chlorophyceae*) are able to form lichens. Among the blue-green algae the genus *Nostoc* is the most abundant; and among green algae the single-cell *Trebouxia* predominates and, for example, forms about 80% of Scandinavian lichens[2].

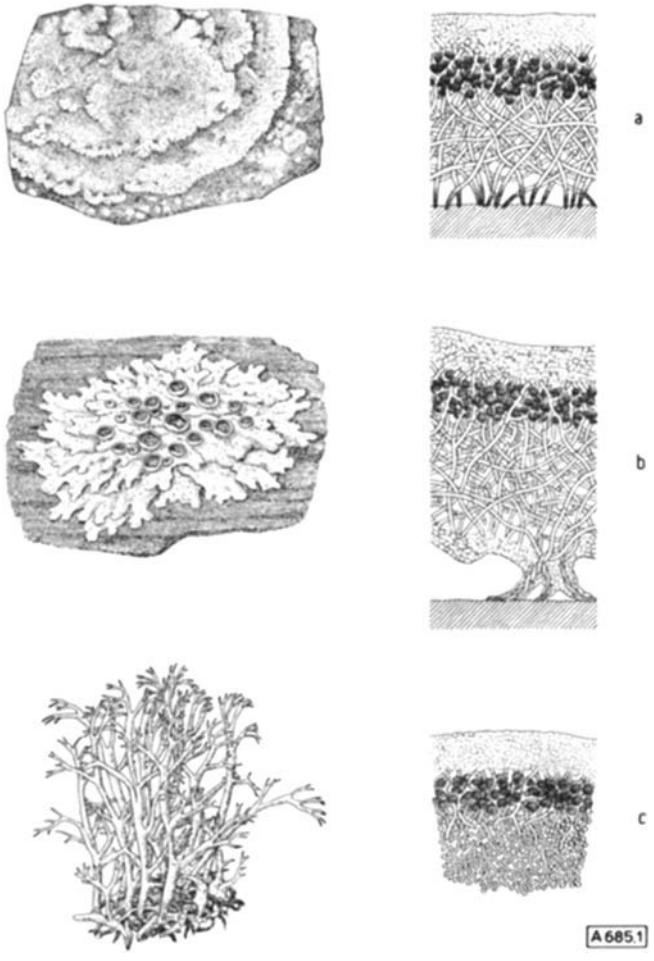


Fig. 1. Left: The three principal forms of lichens: crustose, foliose, and fruticose.

Right: (a) and (b) longitudinal sections through the lichen thallus, (c) cross-section through a stem. The lichen tissue is composed of the algal layer (dark) and the fungal hyphae (after *V. Ahmadjian* [1], reproduced by kind permission of the copyright holder).

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[1] *V. Ahmadjian*, Sci. American No. 2, 124 (1963).

[2] *R. Santesson*, Symbolae bot. upsal. *12*, 1 (1952).

A lichen alga can form associations with different lichen fungi to form varying types of lichens. Mostly, the lichen thalli contain only a single type of alga but in a few cases two are present; for example, in the Alpine sac lichen *Solorina crocea* a separate nitrogen-fixing blue-green algal zone is located underneath the peripheral green algal layer. Such a combination is known as trisymbiosis. On the other hand, one lichen fungus can associate with different algae [3]. For example, the morphologically indistinguishable lichen types *Lobaria pulmonaria* and *L. retigeria* represent fungus-green algae and fungus-blue-green algae associations respectively [4].

The lichen components can be separated and cultivated relatively easily. While the morphology of the isolated lichen fungus generally differs sharply from that in the natural lichen combination, the isolated lichen algae do not alter their appearance to the same extent. The aim of the lichen biologist to recombine isolated symbionts by a "lichen synthesis" has recently moved nearer to being achieved. The two symbionts have been cultivated together under special conditions, with the fungal hyphae enveloping the algae to form of a pseudo-parenchyma (Fig. 2) [5a]. *Ahmadjian* [6] has recently succeeded in obtaining differentiated lichen-like structures by this method, and these studies should provide a deeper insight into the course of "lichenization", a phenomenon difficult to observe in nature. In addition, it should be possible to create new types of artificial lichens by combining mycobionts and phycobionts.

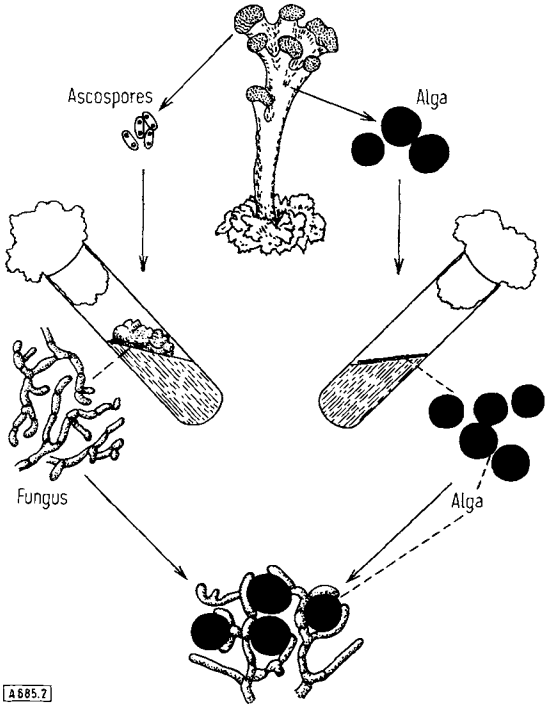


Fig. 2. Isolation of the two symbionts from a lichen and their recombination (schematic) (after *M. E. Hale* [5a], reproduced by kind permission of the copyright holder).

The two symbionts are very closely bound, with the fungal cells generally enveloping the algal cells or penetrating them with special sucking organs (haustoria) to ensure rapid exchange of metabolites (Fig. 3) [7]. (Regarding the biology of the lichens, see [5, 7–10].)

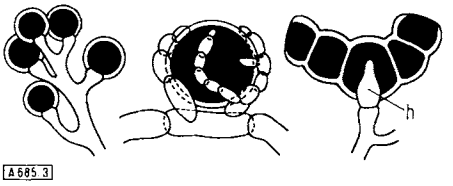


Fig. 3. Several forms of coupling between lichen algae and lichen fungi (h = haustoria) (after *G. Follmann* [7], reproduced by kind permission of the copyright holder).

The study of lichen physiology can be approached from two directions. Either the physiology of the individual symbionts or that of the intact lichen thallus is investigated. Many of the physiological studies that have been carried out on lichen components will not be discussed here, for the physiology of the lichen is not simply that of the sum of the properties of the two symbionts. The lichen organism must rather be regarded as a new functional entity.

2. The Metabolism of Lichens

Carbon for the lichen is furnished primarily by the photosynthetic activity of the algal partner. *D. C. Smith* succeeded in identifying the carbon compounds that participate in the transport of the fixed carbon from the alga to the fungus [11–13]. Pieces of identical shape were cut from the thallus of *Peltigera polydactyla*, a lichen with a blue-green *Nostoc* alga, and introduced into a medium containing $NaH^{14}CO_3$. Individual thallus pieces were collected at intervals, and the algal layer was separated from the medulla layer consisting only of fungal hyphae. As expected, the activity initially appeared in the algal layer and the [^{14}C]-glucose formed migrated from there into the fungal portion. After a 45-min incubation period in light, 60% of the fixed carbon was present in the fungal part in the form of mannitol [11, 12]. By contrast, in *Xanthoria aureola* lichen, which contains the green alga *Trebouxia* as phycobiont, the first labeled product was ribitol which was subsequently converted into mannitol and arabitol in the mycobiont [13]. A comparative study with four different *Lobaria* lichens containing *Trebouxia* and *Nostoc* algae led to the establishment of the two following principal patterns of carbohydrate movement [14].

Alga		Fungus
(*Trebouxia*) → Ribitol	→ (→Ribitol	→ Mannitol and Arabitol)
(*Nostoc*) → Glucose	→ (→Glucose	→ Mannitol)

[3] *E. G. Roms*, Ukrains'kyj botaničnyj Ž. *20*, 57 (1963).

[4] *Y. Asahina*, Bot. Mag. (Tokyo) *51*, 759 (1937).

[5] a) *M. E. Hale*: Lichen Handbook. Smithsonian Institution, Washington 1961, p. 52; b) The Biology of Lichens. Edward Arnold Publishers, Ltd., London 1967.

[6] *V. Ahmadjian*, Science (Washington) *151*, 199 (1966).

[7] *G. Follmann*: Flechten (Lichenes). Franckh'sche Verlagshandlung, Stuttgart 1960, p. 6.

[8] *V. Ahmadjian*: The Lichen Symbiosis. Blaisdell Publishing Co., London 1967.

[9] *R. Schaede*, revised by *F. H. Meyer*: Die pflanzlichen Symbiosen. G. Fischer-Verlag, Stuttgart 1962.

[10] *V. Ahmadjian*, Annu. Rev. Microbiol. *19*, 1 (1965).

[11] *E. A. Drew* and *D. C. Smith*, Lichenologist *3*, 197 (1966).

[12] *E. A. Drew* and *D. C. Smith*, New Phytologist *66*, 379 (1967).

[13] *D. H. S. Richardson* and *D. C. Smith*, Lichenologist *3*, 202 (1966).

[14] *D. H. S. Richardson*, *D. C. Smith*, and *D. H. Lewis*, Nature (London) *214*, 879 (1967).

Accordingly, the algal partner participating in the symbiosis appears to influence the type of pattern of carbohydrate movement. *Fox* and *Mosbach*[15,16] have determined the appearance of ^{14}C-activities in the tridepside gyrophoric acid [see *(15)* in Fig. 8] following incubation of the lichen *Umbilicaria papulosa* in light by a different technique. Labeling of the depside occurred within 1 min. Since at least the monocyclic units of these compounds must be synthesized in the fungal part, the entire sequence takes place during this short time, *i.e.* photosynthesis in the alga, transport of the sugar alcohols to the fungus, and biosynthesis of the depside from acetate and malonate units formed from the sugar alcohol.

Lichens from Arctic and Alpine regions display a high photosynthetic activity even at low temperatures. Thus, carbon fixation of *Letharia vulpina* at $-5\,^{\circ}C$ and ice formation in the pith layer still occur at half the rate measured under optimum conditions, and some lichens even continue photosynthesis at $-24\,^{\circ}C$[17,18]. The supply of carbon by photosynthesis is likely to be supplemented by saprophytic feeding in the natural environment of the lichens, *i.e.* by absorption of organic substances through the thallus or rhizines (adherent fibers).

Nitrogen is supplied to the organism by absorption of both organic and inorganic nitrogen compounds by the lichen thallus, *i.e.* mainly by the fungal partner. *Henriksson*[19] and *Scott*[20] were able to show with ^{15}N that lichens with blue-green algae can also fix atmospheric nitrogen. Undoubtedly, the lichens seldom contain sufficient nitrogen compounds, and for this reason the slow growth and the slow protein synthesis of the lichens can be interpreted as an adaptation to the given conditions during the course of evolution.

Little is known about the vitamin balance of intact lichens, but thiamine and biotin are known to be essential to the isolated mycobiont. Pure cultures of the phycobionts secrete large amounts of vitamins into the medium[21]. From the above data, which were obtained for individual symbionts, it may be concluded that the intact lichen is at least in part provided with vitamins by the phycobionts.

Mineral salts are supplied to the lichen by the thallus, which absorbs the salts dissolved in rain water. The mineral content in the thallus is often remarkably high; for instance, the *Diploschistes scruposus* lichen contains 10% of zinc calculated on the dry weight[22].

Radioactive fallout was also found in high concentrations in living lichens[23], which are characterized by a pronounced resistance to γ-radiation[24]. Finally, the water balance is determined by the mycobiont, which serves also to protect the algal partner against drying out and strong sunlight.

3. Biosynthesis of Lichen Substances

3.1. General

Lichen substances are generally low-molecular organic compounds. They represent secondary metabolites which, like the many corresponding fungal metabolites, have so far been ascribed a direct biological role in only few instances. The structures of about 120 lichen substances are known at the present time. *Emil Fischer*'s original synthesis of a depside represented an important contribution to this subject[25]. Work by *Robertson* and *Barton*[26,27] on the dibenzofuran derivative usnic acid [see *(20)* in Fig. 11] deserves special mention, as do also the investigations by the study groups led by *Asahina*, *Sheshadri*, and *Shibata*. Comparative mass spectrometry with positive and negative ions is a valuable tool for these studies, particularly for the elucidation of depside structures in which the acid and alcohol portions yield strong mass peaks[28]. (For a survey of lichen chemistry see[28–34], bibliography in[35].)

Is a separate treatment of the biosynthesis of lichen substances justified? The fact that particularly the important aromatic lichen substances, *i.e.* depsides, depsidones, depsones, dibenzofurans, and pulvic acid derivatives (see Figs. 6 and 15) almost all occur solely in lichens speaks in favor of this approach. Furthermore, an investigation should embrace a study of whether, and to what extent, the two symbionts participate in the biosynthesis of such structures. It is characteristic of aromatic lichen compounds that they

[15] *K. Mosbach* and *C. H. Fox*, IUPAC, X. International Congress, Abstracts 152 (1966).

[16] *C. H. Fox* and *K. Mosbach*, Acta chem. scand. *21*, 2327 (1967).

[17] *O. L. Lange* and *H. Metzner*, Naturwissenschaften *8*, 191 (1965).

[18] *O. L. Lange*, Planta *64*, 1 (1965).

[19] *E. Henriksson*, Physiol. Plantarum (Copenhagen) *10*, 943 (1957).

[20] *G. D. Scott*, New Phytologist *55*, 111 (1956).

[21] *T. W. Bednar* and *O. Holm-Hansen*, Plant Cell Physiol. (Tokyo) *5*, 297 (1964).

[22] *J. Lambinon*, *A. Maquinay*, and *J. L. Ramaut*, Bull. Jard. Etat Bruxelles *34*, 273 (1964).

[23] *E. Gorham*, Canad. J. Botany *37*, 327 (1959).

[24] *I. M. Brodo*, Bryologist *67*, 76 (1964).

[25] *E. Fischer* and *O. Fischer*, Ber. dtsch. chem. Ges. *46*, 1138 (1913).

[26] *F. H. Curd* and *A. Robertson*, J. chem. Soc. (London) *1937*, 894.

[27] *D. H. R. Barton*, *A. M. Deflorin*, and *O. E. Edwards*, J. chem. Soc. (London) *1965*, 530.

[28] *S. Huneck*, Progr. Phytochemistry, *1968*, 223.

[29] *S. Neelakantan*: Advancing Frontiers in the Chemistry of Natural Products. Hindustani Publishing Corp., Delhi 1965, p. 35.

[30] *S. Shibata* in *F. Linskens* and *M. V. Tracey*: Moderne Methoden der Pflanzenanalyse. Springer-Verlag, Heidelberg 1963, Vol. 6, p. 155.

[31] *Y. Asahina* and *A. Shibata*: Chemistry of Lichen Substances, Japanese Society for the Promotion of Science Ueno, Tokyo 1954.

[32] *J. Santesson*, Lic.-Dissertation, Uppsala University (Sweden), 1967.

[33] *C. A. Wachtmeister*, Svensk kem. Tidskr. *70*, 117 (1958).

[34] *B. Åkermark*, Svensk kem. Tidskr. *79*, 3 (1967).

[35] *W. L. Culbertson*, Recent Literature on Lichens, Quarterly review of all publications in the field of lichens, in "The Bryologist".

are all dicyclic or tricyclic, unlike the monocyclic aromatic metabolites occurring, for example, in molds. Generally, they form a high percentage of the dry weight of the lichens, *e.g.* the depside lecanoric acid forms up to 20%[36]. In molds secondary aromatic compounds are generally formed in corresponding amounts only under normal culture conditions, *i.e.* when the medium contains much glucose. Finally, any elucidation of the biosynthetic pathways leading to the lichen substance should put the chemotaxonomy of the lichens on a sounder basis.

Until recently knowledge regarding the biosynthesis of lichen substances was restricted to theoretical postulates, since it was assumed that the slow-growing organisms are unsuitable for direct experiments. However, *Mosbach* was able to show[37] that the lichen *Umbilicaria papulosa* incorporated 4% of [^{14}C]-diethyl malonate, which was added as a precursor, in the tridepside gyrophoric acid *(15)*. Such a high rate of incorporation is comparable with that found in molds. *Shibata*'s classification in somewhat modified form is a suitable basis for a detailed discussion of the biosynthesis of lichen substances[38] (Table 1).

Table 1. Classification of lichen substances with references to the Sections in which they occur.

carbohydrates (3.2.)	polyols polyglycosides polysaccharides (3.2.)	
acetate-polymalonate group (3.3.)	higher fatty acids and lactones (3.3.1.), aromatic polyketides (3.3.2.)	depsides (3.3.2.1.), depsidones and depsones (3.3.2.2.), bibenzoquinones (3.3.2.3.) dibenzofurans (3.3.2.4.) chromones, xanthones, anthraquinones, and chromanones (3.3.2.5.)
mevalonic acid group (3.4.)	di- and triterpenes, steroids, carotinoids (3.4.)	
shikimic acid group (3.5.)	diketopiperazines, terphenylquinones, pulvic acid derivatives (3.5.)	
others		dimethyl sulfone, cholinesulfuric acid

3.2. Carbohydrates

Lichens are distinguished by their high polyol content. The compounds that have been found so far are *meso*-erythritol, D-arabitol, D-ribitol, D-mannitol, D-volemitol ($C_7H_{16}O_7$), and siphulitol ($C_7H_{16}O_6$), the first deoxy-sugar alcohol found in nature[39]. According to investigations by *Lindberg et al.*[40] on 60 types of lichens, the occurrence of the individual sugar alcohols appears to vary with the lichen genus. However, D-mannitol occurred in all the species investigated. Erythritol occurs in some lichens as the ester of orsellinic acid (montagnetol) and of lecanoric acid (erythrin). Polyol glycosides have only recently been found in lichens. Of the three known glycosides, umbilicin (2-*O*-β-D-galactofuranosyl-D-arabitol) may be mentioned here[41].

The cell walls of the hyphae consist mainly of lichenin or isolichenin, and more rarely of pustulan, glucan, and other, as yet unidentified, polysaccharides, some of which occur solely in lichens. Lichenin, which is found in several lichens, is a linear polymer built up from β-D-glucopyranose units; its molecular weight (20000–40000) lies between those of starch and cellulose[42]. Although investigations have not been carried out on the biosynthesis of lichen carbohydrates, it would appear that the relevant pathways probably follow other familiar patterns. The sugar alcohols which are generally present as intermediates during the carbon flow from the alga to the fungal partner seem to have a special significance.

3.3. The Acetate-Polymalonate Group

The group of compounds derived from acetate-polymalonate comprises by far the greatest number of lichen substances, their biosynthesis proceeding *via* condensation of a "starter" acetyl-SCoA[*] unit with *n* malonyl-SCoA units. Another name for compounds of this type is polyketides, a term coined by *Collie*[43], who interpreted these structures as polymeric ketenes. In the widest sense, saturated fatty acids belong to this group as reduced polyketides, but it is better for the term to be restricted to aromatic compounds.

3.3.1. Higher Fatty Acids and Lactones

The higher fatty acids occurring in lichens and their lactones can be divided into three groups: γ-lactone acid derivatives (seven members *e.g.* lichesterinic acid *(1)*), dibasic fatty acids [rocellic acid *(2)*], and tribasic fatty acids [caperatic and rangiformic acids *(4)*]. In addition, two tetrahydroxy fatty acids have been detected[44] (*e.g.*: ventosic acid $CH_3(CH_2)_8(CHOH)_2$-CH_2-$(CHOH)_2(CH_2)_7COOH$]. All aliphatic lichen acids are optically active. So far the absolute configurations of only rangiformic and rocellic acids are known[45] (rangiformic acid = methyl dihydrogen (+)-(2*S*:3*S*)-1,2,3-heptadecanetricarboxylate; rocellic acid

[36] *T. R. Seshadri* and *S. S. Subramanian*, J. sci. ind. Res. (New Delhi) *8b*, 170 (1949).

[37] *K. Mosbach*, Acta chem. scand. *18*, 329 (1964).

[38] *S. Shibata*, Beitr. Biolog. Physiol. Naturstoffen *1965*, 451.

[39] *B. Lindberg* and *H. Meier*, Acta chem. scand. *16*, 543 (1962).

[40] *B. Lindberg*, *A. Misiorny*, and *C. A. Wachtmeister*, Acta chem. scand. *7*, 591 (1953).

[41] *B. Lindberg* and *B. Wickberg*, Acta chem. scand. *16*, 2240 (1962).

[42] *S. Peat*, *W. J. Whelan*, *J. R. Turvey*, and *K. Morgon*, J. chem. Soc. (London) *1961*, 623.

[*] HS–CoA = coenzyme A.

[43] *J. N. Collie*, J. chem. Soc. (London) *91*, 1806 (1907).

[44] *Y. T. Solberg*, Acta chem. scand. *11*, 1477 (1957).

[45] *B. Åkermark*, Svensk kem. Tidskr. *79*, 11 (1967).

= (+)-(2*S*:3*R*)-2-methyl-3-dodecylsuccinic acid). No biosynthetic investigations on the lichen substances listed here are as yet available.

Gatenbeck and *Måhlén* have recently succeeded in synthesizing enzymatically the related compounds decylcitric acid *(3a)* and spiculisporic acid occurring in fungi by condensation of lauryl-SCoA with oxalacetate or α-ketoglutarate respectively [46,47]. Formation of the lichen acids is likely to proceed analogously by an aldol condensation of long-chain alkanoyl-SCoA units with keto acids, which, in turn, are formed by condensation of "starter"-acetyl-SCoA with *n* molecules of malonyl-SCoA. The lichen substances shown in Fig. 4 are therefore probably formed by condensation of myristoyl- or palmitoyl-SCoA with oxalacetic acid or pyruvic acid. In the γ-lactone acids the corresponding β-hydroxy fatty acids are possible condensation units. According to a recent publication [47a], the protolichesterinic acid occurring in lichens is formed by condensation of palmitic acid with pyruvic acid as suggested above.

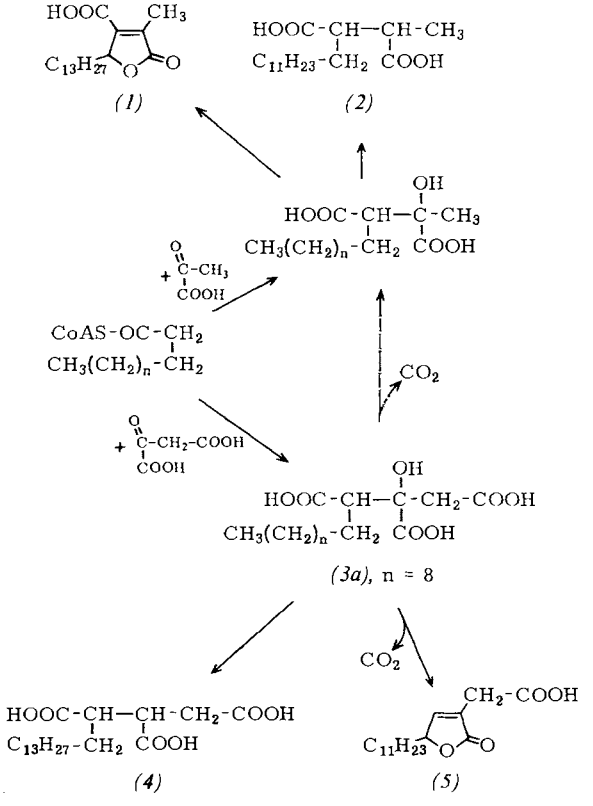


Fig. 4. Proposed biosynthesis of lichesterinic acid *(1)*, rocellic acid *(2)*, rangiformic acid *(4)*, acarenoic acid *(5)*, and decylcitric acid *(3a)*, $n = 8$, (fungus).

3.3.2. Aromatic Polyketides

The structures of about 100 aromatic lichen substances have so far been elucidated; a number of these compounds exhibit antibiotic properties and no less than 90 of them are aromatic polyketides. In most cases orsellinic acid and its homologs are the principal structural units. In molds, orsellinic acid *(6)* occurs in the free form [48,49]; in lichens, however, it is present almost exclusively in the form of condensed dicyclic or tricyclic compounds. According to isotopic studies with ^{14}C and ^{18}O [50–53], *(6)* is formed by the condensation of an acetyl-SCoA unit with three malonyl-SCoA units to form a (tentatively) hypothetical 3,5,7-trioxooctanoic acid, which is probably bound enzymatically as a thiol ester and cyclizes by an internal aldol condensation. Alternatively, aldol condensation can lead to 3,5-dihydroxyphenylacetic acid *(8)*, and Claisen condensation to acetylphloroglucinol *(7)* (Fig. 5).

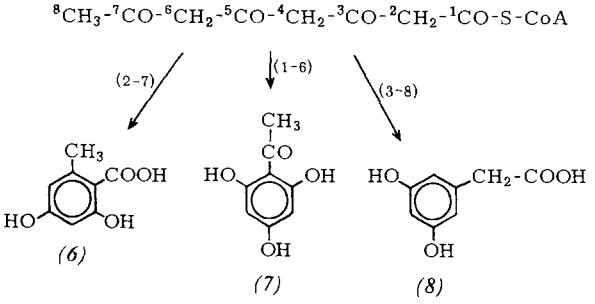
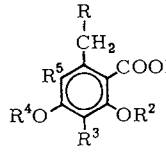


Fig. 5. Three possible alternative cyclizations of 3,5,7-trioxooctanoic acid to the aromatic compounds *(6)*–*(8)*. (The acid is bound to coenzyme A or more likely to a multienzyme).

The formation of these compounds very probably occurs on a multienzyme complex in analogy with fatty acid biosynthesis [54], as indicated by enzymatic experiments with other polyketides, *e.g.* 6-methylsalicylic acid and alternariol [54,55]. Orsellinic acid and its homologs, the principal structural units of the aromatic lichen substances, appear in many derivatives (Table 2), in which the β-orsellinic acid group (position



(6), $R=R^1=R^2=R^3=R^4=R^5=H$

Table 2. List of substituents of orsellinic acid *(6)* found so far in lichen substances.

R	R^1	R^2, R^4	R^3	R^5
C_2H_5	CH_3	CH_3	CH_3	
n-C_4H_9	erythrityl		CH_2OH	
CO-*n*-C_3H_7			CH_2O–$COCH_3$	
n-C_6H_{13}			*trans*-CH_2O–CO-CH=CH–COOH	
CO-*n*-C_5H_{11}			CHO	CHO
			COOH	
OH			OH	OH
			Cl	Cl

[46] *S. Gatenbeck* and *A. Måhlén*: Proceedings of the Congress on Antibiotics, Prague 1964. Butterworth 1966, p. 540.

[47] *S. Gatenbeck* and *A. Måhlén*, Acta chem. scand. *22*, 2613 (1968).

[47a] *J. L. Bloomer*, *W. R. Eder*, and *W. F. Hoffmann*, chem. Commun. *1968*, 354.

[48] *L. Reio*, J. Chromatogr. (Amsterdam) *1*, 338 (1958).

[49] *K. Mosbach*, Z. Naturforsch. *14b*, 69 (1959).

[50] *K. Mosbach*, Acta chem. scand. *14*, 457 (1960).

[51] *S. Gatenbeck* and *K. Mosbach*, Acta chem. scand. *13*, 1561 (1959).

[52] *K. Mosbach*, Naturwissenschaften *48*, 525 (1961).

[53] *R. Bentley* and *J. G. Keil*, Proc. chem. Soc. *1961*, 111.

[54] *F. Lynen* and *M. Tada*, Angew. Chem. *73*, 513 (1961).

[55] *S. Gatenbeck* and *S. Hermodsson*, Acta chem. scand. *19*, 65 (1965).

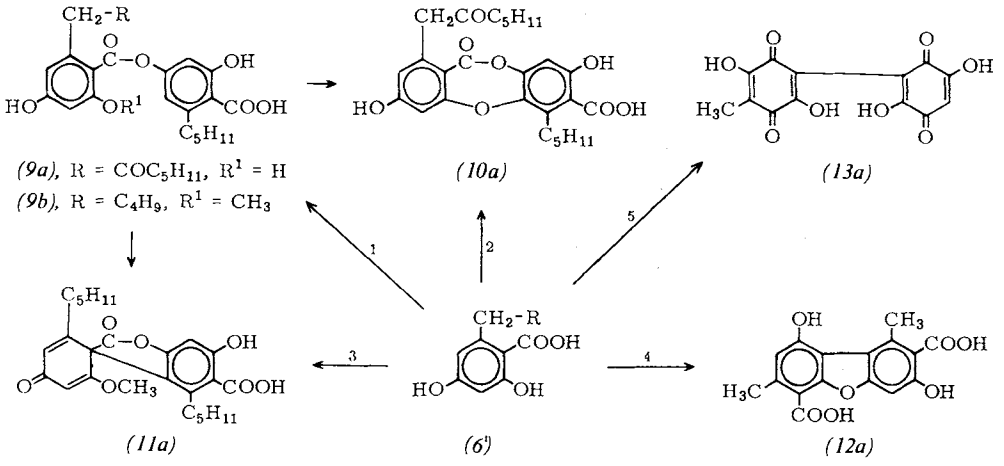


Fig. 6. Proposed biosynthesis of the five types of condensation products of orsellinic acid *(6)*, and its homologs occurring in lichens. *(9a)* = olivetoric acid, *(9b)* = dihydropicrolichenic acid, *(10a)* = physodic acid, *(11a)* = picrolichenic acid, *(12a)* = pannaric acid, *(13a)* = pyxiferin.

3 substituted with C_1 units) generally contains no aliphatic side chains (R=H). These structural units can form five types of condensation products (Fig. 6):

1. Esterification forming a depside *(9)*.
2. A cyclic depside (depsidone) *(10)*.
3. A depside with an additional C–C bond (depsone) *(11)*.
4. A cyclic ether with an additional C–C bond (dibenzofuran) *(12)*.
5. Products with a central C–C bond (bibenzoquinone) *(13)*.

Together with the pulvic acid derivatives (see Section 3.5) the first four types form the actual aromatic lichen substances. Except for the nidulins (mold depsidones) and the *m*-digallic acid occurring in tannins (depsides in algae and higher plants) they are restricted to the lichens.

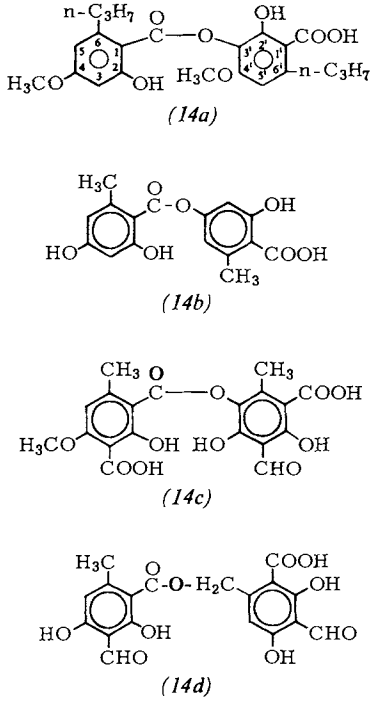


Fig. 7. Representatives of the four depside subgroups. *(14a)* = sekikaic acid, *(14b)* = lecanoric acid, *(14c)* = thamnolic acid, *(14d)* = barbatolic acid.

3.3.2.1. Depsides

The depsides have 40 known representatives and thus constitute the largest group of aromatic lichen substances; according to the type of linkage they can be divided into four subgroups (Fig. 7).

The first biosynthetic work on aromatic lichen substances was carried out with the gyrophoric acid-producing *Umbilicaria papulosa* [37]. $CH_2(^{14}COOC_2H_5)_2$ was added to the lichen thallus in agitated cultures; after a 3-day incubation period, 4% of the added activity was incorporated into gyrophoric acid *(15)*. As expected, subsequent degradation of labeled *(15)* gave the same specific activity for all three

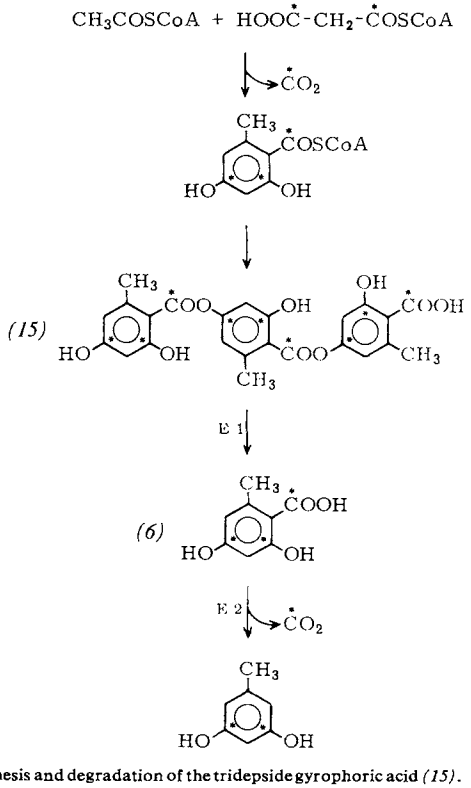
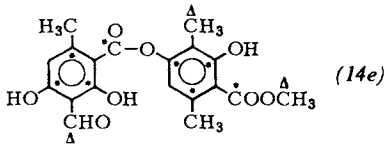


Fig. 8. Biosynthesis and degradation of the tridepside gyrophoric acid *(15)*. Labeling pattern (*) obtained after incubation with $CH_2(^{14}COOC_2H_5)_2$. Degradation is effected by means of depsidase (E1) from the alga and with orsellinic acid decarboxylase (E2) from the fungus. (The orsellinic acid is bound to coenzyme A or to an enzyme during depside formation.)

orsellinic acid molecules in the positions emanating from the malonyl-SCoA, while only a very slight activity appeared in the positions derived from the acetyl-SCoA "starters" (Fig. 8).

The subsequent experiments with the depside atranorin *(14e)*, which belongs to the β-orsellinic acid group, with ^{14}C-labeled acetic and formic acids demonstrated specific incorporation of formic acid in the CHO and CH_3 groups of the depside [56] (Fig. 9).



(14e)

Fig. 9. Labeling pattern in the depside atranorin *(14e)* after incubation with $CH_3{}^{14}COOH$ (*) and $H^{14}COOH$ (Δ).

S-Adenosylmethionine is a possible activated form of these groups derived from the C_1-fragment pool. Subsequently is was shown by using tritium-labeled compounds that the monocyclic units of atranorin can once more be reunited by the lichen to form the depside [57].

Little is known about the individual steps of this process. It may be taken as certain that the monocyclic units are formed by the fungal partner. The evidence is firstly that they occur in molds, and secondly that in lichen fungi that normally form depsides while in lichen association in pure culture, only orsellinic acid or haematommic acid (3-formylorsellinic acid) have been found [58]. It is possible that the algal partner subsequently enzymatically condenses these compounds, which are probably present as activated orsellinoyl-SCoA esters. A parallel to such work distribution between the two symbionts is found in the enzymatic degradation of lichen depsides (see Fig. 8) [59].

On the other hand, such enzymatic condensation of activated monomers can also take place in the fungal part. A third alternative is the possibility that the whole depside biosynthesis takes place on a single multienzyme complex, in which two or three orsellinic acid synthetase complexes are so closely coupled together that a direct condensation of the enzyme-bound monomers can occur. This could be one explanation why tridepsides but no didepsides occur in certain lichens.

It may be assumed that higher orsellinic acid homologs such as olivetoric acid *(9a)* are built up of one acetyl-SCoA and *n* malonyl-SCoA units in analogy with the "C_{10} acid" (6-acetonyl-2,4-dihydroxybenzoic acid) [60]. A condensation of separately formed alkanoyl-SCoA units with orsellinic acids is less likely.

3.3.2.2. Depsidones and Depsones

Approximately 20 depsidones occur among the lichen substances. It is not yet possible to distinguish between the following alternative biosynthetic pathways:

1. intramolecular oxidative phenol coupling [61,62] of the depside by a "depside dehydrogenase".

2. formation without the participation of a free intermediate depside on a separate "depsidone multienzyme complex".

The first alternative is supported by the appearance in lichens of depsidones that correspond to several of the depsides. In addition to the depside-depsidone pair olivetoric acid *(9a)* – physodic acid *(10a)* reproduced in Fig. 6, the pairs atranorin-virensic acid *(14e)*, microphyllinic acid – α-collatolic acid and sphaerophorin-grayanic acid occur. In some types of lichens olivetoric acid and physodic acid also appear together [63], and, finally, further evidence is provided by the synthesis of the depsidone diploicin by oxidation of the corresponding depside with manganese dioxide [64]. Depsidones derived from depsides such as sekikaic acid *(14a)* or thamnolic acid *(14c)* have not been found. In the first case the methoxy group prevents the otherwise biosynthetically plausible $C^{\bullet}-O^{\bullet}$ coupling. Instead, the depsides that are probably present as biradicals during phenol dehydrogenations can undergo an alternative $C^{\bullet}-C^{\bullet}$ coupling of the type that is realized in the depsones.

Only one depsone, picrolichenic acid *(11a)* has so far become known [65]. It is probably formed from the corresponding depside, dihydropicrolichenic acid *(9b)* by such an intramolecular oxidation. The recent synthesis of *(11a)* by oxidation of *(9b)* with manganese dioxide is in agreement with this postulate [66].

3.3.2.3. Bibenzoquinones

Despite the frequent occurrence of bibenzoquinones in independently living fungi, a lichen representative, pyxiferin *(13a)*, has only recently been found [67]. Fig. 10 demonstrates that pyxiferin is closely related structurally to the fungal bibenzoquinon esoosporein

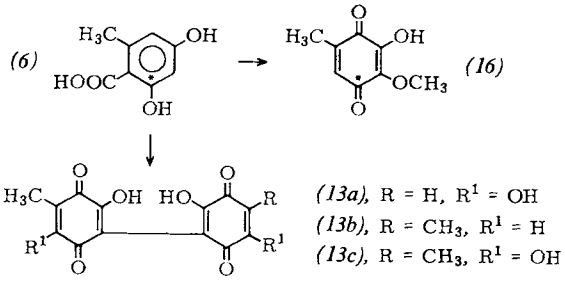


Fig. 10. Proposed biosynthesis of pyxiferin *(13a)*, R = H, R^1 = OH; structures of the fungal bibenzoquinones phoenicin *(13b)*, R = CH_3, R^1 = H, and oosporein *(13c)*, R = CH_3, R^1 = OH. Labeling pattern in fungal toluquinone fumigatin *(16)* after incubatin with [2-^{14}C]-orsellinic acid *(6)*.

[56] *S. Shibata, M. Yamazaki,* and *M. Matsuo,* Chem. pharmac. Bull. (Tokyo) *13,* 1015 (1965).

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[60] *A. H. Manchanda* and *C. E. Stickings,* IUPAC, XIX. International Congress, Abstracts 209 (1963).

[61] *D. H. R. Barton* and *T. Cohen:* Festschrift A. Stoll Birkhäuser, Basel 1957, p. 117.

[62] *H. Erdtman* and *C. A. Wachtmeister,* see ref. [61], p. 144.

[63] *C. Culberson,* Science (Washington) *143,* 255 (1964).

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[65] *C. A. Wachtmeister,* Acta chem. scand. *12,* 147 (1958).

[66] *T. A. Davidson* and *A. I. Scott,* J. chem. Soc. *1961,* 4075.

[67] *S. Neelakantan,* see ref. [29], p. 58.

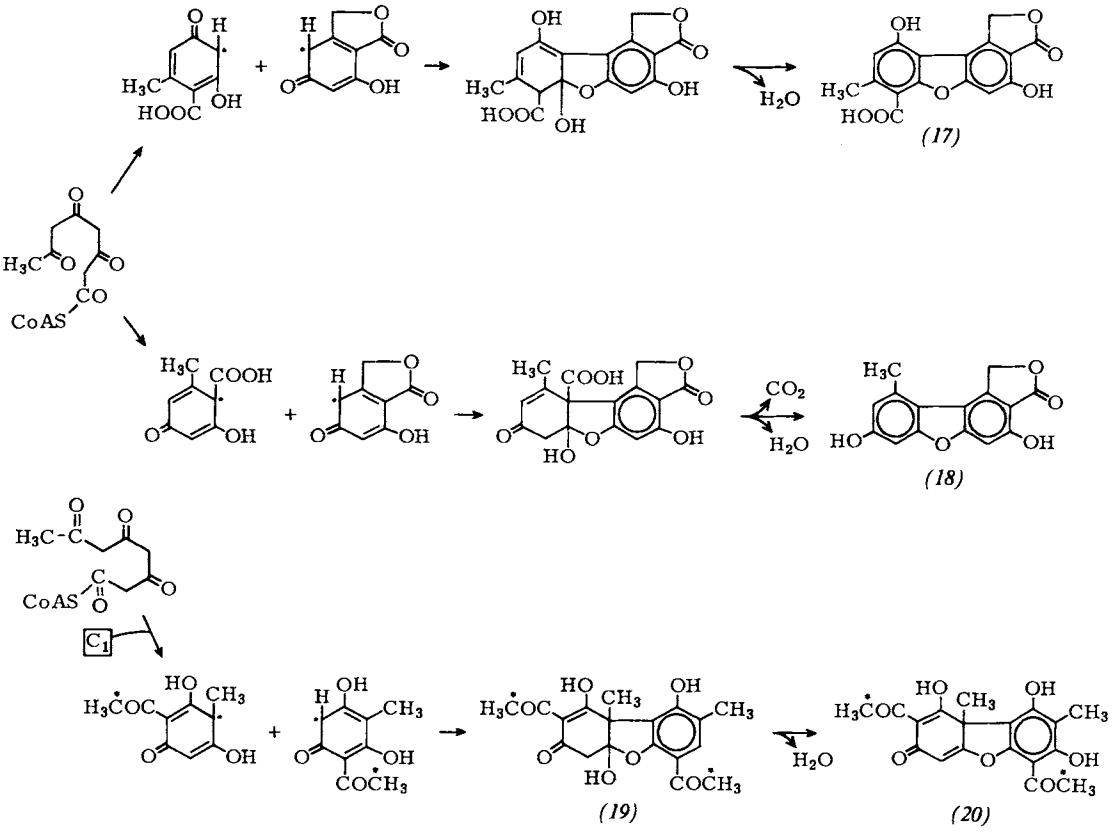


Fig. 11. Proposed biosynthesis of dibenzofurans: porphyrilic acid *(17)*, strepsilin *(18)*, and usnic acid *(20)*. Labeling pattern in *(20)* after incubation with [$^{14}CH_3$—CO]-acetylmethylphloroglucinol. (The condensing units are bound to coenzyme A or to an enzyme.)

(13c) and phoenicin *(13b)*. The biosynthesis of the monocyclic quinones probably proceeds *via* orsellinic acid, as was shown for the fungal toluquinone fumigatin *(16)* [68]. The two monocyclic portions are thought to combine by oxidative phenolic coupling [69]. Furthermore, it has been shown that in the biosynthesis of phoenicin *(13b)* added orsellinic acid and also orcin are incorporated in specific manner [70].

3.3.2.4. Dibenzofurans

Dibenzofurans are essentially encountered only in lichens. Rhodomyrtoxin [71] is the only representative yet to have been found outside the lichen group. Of the seven dibenzofurans whose structures have been elucidated, five can be interpreted as condensation products of orsellinic acid and its homologs; only usnic acid *(20)* and isousnic acid [72] are composed of two acetylphloroglucinol units. The usnic acids are the sole aromatic lichen substances to contain acetylphloroglucinol in place of orsellinic acid as the skeleton unit; methylation of the nucleus, which probably occurs before aromatization, apparently determines the type of cyclization (Claisen) involved. *Barton et al.* [73] were the first to succeed in synthesizing usnic acid *(20)* in their classical work involving oxidation of acetylmethylphloroglucinol with potassium hexacyanoferrate(III). The initially formed hydroxydihydrousnic acid *(19)* was subsequently dehydrated with sulfuric acid to form *(20)*. Recently, *Pentilla* and *Fales* succeeded in effecting the same coupling enzymatically with a peroxidase system [74]. Finally, *Shibata et al.* [75] were able to demonstrate with ^3H- and ^{14}C-labeled acetylmethylphloroglucinol that usnic acid is formed from these units in the lichen thallus. By contrast, labeled acetylphloroglucinol was not incorporated in usnic acid *(20)* (Fig. 11). According to these findings, the biosynthesis of usnic acid and probably that of other dibenzofurans proceeds by oxidative phenol coupling and subsequent dehydration. The question whether separate dehydrogenases and dehydratases, or a multienzyme complex are involved had admittedly not yet been answered.

3.3.2.5. Chromones, Xanthones, Anthraquinone, and Chromanone

Chromones *(21)*, xanthones *(22)*, anthraquinones *(23)*, and chromanones *(24)* cannot be regarded as typical lichen metabolites since they also occur in other organisms. Biosynthetic investigations of such lichen compounds are not so far available; their common property is the postulate of a β-polyoxomethylene chain as a precursor, as is indicated in Fig. 12, al-

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[73] *D. H. R. Barton, A. M. Deflorin*, and *O. E. Edwards*, J. chem. Soc. (London) *1956*, 530.

[74] *A. Pentilla* and *H. M. Fales*, Chem. Commun. *1966*, 656.

[75] *H. Taguchi, U. Sankawa*, and *S. Shibata*, Tetrahedron Letters *1966*, 5211.

though the less probable formation by condensation of two separately formed polyketide chains or their cyclized products, as was demonstrated for the biosynthesis of citromycetin [76], cannot yet be entirely ruled out.

The two known chromones, lepraric acid [77] and rupicolin *(21a)* [78], probably result from the condensation of an acetyl-SCoA unit with four malonyl-SCoA units.

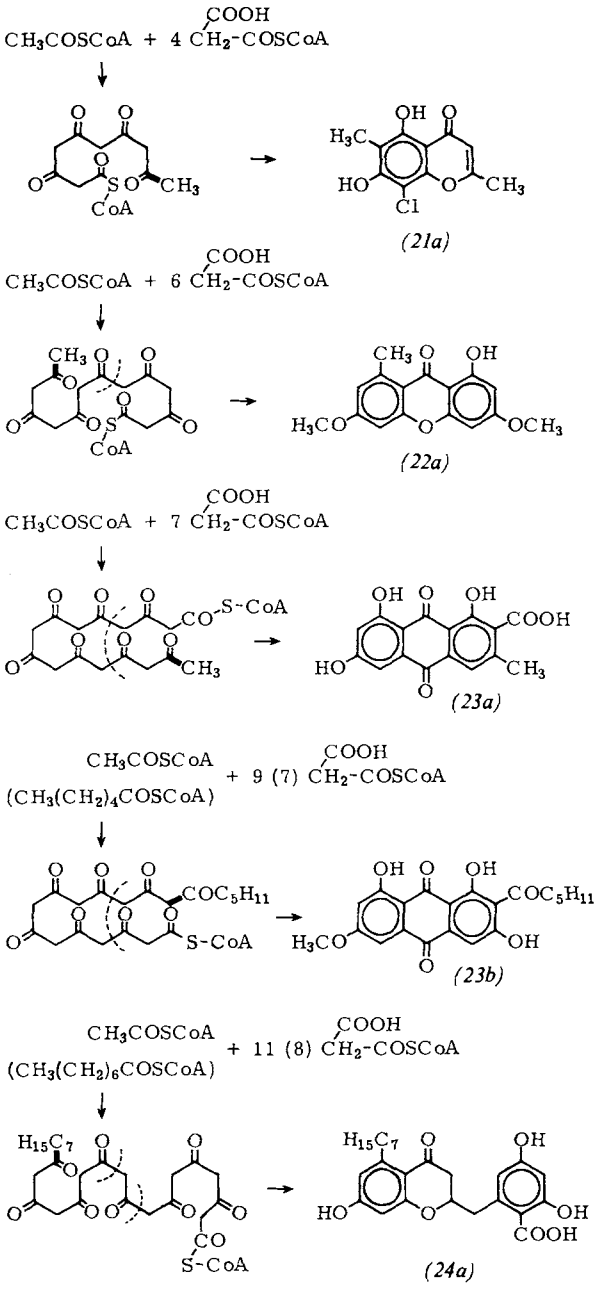


Fig. 12. Proposed biosynthetic pathways of non-condensed aromatic lichen polyketides from a β-polyoxomethylene chain. The "starting" positions are indicated by heavy lines, while the dotted lines show the theoretically possible formation of such compounds from two separate units. (The above polyoxomethylene chains are bound to coenzyme A or more likely to a multienzyme.)

The six xanthones *(22)* are probably formed analogously from one acetyl-SCoA molecule and six malonyl-SCoA molecules. The recently established structure for thiophanic acid (2,4,5,7-tetrachloro-1,3,6-trihydroxy-8-methylxanthone), a tetrachloroxanthone [79], is of interest, as is also the large number of chlorine-substituted aromatic lichen metabolites.

The structures of ten anthraquinones *(23)* from lichens have so far been elucidated. Biosynthetic investigations on fungal anthraquinones by *Gatenbeck* [80] and *Shibata* [81] point to a formation from an acetyl-SCoA molecule and *n* malonyl-SCoA units. While the cyclization step leading to endocrocin *(23a)* corresponds to the ring closure leading to orsellinic acid, solorinic acid *(23b)* exhibits a parallel to the acetylphloroglucinol cyclization (cf. Section 3.3.2.1 for the pentanoyl side-chain). Finally, siphulin *(24a)* [82] is the only chromanone *(24)* yet to have been found. Here too a formation *via* a long C_{24} β-polyoxomethylene chain is the most probable alternative.

3.4. The Mevalonic Acid Group

One diterpene, (−)-16α-hydroxykaurane [83], a series of interesting triterpenes [28], and several steroids (ergosterol, β-sitosterol, Vitamin D_2) and carotenoids (β- and γ-carotene as well as several xanthophylls) have been found among the lichen substances whose biosynthesis can be derived from mevalonic acid *(25)*. Results of biosynthetic investigations on these lichen metabolites are not available, but it may be assumed that their formation follows the familiar pattern (Fig. 13) [84].

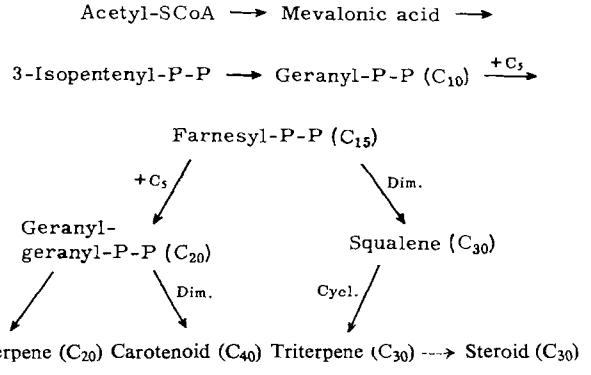


Fig. 13. Biosynthetic pathways of mevalonic acid group compounds.

The triterpenes are all pentacyclic; zeorin and leukotylin are distinguished by a rare five-membered ring E. Zeorin *(26)*, the most frequently occurring lichen

[76] *S. Gatenbeck* and *K. Mosbach*, Biochem. biophysic. Res. Commun. *11*, 166 (1963).

[77] *K. Soviar, O. Motl, Z. Samek*, and *J. Smolikowa*, Tetrahedron Letters *1967*, 2277.

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[84] *J. H. Richards* and *J. B. Henrickson*: The Biosynthesis of Steroids, Terpenes, and Acetogenins. W. A. Benjamin, Inc., New York 1964, p. 205.

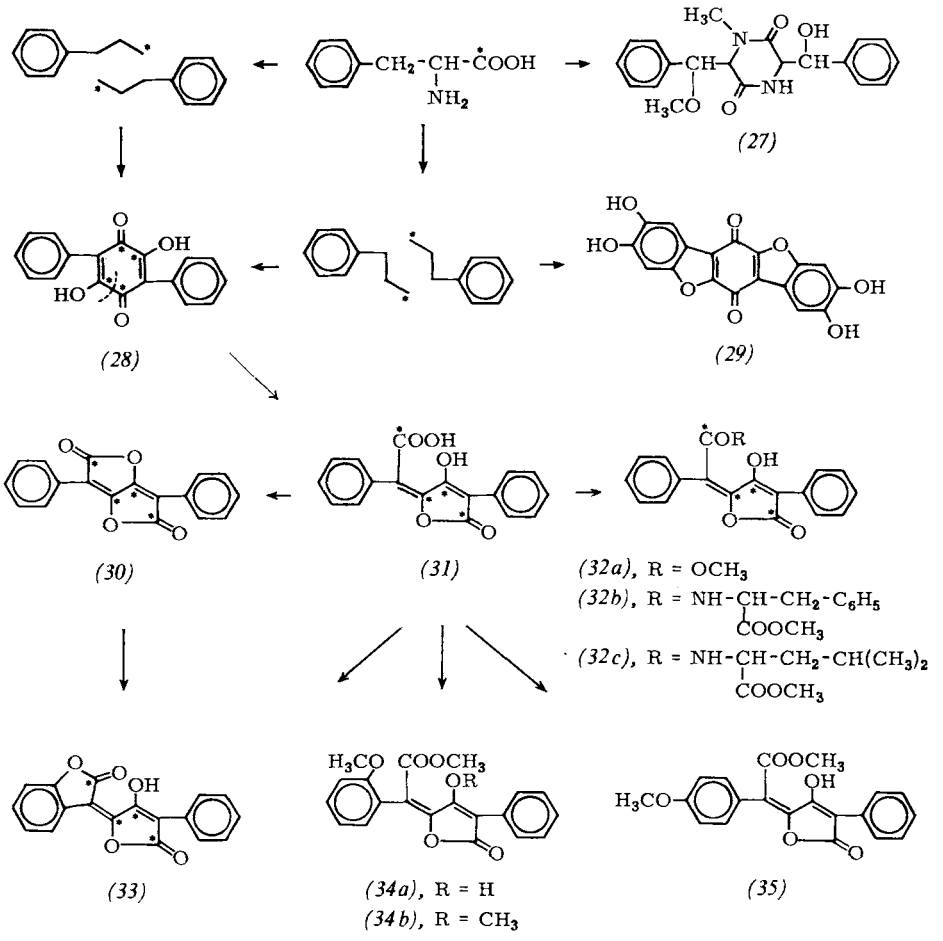


Fig. 15. Biosynthesis of aromatic lichen compounds of the shikimic acid group from C_6–C_3 fragments. In compounds whose formation was demonstrated experimentally from [1-^{14}C]-phenylalanine the ^{14}C-labeling obtained has been marked with an asterisk. *(32b)* = rhizocarpic acid, *(32c)* = epanorin, *(34a)* = leprapinic acid, *(35)* = pinastric acid.

terpene (6α,22-dihydroxyhopane)[85,86] is probably formed by the cyclization of squalene *(25)* (Fig. 14). A direct precursor of lichen triterpenes with an oxygen function in position 3 (as in friedelin) may be 2,3-epoxysqualene[87].

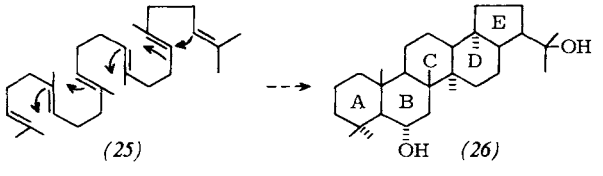


Fig. 14. Cyclization of squalene *(25)* to form zeorin *(26)*.

3.5. The Shikimic Acid Group

Only twelve aromatic lichen compounds belong to the shikimic acid group. *i.e.* their biosynthesis proceeds in the sequence: phosphoenolpyruvic acid + erithrytyl 4-phosphate → shikimic acid → chorismic acid → prephenic acid → C_6–C_3 derivatives. A diketopiperazine, picrorocellin *(27)*, two terphenylquinones, telephoric acid *(29)*, and polyporic acid *(28)*, as well as nine pulvic acid derivatives *(30)–(35)* have so far been found in lichens (Fig. 15). Phenylquinones are widespread especially among fungi; in contrast, the mainly yellow pulvic acid derivatives must be regarded as typical lichen substances. While picrorocellin *(27)* is evidently formed by direct condensation of two phenylalanine units, the terphenylquinones are formed by condensation of two (probably activated) phenylpyruvic acid derivatives, as has been shown for the fungal quinone volucrisporin, a *meta*-dihydroxyterphenylquinone[88]. The subsequent oxidative ring opening of the symmetrical terphenyls such as polyporic acid then leads to the pulvic acid derivatives with their characteristic diphenylbutadiene system, as experiments with [1-^{14}C]-DL-3-phenylalanine[89,90] and [^{14}C]-polyporic acid quinone[91] have shown.

The role played by the two symbionts in the biosynthesis of lichen substances has recently been established for the pulvic acid derivatives. *Thomas*[92] had shown that isolated lichen fungi are able to form "stictaurin", subsequently shown to be a mixture of calycin *(33)*

[85] *S. Huneck* and *J. M. Lehn*, Bull. Soc. chim. France *1963*, 1702.

[86] *T. Nakanishi* and *J. Kitagawa*, Tetrahedron Letters *1968*, 1485.

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[91] *W. Maas* and *A. Neish*, Canad. J. Botany *45*, 59 (1967).

[92] *E. Thomas*, Beitr. Kryptogamenflora der Schweiz *9*, 1 (1939).

and pulvic acid dilactone *(30)*. Recently the four pigments pulvic acid *(31)*, pulvic dilactone *(30)*, calycin *(33)*, and vulpinic acid *(32a)* were isolated from the extract of a lichen fungus culture of *Candellariella vitellina* [93]. Here, the algal component apparently plays no direct part in the biosynthesis.

The appearance of vulpinic acid was surprising, because it is not formed in the corresponding natural lichen associations. Recently, pulvic acid derivatives have also been found in independent living lichen-like fungi [94].

4. Conclusions

As has been stated previously, the lichen symbionts can collaborate during the degradation of compounds such as depsides to phenols. The question whether such a collaboration takes place, and if so to what extent, during the biosynthesis of such compounds, has not yet been clarified. Even if the algal component contains none of the enzyme systems that participate directly in these syntheses, its metabolic activity, and particularly its photosynthesis, provides the prerequisites for collaboration.

In general, both symbionts profit from the association in the various symbiotic forms of life that occur in nature, *inter alia* through exchange of metabolites. It is known that the bacteria present in the digestive tract of mammals imbibe the foodstuffs present and in turn supply a number of vitamins to the host. During the symbiosis of the nitrogen-fixing nodular bacteria with legumes, the nitrogen fixed in the nodules is given up to the plant partner which, in turn, furnishes carbon compounds. In mycorrhiza, the symbiotic association of fungi with higher plants, the fungal partner supplies the water and mineral salts required, and abstracts assimilates from its plant partner. The high degree of integration in symbiotic associations is demonstrated particularly clearly by the appearance of substances and structures that the individual substances could not produce [95]. Examples are a special hemoglobin, leghemoglobin, that participates in the fixation of nitrogen in the nodules of legumes [96,97], the development of rhizotamines (root nodules) in actinomycetes symbioses, and the morphogenetic effect of the intestinal flora in mammals on the development of the lymphatic system. The related problems of the nature and degree of exchange of metabolic products and its regulation, and the nature of the substances that influence the morphology of the symbiotic organism, in short the "biochemistry of symbiosis", are still largely unresolved.

In conclusion a parallel is drawn, as *Dubos* [98] has already indicated, between the intact lichen thallus and an individual cell. For this purpose the cell is regarded as a small-scale symbiotic form of life made up of semiautonomic, genetically independent, closely integrated small organs. Evidence for such a view is provided by the presence of DNA in chloroplasts [99] and mitochondria [100] and by the existence of a special messenger-RNA fraction on the polysomes of plasmatic membranes [101]

I wish to thank the Swedish Scientific Research Council for their generous support.

Received: July 1, 1968 [A 685 IE]
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Structure and Biosynthesis of the Ergot Pigments[1]

By B. Franck[*]

In addition to the well known alkaloids, ergot contains two groups of yellow to red pigments, between which there is a close and novel biogenetic relation. The pigments are anthraquinonecarboxylic acids and dimeric hydroxanthone derivatives (ergochromes), the structures of which, including the absolute configurations at 80 centers of chirality, have been completely determined. The intermediates involved in the biosynthesis have been largely established by feeding with labeled precursors, and its course by model experiments.

1. Introduction

Whereas interest in natural products chemistry was formerly centered mainly on the isolation of new physiologically active compounds, the determination of their structure, and their synthesis, attention is now also being given to their biosynthesis. Some years ago, pigments that are present in ergot drugs attracted our interest from this point of view. The properties of these pigments were indicative of unusual structures. Natural products with new structural principles frequently permit significant advances in the explanation of biogenetic relationships, and the ergot pigments did not disappoint us in this respect.

Ergot (Fig. 1) is found in nature on ears of rye. It is the permanent mycelium of the filamentous fungus *Claviceps purpurea*. The dramatic history of its investigation is divided into three phases: the discovery of its toxicity, its use as a medication, and the elucidation of the structures and biosynthesis of its ingredients[3].

From early times right up to the present century, the consumption of unpurified grain containing ergot has repeatedly led to devastating mass poisonings, which spread like an epidemic with the ergot fungus. This poisoning, which was known as ergotism, could lead to mutilation and death as a result of severe contraction of the peripheral blood vessels. It was only around 1600 that ergot was recognized as the cause of ergotism. It had previously been recorded in writing that with careful dosage, ergot is a valuable drug in midwifery[4]. The isolation and complete structural elucidation of the ergot alkaloids is mainly due to *Stoll et al.*[5].

Ergot research reached a climax in the last decade with the elucidation of the biosynthesis of these alkaloids with the aid of radioactively labeled precursors and the recently discovered methods for the cultivation of the ergot fungus on synthetic nutrient solution[6,7]. This led to the important



Fig. 1. Ergot *(Claviceps purpurea)*; (a) on rye ears (after *O. Gessner* [2], reproduced with permission of the copyright holder); (b) with sprouting fungus heads (photograph: Dr. *D. Claus*, Institut für Mikrobiologie der Universität, Göttingen).

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44 Münster, Orléans-Ring 23 (Germany)

[1] Ergot Pigments, Part 19. For Part 18 see [55].

[2] *O. Gessner*: Gift- und Arzneipflanzen von Mitteleuropa. Winter-Universitätsverlag, 2nd Edit. Heidelberg 1953.

[3] *A. Hofmann*: Die Mutterkorn-Alkaloide. Enke-Verlag, Stuttgart 1964.

[4] *G. Barger*: Ergot and Ergotism. Gurney and Jackson, London 1931.

[5] *A. Stoll*, Fortschr. Chem. org. Naturstoffe *9*, 114 (1952).

[6] *K. Mothes, F. Weygand, D. Gröger*, and *H. Grisebach*, Z. Naturforsch. *13b*, 41 (1958); *K. Winkler* and *D. Gröger*, Pharmazie *17*, 658 (1962).

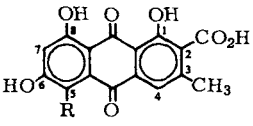
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realization, which has since been confirmed in many other examples[8], that terpene units are involved in the biosynthesis of indole alkaloids.

As with the ergot alkaloids, the investigation of the ergot pigments has also led to a fundamental biogenetic discovery. One group of these pigments, the ergochromes, are formed from anthraquinones[9–11] by oxidative ring opening[54–56]. No such ring opening of the very stable anthraquinones had previously been known either in the extensively studied chemistry of the anthraquinones or in their metabolism. The anthraquinones, which occur widely in nature (more than 100 are known at present) were therefore mostly regarded as "metabolic end products". This unsatisfactory view has now been refuted by the ring opening of anthraquinones in the ergot fungus.

2. The Anthraquinonecarboxylic Acids Endocrocin and Clavorubin

When aqueous methanol is poured over crushed ergot or dried mycelium of liquid cultures of the ergot fungus, a cherry-red extract is formed. Separation by partition chromatography on cellulose (Fig. 2) showed that this color is due to two hydroxyanthraquinonecarboxylic acids, which were isolated in the crystalline form[9]. The orange-red anthraquinone derivative was found to be endocrocin[9] *(1)*, which had previously been isolated from the Japanese tree lichen *Nephromopsis endocrocea*[10] and from *Aspergillus amstelodami*[11], and was found shortly afterwards in *Penicillium islandicum*[12]. The red compound known as clavorubin is a very similar compound; since it dissolves much less readily in the pure state[13], it was converted into the crystalline methyl ester for structural investigation. It was found that clavorubin *(2)* has the same structure as endocrocin, with the addition of a hydroxyl group on C-5; it can accordingly be prepared by specific oxidation[14] of endocrocin with manganese dioxide in concentrated sulfuric acid[15].



(1), R = H
(2), R = OH

Endocrocin and clavorubin were the first group of intensely colored and acidic (pK_a = 4.2) ergot pigments to be characterized. The concentration of these pigments in ergot (40 mg/kg), however, is much lower than that of the ergochromes described in the next section.

3. Isolation of the Light Yellow Ergochromes

The ergochromes are a group of light yellow, weakly acidic (pK_a = 8.5–9.4) ergot pigments, which can be obtained from the chloroform extract of ergot that has been degreased and pretreated with aqueous tartaric acid. The ergochrome content of ergot is about 5 g/kg, which is much higher than that of endocrocin *(1)* and clavorubin *(2)*, and is even higher than the yield of ergot alkaloids (approx. 2 g/kg)[2].

Though the first ergochrome preparations were isolated by *Dragendorff*[16] around 1877 (Table 1), the structure of the ergochromes was unknown until recently. The difficulties in the investigation of these compounds can now be traced to their great sensitivity to hydrolysis and the extreme similarity of their properties. Since many differ only in the configura-

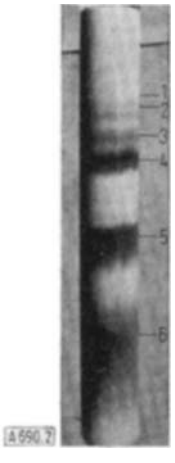


Fig. 2. Separation of the anthraquinonecarboxylic acids from ergot by partition chromatography on cellulose powder. 1–4 = cherry-red, clavorubin, and tail zones; 5 = orange-red, endocrocin; 6 = impurities.

Table 1. Ergochrome preparations isolated from ergot without chromatographic purification.

Ergochrome	Year	Ref.
Sclererythrin	1877	[16]
Sclerocrystallin	1877	[16]
Scleroxanthine	1877	[16]
Scleroiodinin	1877	[16]
Ergochrysin	1897	[17]
Secalonic acid	1906	[18]
Ergoxanthine	1910	[19]
Ergoflavin	1912	[20]
Chrysergonic acid	1952	[21]

[8] *A. R. Battersby, R. T. Brown, R. S. Kapil, J. A. Knight, J. A. Martin,* and *A. O. Plunkett,* Chem. Commun. *1966*, 888, and literature cited therein.

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tions of a few of the many centers of chirality, it was not possible to obtain them in the pure and homogeneous state by classical separation methods.

We achieved the complete separation of the ergochromes only by chromatographic methods. The mixtures of ergochromes were first isolated from ergot from various sources [22], and all the preparation methods for the pigment samples described previously [16–21] were repeated [24]. The chromatographic separation (which is made difficult by the low solubility of the ergochromes) and characterization was first carried out with a basic solvent system on buffered paper [23]. Diastereoisomeric ergochromes, however, were separated for the first time by *Gottschalk* [24,25] with chloroform/2-pentanone (9:1) on silica gel G, which is impregnated with oxalic or tartaric acid. It was found that the preparations described earlier (Table 1) are mixtures containing up to 13 components. The only exception was ergoflavin, which is not accompanied by diastereoisomers, and which *Freeborn* [20] obtained in the pure state by crystallization. Apart from ergoflavin, a total of nine ergochromes have been isolated in the pure and sterically homogeneous state by preparative chromatography using the above-mentioned system on columns of thin layer silica gel. Figure 3 shows the zones due to these ten pigments, as well as those of two unidentified trace components X_1 and X_2, in the thin layer chromatogram of an ergochrome mixture.

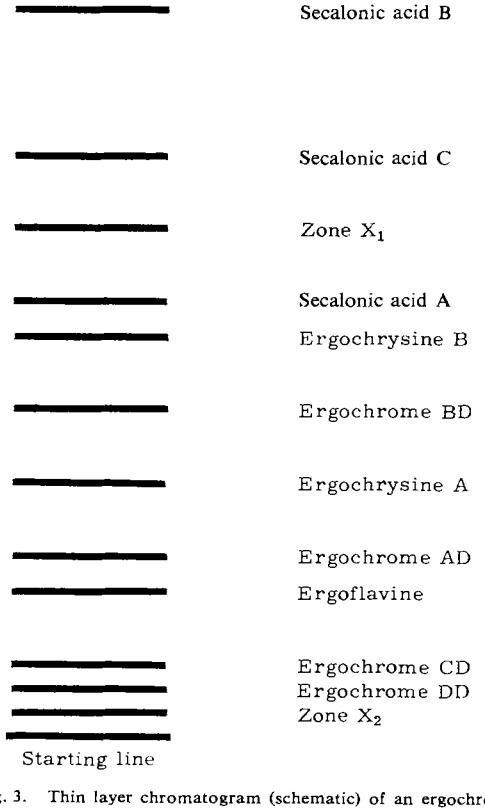
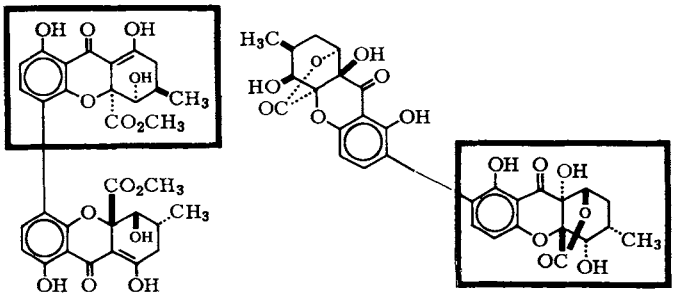


Fig. 3. Thin layer chromatogram (schematic) of an ergochrome mixture (chloroform/methanol = 100:1 on silica gel G containing tartaric acid).

4. Determination of the Constitution of Ergoflavin and of the Diastereoisomeric Secalonic Acids A and B

The principal component of the ergochromes is secalonic acid A. On the basis of degradation with alkali and ozone, partial synthesis, and NMR and mass spectra, we have obtained the structure *(3a)* for this compound [23,25,26]. The structure of ergoflavin *(4)* was established independently and almost simultaneously by *Whalley et al.* [27] and *McPhail et al.* [28] by a combination of chemical investigation with X-ray structure analysis. The pigments are symmetrical dimerization products of two xanthone derivatives, and differ in that the halves of the secalonic A molecule are linked in the *p* position with respect to the free hydroxyl group, while those of the ergoflavin molecule are linked in the *o* position.



(3a) *(4)*

Two other ergochromes, secalonic acids B and C, differ only in the configuration of some centers of chirality, and are therefore diastereoisomers [26,29].

As with other aromatic-hydroaromatic natural products, the determination of the constitution of secalonic acid A took place in two parts. The aromatic skeleton was first established by UV spectroscopy and vigorous degradation with alkali, and the saturated part of the molecule was then characterized by ozonolysis and by NMR and mass spectroscopy. The UV spectrum is very similar to that of 5-hydroxy-2-methylchromone *(8)*. As was found by *Bergmann* [30] and *Stoll* [21] for

[22] These were ergot drugs from Canada, Portugal, Spain, Germany, Austria, Hungary, Poland, Russia, and Japan, most of which had been obtained by artificial inoculation of rye plants with *Claviceps* strains.

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[26] *B. Franck, E. M. Gottschalk, U. Ohnsorge,* and *F. Hüper,* Chem. Ber. *99,* 3842 (1966).

[27] *J. W. Apsimon, J. A. Corran, N. G. Creasey, K. Y. Sim,* and *W. B. Whalley,* J. chem. Soc. (London) *1965,* 4130; Proc. chem. Soc. (London) *1963,* 209.

[28] *A. T. McPhail, G. A. Sim, J. D. M. Asher, J. M. Robertson,* and *J. V. Silverton,* J. chem. Soc. (London) *B 1966,* 18; Proc. chem. Soc. (London) *1963,* 210.

[29] *B. Franck* and *E. M. Gottschalk,* Angew. Chem. *76,* 438 (1964); Angew. Chem. internat. Edit. *3,* 44 (1964).

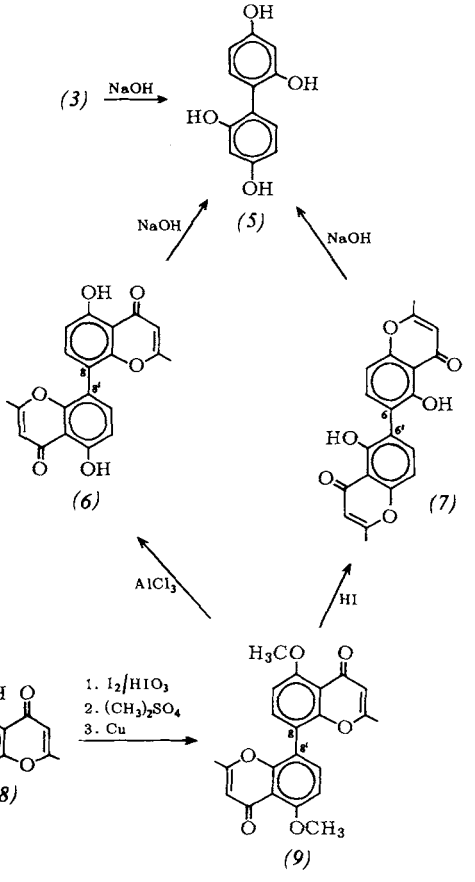
[30] *W. Bergmann,* Ber. dtsch. chem. Ges. *65,* 1486 (1932).

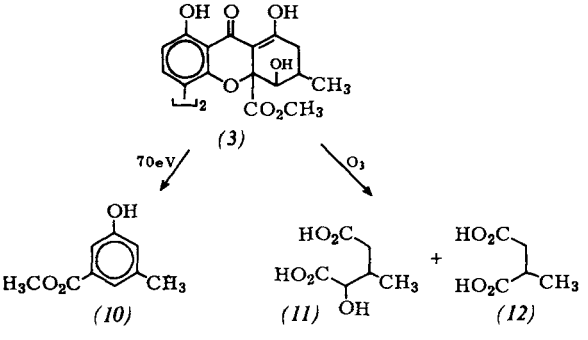
mixtures of ergochromes, secalonic acid A gives 2,4,2′,4′-tetrahydroxybiphenyl *(5)* on alkali fusion, so that two 5-hydroxychromonyls must be joined *via* the phenyl nuclei. Possibilities for the chromophore of the pigment were therefore an 8,8′-bichromonyl *(6)* or a 6,6′-bichromonyl *(7)*. The two bichromonyls, which had not previously been described, were synthesized by the reaction sequence shown in the scheme [31]. The 5,5′-dimethoxy-2,2′-dimethyl-8,8′-bichromonyl *(9)* obtained by Ullmann condensation could be converted into *(6)* by normal dimethylation, and into *(7)* by a new variant of the Wessely-Moser rearrangement [32, 33]. Thus both bichromonyls were available in good yields by a simple reaction sequence. Comparisons using the Gibbs color reaction [34], which is specific for phenols with the *p* position unoccupied, showed that secalonic acid A is an 8,8′-bichromonyl derivative, and therefore contains a basic skeleton that had not previously been known in natural products [23, 31].

According to its mass spectrum and elemental analysis, secalonic acid A has the empirical formula $C_{32}H_{30}O_{14}$. Two C-methyl groups, two aliphatic methoxycarbonyl groups, and six acetylatable hydroxyl groups were found [23]. The attachment of the functional groups and the other parts of the molecule indicated by the empirical formula to the 8,8′-bichromonyl skeleton was determined from the NMR and mass spectra and from the ozonolysis [23, 26]. Two doublets in the aromatic region of the NMR spectrum of secalonic acid A must be attributed to two pairs of adjacent aromatic protons, on the basis of their intensity and spin coupling (J = 8.5 Hz). The positions on the aromatic nuclei of the 8,8′-bichromonyl skeleton *(6)* in secalonic acid A *(3)* are therefore unoccupied. The NMR spectrum also showed that the basic skeleton of this pigment is symmetrically substituted, since instead of two doublets one would otherwise expect four with half the intensity [23].

The mass spectrum of the secalonic acid contains an intense fragment at m/e = 166 and derived fragments at m/e = 135 and 107, showing that a molecule of methyl cresotate *(10)* is readily split off on electron bombardment. According to this observation, each half of the basic bichromonyl skeleton must carry a six-membered carbocycle on the heterocycle. This carbocycle is readily aromatized, and carries a hydroxyl group, a methoxycarbonyl group, and a methyl group.

Ozonolysis of secalonic acid at 0 °C in ethyl acetate gave methylsuccinic acid and α-hydroxy-β-methylglutaric acid *(11)*, the carbon atoms of which must have been arranged in the ergochrome as shown. This together with the NMR spectrum shows that secalonic acid A has the structure *(3)* [26], and the cresotic acid split off in the mass spectrometer is the 1,3,5-isomer [35].





The similarity of the UV spectrum of secalonic acid A to that of 5-hydroxy-2-methylchromone *(8)* and the NMR spectrum indicate that, as in decalin-1,8-dione [36], the β-dicarbonyl system must be enolized [37]. According to the UV, IR, NMR, and mass spectra and the pK_a value, secalonic acid B is practically the same as secalonic acid A, but differs in its melting point, R_f value, and molar rotation. Experiments carried out in the same way show that secalonic acid B *(3b)* is a diastereoisomer of secalonic acid A *(3a)* [26].

[31] *B. Franck* and *G. Baumann*, Chem. Ber. *96*, 3209 (1963).

[32] *F. Wessely* and *H. G. Moser*, Mh. Chem. *56*, 97 (1930).

[33] *H. Schmid* and *A. Bolleter*, Helv. chim. Acta *33*, 917 (1950).

[34] *H. D. Gibbs*, J. biol. Chemistry *73*, 649 (1927); *F. E. King*, *T. J. King*, and *L. C. Manning*, J. chem. Soc. (London) *1957*, 563.

[35] *Bergmann* [30] and *Stoll et al.* [21] had also obtained 1,3,5-cresotic acid and methylsuccinic acid as well as 2,4,2′,4′-tetrahydroxybiphenyl on degradation of ergochromes with alkali.

[36] *H. Stetter* and *U. Milbers*, Chem. Ber. *91*, 977 (1958).

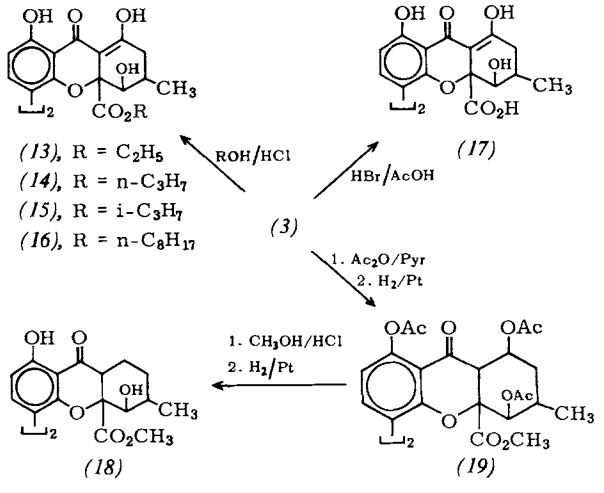
[37] *Whalley et al.* [38] carried out independent investigations on secalonic acid mixtures, the results of which also agree with the structure *(3)* and largely confirm our results.

[38] *J. W. Apsimon*, *J. A. Corran*, *N. G. Creasey*, *W. Marlow*, *W. B. Whalley*, and *K. Y. Sim*, J. chem. Soc. (London) *1965*, 4144.

5. Derivatives of Secalonic Acids A and B

Derivatives were required for the investigations on the configuration of the secalonic acids and for the elucidation of their biosynthesis. The possibilities for the conversion of secalonic acids into derivatives are however limited by the sensitivity of the allyl ether grouping to hydrolysis and the tautomerism of the enol system. Methylation under mild conditions with dimethyl sulfate or diazomethane gives reaction mixtures containing many components, no hydrogen is absorbed on catalytic hydrogenation [23], and acetylation by warming with acetic anhydride/sodium acetate leads to extensive changes [21]. The secalonic acids *(3)* can however be converted into crystalline diethyl *(13)*, di-*n*-propyl *(14)*, diisopropyl *(15)*, and di-*n*-octyl derivatives by transesterification with HCl/alcohol mixtures [39], and into desmethoxysecalonic acids *(17)* by treatment with HBr/glacial acetic acid [40, 54].

A stable, well-crystallized derivative of secalonic acid A *(3a)* has been prepared by removal of the enol group as follows [41]. After blockage of the tautomerism by acetylation under particularly mild conditions to form the hexaacetate [23], the enol double bonds could be readily hydrogenated.



On subsequent removal of the acetyl groups, the resulting aldol was simultaneously dehydrated. Rehydrogenation gave *(18)*, which, unlike secalonic acid A, no longer has an acidic group, and is therefore called "secalon A" [41].

6. Relative and Absolute Configuration of Secalonic Acids A and B

The configuration of the ergochromes, and particularly of the secalonic acids, at their various centers of chirality is important to the understanding of their structural variability and their biosynthesis. The NMR spectra of secalonic acids A and B (Fig. 4) are surprisingly simple when one considers the high molecular weights and complicated structures of these compounds. When the complete constitution was known, it could be deduced from these spectra that these two ergochromes are perfectly symmetrical, *i.e.* they consist of two halves that are identical even in their stereochemistry. This greatly simplified the determination of the configuration, since each of the two secalonic acids could be treated as if it consisted of only one half of its molecule, with three centers of chirality on C-6, C-5, and C-10.

Of these, the methyl-substituted C-6 can be cut out with ozone, as described earlier. Since the dextrorotatory methylsuccinic acid formed on ozonolysis of secalonic acid A has the *R* configuration, this is also the configuration of C-6 in the secalonic acid. With this absolutely fixed center of chirality as a basis, the relative arrangement of the adjacent hydroxyl group was found from the NMR spectrum (Fig. 4) [26].

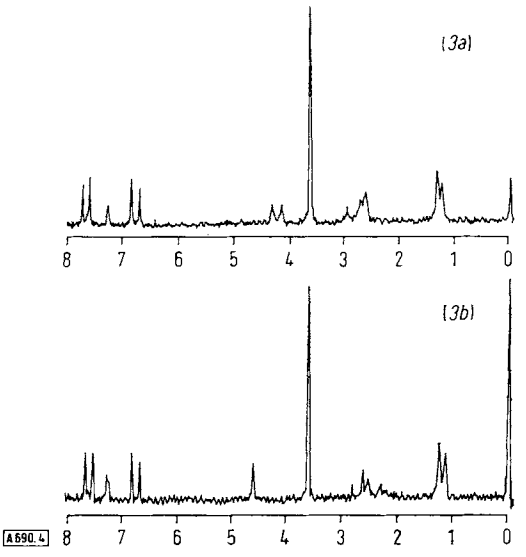


Fig. 4. NMR spectra of secalonic acids A *(3a)* and B *(3b)* in deuteriopyridine (from [26], data in δ values).

Since the spin coupling of the two protons on C-5 and C-6 showed that these are *trans*-diaxial with respect to each other, the methyl group and the hydroxyl group are also *trans* to each other *(3a)*. Similarly, the methyl center C-6 in secalonic acid B is found to have the *S* configuration, and is *cis* to the adjacent hydroxyl group *(3b)*.

To determine the configuration of the ring fusion center C-10, which carries the methoxycarbonyl group, the rotatory dispersion and mass spectra of the two diastereoisomeric secalonic acids were first compared [26]. The rotatory dispersions of secalonic acids A and B are practically mirror images, with opposite Cotton effects (Fig. 5). This indicates that the centers of chirality nearest to the chromophore, which cause the greatest chiralic disturbance, *i.e.* those at C-10, have opposite configurations (cf. [42,43]).

The configuration at the ring fusion center could not be assigned on the basis of the rotatory dispersion, *i.e.* the question which secalonic acid has the methoxycarbonyl group *cis*, and which *trans*, to the adjacent hydroxyl group could not be answered directly. A

[39] *O. v. d. Heyde*, Diplomarbeit, Universität Kiel, 1966.
[40] *F. Hüper*, Dissertation, Universität Kiel, 1967.
[41] *W. Beinert*, Diplomarbeit, Universität Kiel, 1967.
[42] *C. Djerassi, R. Riniker*, and *B. Riniker*, J. Amer. chem. Soc. *78*, 6362 (1956).
[43] *C. Djerassi*: Optical Rotatory Dispersion. McGraw-Hill, New York 1960, p. 64.

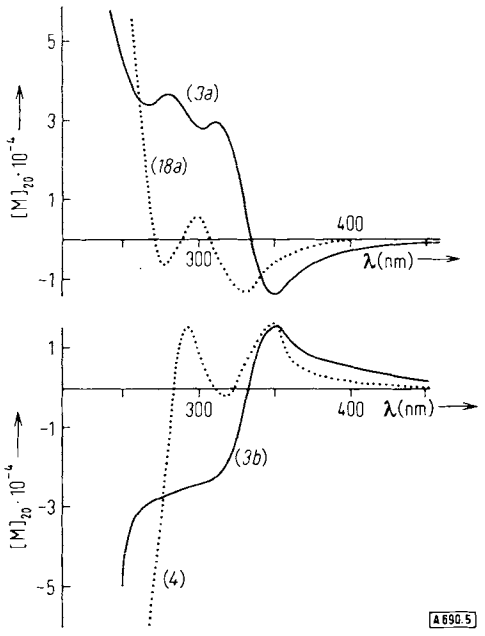
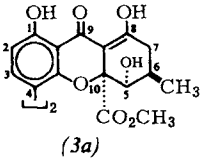
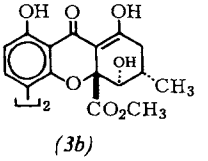


Fig. 5. ORD curves of secalonic acid A *(3a)*, secalonic acid B *(3b)*, secalon A *(18a)* [configuration as *(3a)*], and ergoflavin *(4)* [configuration as *(3b)*] in chloroform.

mass-spectrometric comparison of stability at C-10 was helpful in this respect. It is clear from the mass spectra of secalonic acids A and B that the ester group in secalonic acid A has the less stable *cis* configuration, and can be split off particularly readily by electron bombardment. This difference in stability became even more impressive when the energy of the electrons was decreased from 70 to 21 eV, as well as in the transesterification products of secalonic acids A and B [*(13)*, *(14)*, and *(15)*] with large alkyl residues on the ester group on C-10 [26,39,44].



(3a)



(3b)

The assignment of the configuration at C-10 in the secalonic acids in accordance with *(3a)* and *(3b)* was confirmed as follows by comparison with ergoflavin *(4)*, the configuration of which has been established by X-ray analysis [28]. Since the center of chirality at the ring fusion in the secalonic acids and similar ergochromes determines the course of the rotatory dispersion, this course should be similar for the same configuration on C-10 and the same chromophore. To allow a comparison of the C-10 configuration of a secalonic acid with that of ergoflavin, the secalonic acid must be converted into a derivative having the chromophore of ergoflavin. A suitable derivative of secalonic acid A is secalon A *(18a)* [41]. Since the course of the rotatory dispersion of secalon A is similar to, but in an almost mirror-image relation with, that of ergoflavin *(4)* (Fig. 5), these two compounds must have opposite configurations at the ring fusion center. This provides further confirmation of the absolute configuration of secalonic acid A as shown in *(3a)*, and hence also of secalonic acid B as shown in *(3b)*.

[44] *B. Franck*, *G. Baumann*, *U. Ohnsorge*, and *F. Hüper*: Abstract Book, 4th IUPAC-Symposium "The Chemistry of Natural Products", Stockholm 1966.

7. Structure and Absolute Configuration of the Other Seven Ergochromes

If the half molecules of the three symmetrical ergochromes described so far are denoted by A, B, and C, secalonic acids A and B and ergoflavin have the structures A–A, B–B, and C–C respectively (Table 2). Three other ergochromes, which we call secalonic acid C and ergochrysins A and B [45,46], were also obtained in the pure, sterically homogeneous state by our chromatographic separation method [24,29] for the diastereoisomeric secalonic acids. These were found to be the three *unsymmetric* dimerization products of the xanthone derivatives A, B, and C (Table 2). Their structure was found surprisingly easily from the fact that they behaved in all the investigations like a mixture of two of the symmetric pigments just discussed [45,47]. This is true of the UV, IR, NMR, and mass spectra, rotatory dispersion, circular dichroism, derivatives, and chemical degradation reactions. As an example, Figure 6 shows the UV spectra of ergochrysin A together with those of secalonic acid A and ergoflavin. Thus secalonic acid C, ergochrysin A, and ergochrysin B have the structures A–B, A–C, and B–C (Table 2).

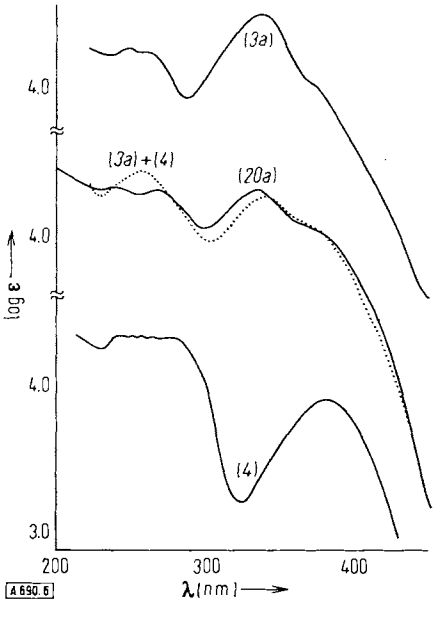


Fig. 6. UV spectra (in methanol) of ergochrysin A *(20a)*, secalonic acid A *(3a)*, ergoflavin *(4)*, and an equimolar mixture of *(3a)* + *(4)* (from [49]).

[45] *B. Franck*, Angew. Chem. *76*, 864 (1964); Angew. Chem. internat. Edit. *3*, 763 (1964).

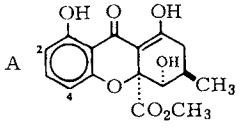
[46] *B. Franck*, *G. Baumann*, and *U. Ohnsorge*, Tetrahedron Letters *1965*, 2031.

[47] *B. Franck*: Festschrift Prof. Dr. K. Mothes. Fischer-Verlag, Jena 1965, p. 153.

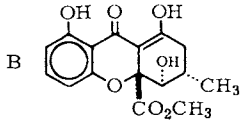
Four other ergochromes[44,46] attracted attention during their chromatographic purification by instability to solvents containing acids. They could be completely converted into one of the ergot pigments described above by heating for a short time in glacial acetic acid. The mass spectra showed that this rearrangement was accompanied by a loss of 32 mass units, corresponding to the removal of methanol. Further spectroscopic and chemical characterization of the pigments and their transformation products showed that the new ergochromes all contain a xanthone derivative of structure D, which is converted into the ergoflavin half C in hot acetic acid, with elimination of methanol and closure of the lactone ring. On the basis of the structures of the ergochrome halves in Table 2, therefore, these four ergochromes have the structures[49] A–D, B–D, C–D, and D–D. They can be readily converted into ergochrysins and ergoflavin by conversion of the ergochrome half D into the ergoflavin half C as follows:

A–D → A–C (ergochrysin A)
B–D → B–C (ergochrysin B)
C–D → C–C (ergoflavin)
D–D → C–C (ergoflavin)

Table 2. Structures of the ergochromes obtained from ergot by chromatography.

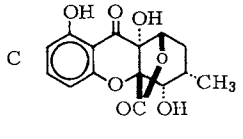


A–A = Ergochrome AA [4,4'] *(3a)* (Secalonic acid A)



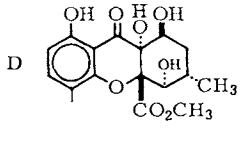
B–B = Ergochrome BB [4,4'] *(3b)* (Secalonic acid B)

C–C = Ergochrome CC [4,4'] *(4)* (Ergoflavin)



A–B = Ergochrome AB [2,2'] *(3c)* (Secalonic acid C) [26]

A–C = Ergochrome AC [2,2'] *(20a)* (Ergochrysin A) [48]

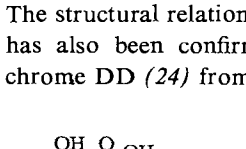


B–C = Ergochrome BC [2,2'] *(20b)* (Ergochrysin B) [48]

A–D = Ergochrome AD [2,2'] *(21)*

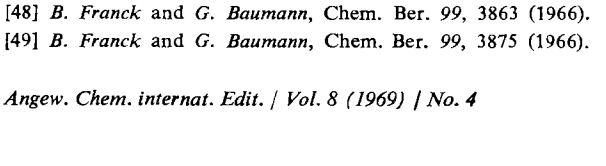
B–D = Ergochrome BD [2,2'] *(22)*

C–D = Ergochrome CD [2,2'] *(23)*



D–D = Ergochrome DD [2,2'] *(24)*

The structural relation between C and D ergochromes has also been confirmed by synthesis of the ergochrome DD *(24)* from ergoflavin *(4)*.



(4) *(24)*

[48] *B. Franck* and *G. Baumann*, Chem. Ber. *99*, 3863 (1966).
[49] *B. Franck* and *G. Baumann*, Chem. Ber. *99*, 3875 (1966).

For the determination of the complete structure of the new ergochromes, it was still necessary to establish the positions in which the halves of their molecules are linked. According to the NMR spectra, only linkage to the phenyl nucleus in the *o* or *p* position with respect to the phenolic hydroxyl group could be considered. Comparison with the synthetic bichromonyls *(6)* and *(7)* showed that the secalonic acids *(3a)* and *(3b)* have *p,p'* linkage[23,31], whereas *o,o'* linkage is found in ergoflavin *(4)*[27]. The *o,o'* linkage in ergoflavin is also shown[48] by its positive Gibbs reaction[34] and the detection of a weakly acidic grouping (pK_{DMF} = 9.4[50]), which can be attributed to the *o,o'*-dihydroxybiphenyl structure[51].

Since the ergochrysins behave in the same way as ergoflavin *(4)* in this respect[48], these must also have *o,o'* linkage of the molecule halves. This simultaneously establishes the type of linkage for the last four ergochromes AD, BD, CD, and DD, since these are converted into *o,o'*-linked ergochrysins or ergoflavin under conditions so mild that a change in the basic skeleton is inconceivable. Thus all ergochromes containing a C or D half exhibit *o,o'* (=2,2') linkage, while the others, *i.e.* the three secalonic acids, have *p,p'* (=4,4') linkage.

Including ergoflavin (the structure of which was established by *Whalley*[27] and *McPhail*[28]), the structures and absolute configurations are completely known for a total of ten ergochromes from ergot. The configurations were determined for not less than 80 centers of asymmetry. The result is remarkable, since the ergochromes form an unusually complete group of natural products, which contains all ten possible combinations of two of the four xanthone derivatives A, B, C, and D (Table 2). This allows the simple nomenclature given in Table 2, which avoids the need for separate names for the ergochromes.

8. Biosynthesis of the Ergochromes from Acetate and Emodin

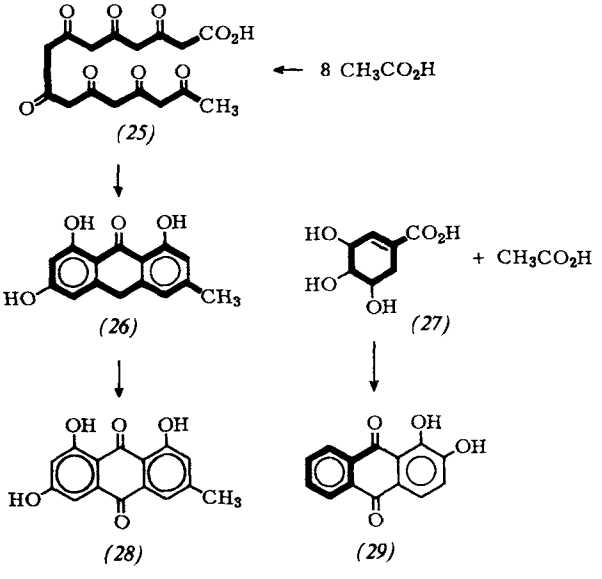
The structures of the ten ergochromes and the two anthraquinone-carboxylic acids from ergot pointed to a biogenetic relationship, since they all contain tricyclic C_{15} systems with similar arrangement of the substituents. There can now be practically no doubt about the biosynthesis of endocrocin *(1)*, since *Gatenbeck*[52] has shown that its decarboxylation product emodin *(28)* is formed by condensation of eight molecules of acetic acid *via* acetyl and malonyl coenzyme A. A heptaoxopalmitic acid *(25)* and emodinanthrone *(26)* may occur as intermediates[52]. Endocrocin may in turn be regarded as a precursor of many natural anthraquinone pigments, and un-

[50] Apparent p*K* value from titration with 0.1 N NaOH in 80% aqueous dimethylformamide at 20 °C.
[51] *H. Musso* and *H. G. Matthies*, Chem. Ber. *94*, 356 (1961).
[52] *S. Gatenbeck*, Acta chem. scand. *12*, 1211 (1958).

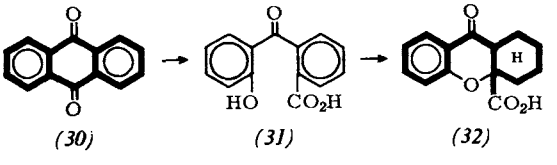
doubtedly also of clavorubin. According to recent results obtained by *Leistner* and *Zenk* [53] a somewhat different biosynthetic route involving shikimic acid *(27)* must be assumed for the formation of alizarin *(29)* in *Rubia tinctorum*. However, alizarin comes from a plant, and not from lower fungi, as do endocrocin and related anthraquinones.

The ten ergochromes can also be derived from endocrocin by a simple, biogenetically possible reaction sequence. They all contain the basic skeleton *(32)* in each half of the molecule. This skeleton could be formed from an anthraquinone *(30)* in two steps: (1) oxidative cleavage of the anthraquinone to form the benzophenone-carboxylic acid *(31)*; (2) ring closure to form the xanthone derivative *(32)* by phenol oxidation.

The ergochrome ring system is thus formally and (as was to be concluded) biogenetically a "*seco*-anthraquinone". Dimerization of the "*seco*-anthraquinone" halves to form the ergochrome should be possible by phenol oxidation in the *p* or *o* position with respect to

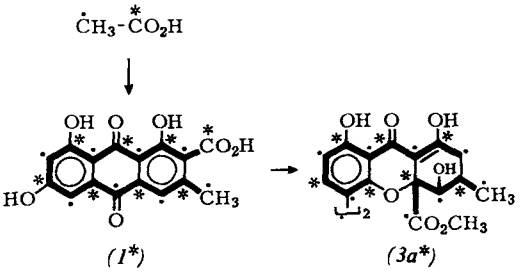


the phenolic hydroxyl group. It has been shown by feeding with radioactively labeled acetate [54] and emodin *(28)* [55] that this biogenetic hypothesis is correct.

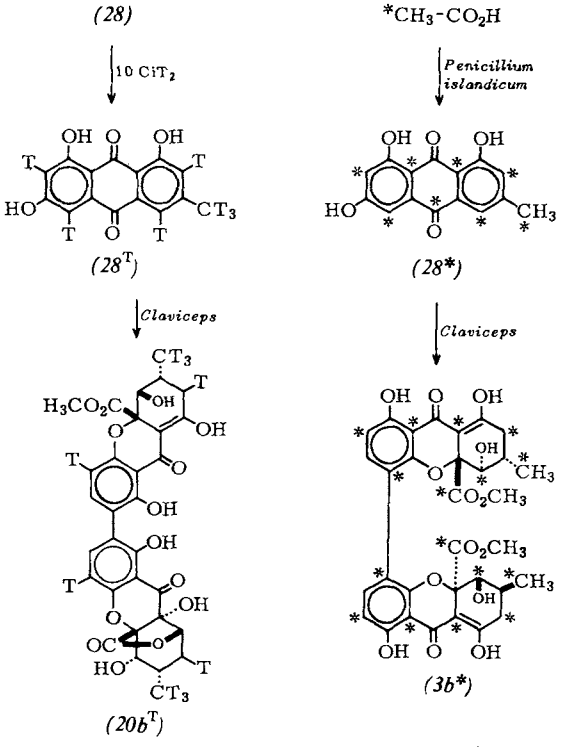


In order to carry out the isotope experiment, it was first necessary to know whether the ergot fungus forms all the ergochromes even when it does not parasitize rye plants, *i.e.* when it is grown on a synthetic nutrient solution. This would prove that the ergot pigments are true metabolic products of the fungus, the biosynthesis of which does not require the cooperation of the rye plant. Furthermore, feeding experiments with labeled precursors are much easier to carry out on liquid cultures. There were fortunately strains of ergot fungus that formed a deep red mycelium containing all the ergochromes as well as endocrocin and clavorubin after cultivation on mannitol/cane sugar solution [56]. Thus the ergot fungus synthesizes the same pigments in liquid cultures as on the rye plant. This is remarkable, and is by no means always the case with the ergot alkaloids [57].

In three experiments, sodium acetates labeled in the carboxyl group with ^{14}C and in the methyl group with ^{14}C or ^{3}H were fed to well established liquid cultures. Degradation of the ergochromes [*e.g. (3a*)*] collected after further growth showed the radioactivity distribution that is to be expected if the pigments are formed from acetic acid *via* endocrocin *(1*)* or emodin and their oxidative ring cleavage.



Direct proof of the biosynthesis of ergochromes from anthraquinones was provided by feeding with emodin which was labeled with ^{14}C in one experiment and with tritium in another. The tritium-labeled emodin was



[53] *E. Leistner* and *M. H. Zenk*, Tetrahedron Letters *1967*, 475; Z. Naturforsch. *22b*, 865 (1967).

[54] *B. Franck, F. Hüper, D. Gröger*, and *D. Erge*, Angew. Chem. *78*, 752 (1966); Angew. Chem. internat. Edit. *5*, 728 (1966); Chem. Ber. *101*, 1954 (1968).

[55] *D. Gröger, D. Erge, B. Franck, U. Ohnsorge, H. Flasch*, and *F. Hüper*, Chem. Ber. *101*, 1970 (1968).

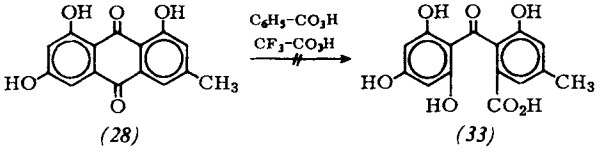
[56] *D. Gröger*, Arch. Pharmaz. *292*, 389 (1959); *D. Gröger* and *D. Erge*, Planta med. *9*, 471 (1961).

[57] *A. Stoll, A. Brack, H. Kobel, H. Hofmann*, and *R. Brunner*, Helv. chim. Acta *37*, 1815 (1954).

obtained by Wilzbach tritiation with 10 Ci of tritium gas, and the ^{14}C-labeled emodin by feeding sodium [2-^{14}C]-acetate to the fungus *Penicillium islandicum* followed by isolation of the biosynthetically formed radioactive emodin. In agreement with the biosynthesis of emodin as elucidated by *Gatenbeck* [52], the radioactive carbon atoms of the emodin *(28*)* formed from sodium [2-^{14}C]-acetate alternate with unlabeled atoms. After the labeled emodins *(28^T)* and *(28*)* had been fed to *Claviceps*, the radioactive ergochromes BC *($20b^T$)* and BB *(3b*)* (incorporation rates 1.2 and 0.5%) and other ergochromes are isolated. Their radioactivity distribution as found by chemical degradation clearly shows that the labeled emodin is completely converted into the ergochromes, with ring opening.

9. Model Experiments on the Biosynthesis of Ergochromes

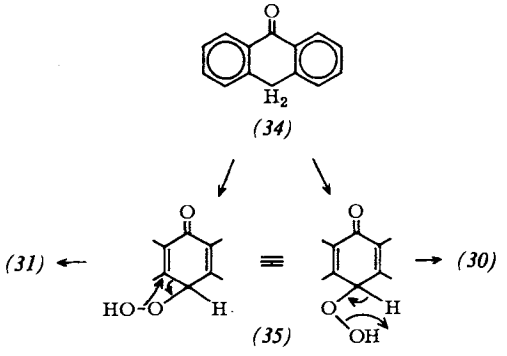
The oxidative ring opening of an anthraquinone during the biosynthesis of ergochromes was puzzling. Though the quinoid ring can be opened by vigorous reagents such as chromic acid or strong bases, the molecule is always halved at the same time [58,59]. It is also surprising that the course of the biological degradation of the natural anthraquinones was still unknown, whereas their biosynthesis had been largely elucidated [52,53]. Since anthraquinones occur in large quantities in nature (the dry matter of many common microorganisms contains 20–30 wt.-% of anthraquinones [60]), whereas accumulation has been observed in only a few places [61], intensive biological degradation must occur. This is also of pharmacological interest, since several anthraquinones are used as drugs.



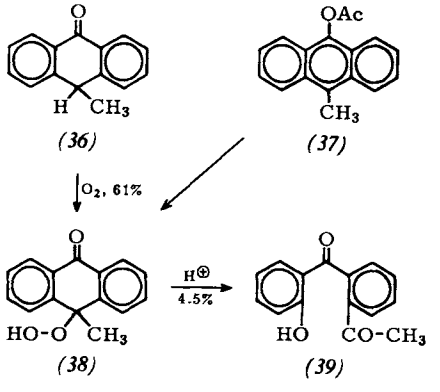
(28) *(33)*

On the basis of these considerations, the behavior of 20 hydroxyanthraquinones, including emodin *(28)* and endocrocin *(1)*, toward peracids under the conditions of the Baeyer-Villiger oxidation was systematically studied [62]. Though benzophenone is readily cleaved all the anthraquinones studied were found to be inert. A reaction of this type is therefore unlikely for metabolism.

Oxidative ring cleavage of an *anthrone (34)*, on the other hand, would be conceivable. Anthrones are precursors of the anthraquinones in their biosynthesis from acetate units, and could also be readily formed by reduction of anthraquinones. According to a hypothesis proposed by *Money* [63] in connection with the biosynthesis of other natural products, autoxidation of an anthrone *(34)* should lead to a hydroperoxide *(35)*, which then rearranges to form the benzophenone derivative *(31)*.



Attempts to verify this hypothesis experimentally with the unsubstituted anthrone *(34)* did not at first have the desired result [62,63], since the very unstable anthrone hydroperoxide *(35)* is dehydrated during its preparation, and yields the anthraquinone *(30)*. On the other hand, 10-methylanthrone hydroperoxide *(38)*, which had not previously been described, and which was obtained in good yields and in the crystalline state by autoxidation of 10-methylanthrone *(36)* in the presence of azodiisobutyronitrile, was found to be stable [62]. *(38)* was also formed by the action of methylmagnesium iodide on 10-methylanthranyl acetate *(37)*, followed by autoxidation [62,64]. The 10-methylanthrone hydroperoxide could be rearranged, with ring opening, into 2-hydroxy-2'-acetylbenzophenone in glacial acetic acid/dilute sulfuric acid. This



proton-catalyzed reaction probably proceeds in the same way as the analogous rearrangement of cumene hydroperoxide. This was the first successful oxidative

[58] *Y. Asahina* and *F. Fuzikawa*, Ber. dtsch. chem. Ges. *68*, 1558 (1935).

[59] *G. A. Swan*, J. chem. Soc. (London) *1948*, 1408.

[60] *R. H. Thomson*: Naturally occurring Quinones. Butterworth, London 1957.

[61] *A. Treibs* and *H. Steinmetz*, Liebigs Ann. Chem. *506*, 171 (1933).

[62] *B. Franck*, *V. Radtke*, and *U. Zeidler*, Angew. Chem. *79*, 935 (1967); Angew. Chem. internat. Edit. *6*, 952 (1967); *V. Radtke*, Dissertation, Universität Kiel, 1968.

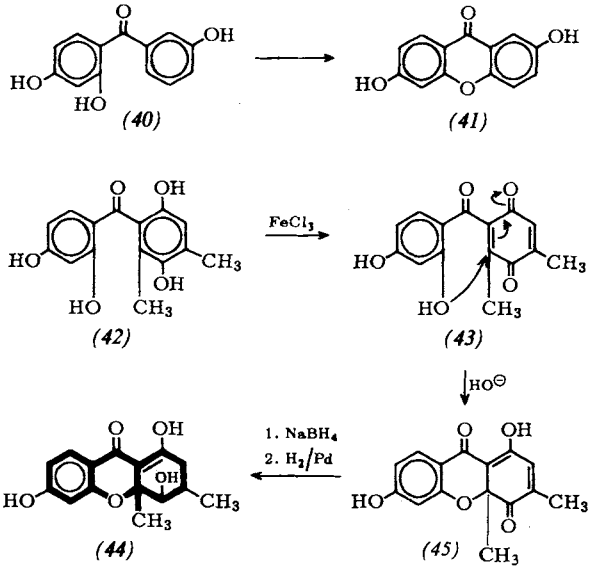
[63] *T. Money*, Nature (London) *199*, 592 (1963).

[64] This reaction does not lead to the transannular peroxide, as was assumed by *Julian*, *Cole*, and *Diemer* [65].

[65] *P. L. Julian*, *W. Cole*, and *G. Diemer*, J. Amer. chem. Soc. *67*, 1721 (1945).

ring opening of an anthrone, which is a conceivable model reaction for biogenetic changes.

The second step in the biosynthesis of ergochromes from anthraquinones consists in the ring closure of a hydroxybenzophenone to form the xanthone derivative. This could proceed as a phenol oxidation. Thus *Lewis* and *Warrington*[66] obtained 2,6-dihydroxyxanthone *(41)* in high yield by oxidation of trihydroxybenzophenone *(40)* with potassium hexacyanoferrate(III). The condensation product *(44)* which



contains the complete basic skeleton of a half molecule of the secalonic acids (bold type) *(3)*, was obtained in a similar manner from 2,5,2′,4′-tetrahydroxy-4,6-dimethylbenzophenone *(42)*[67]. In this case the oxidation with iron(III) chloride leads first to the crystalline *p*-quinone *(43)*, which undergoes alkali-catalyzed condensation to form the dienone *(45)*. Subsequent reduction and catalytic hydrogenation yields *(44)*.

[66] *J. R. Lewis* and *B. H. Warrington*, J. chem. Soc. (London) *1964*, 5074.

[67] *U. Zeidler*, Dissertation, Universität Kiel, 1969.

10. Closing Remarks

As a result of the investigations of recent years, twelve ergot pigments have now taken their place beside the ergot alkaloids. Ten of these pigments, the ergochromes, owe their biosynthesis to a hitherto chemically and metabolically unknown oxidative ring cleavage of anthraquinones, which are formed in nature from acetate units. The ergot fungus thus again proves to be an organism that is characterized by the great versatility of the products and reactions of its metabolism. Since results obtained for this fungus are probably also valid for other organisms[68], the ergot fungus may be regarded as a particularly worthwhile object of study for biogenetic relations.

Several research teams and colleagues have played an important part in obtaining the results described here. The nutrition experiments were carried out with the cooperation of Doz. Dr. Gröger and Dr. Erge from the Institut für Biochemie der Pflanzen der Deutschen Akademie der Wissenschaften at Halle/Saale[54, 55]; *thanks are due to Prof. Dr. S. Shibata (University of Tokyo), Doz. Dr. G. Snatzke (Bonn University), and Messrs. Carl Zeiss, Oberkochen, for rotatory dispersion and circular dichroism measurements. I am particularly grateful to my colleagues mentioned in the references, who participated in the investigation of the ergot pigments at the Universities of Göttingen and of Kiel. The investigations were generously supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and Farbenfabriken Bayer, Werk Elberfeld. I am also grateful to the Stiftung Volkswagenwerk for the use of a mass spectrometer. Valuable drugs were supplied by the Dr. Schwarz Arzneimittelfabrik, Monheim.*

Received: July 24, 1968 [A 690 IE]
German version: Angew. Chem. *81*, 269 (1969)
Translated by Express Translation Service, London.

[68] It is interesting in this connection to note that the secalonic acids A *(3a)* and C *(3c)* have recently also been isolated from the lichen *Parmelia entotheiochroa* by *I. Yosioka*, University of Osaka (private communication).

Deactivation of Excited States[**]

By L. M. Stephenson and G. S. Hammond[*]

Nature abhors an electronically excited state and strives to convert this energy to other forms. This article is concerned with the various pathways involved in the degradation of electronic excitation to ordinary "thermal" forms, but will primarily discuss the quenching of excited states by other molecules. The authors include as examples only those photo-transformations and interactions encountered in solution.

1. Introduction

During phototransformations and interactions occurring in solution, the high frequency of collision with solvent in general establishes a Boltzmann distribution among vibrational and rotational levels in the *lowest* lying, electronically excited states within a very short time span ($< 10^{-11}$ sec) following excitation. Reference to a Jablonski energy diagram (Figure 1)

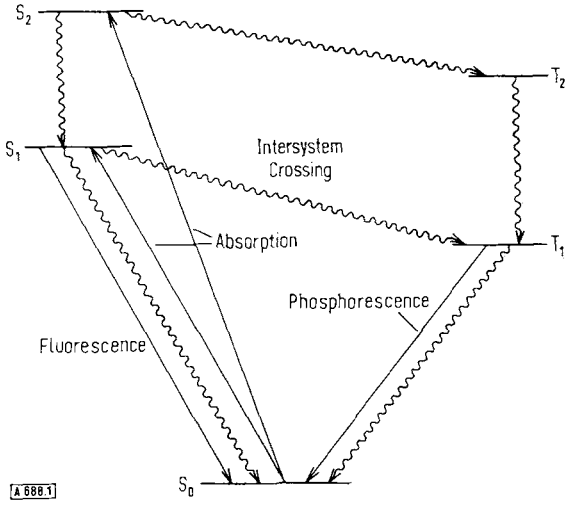


Fig. 1. Jablonski diagram. Solid arrows show absorption and emission of light, wavy arrows indicate radiationless processes.

will serve to clarify this point. The energy gap between the ground state and the lowest lying excited states is generally sufficiently large so that the vibrational overlap [1] between these states is slight. As a consequence, modes of deactivation other than nonradiative decay are frequently sought from lowest excited singlet and triplet states. Vibrational overlap between higher excited states, which are often separated by only small energy gaps, is much larger and leads to extremely rapid rates of nonradiative decay to the lowest excited states in any multiplicity manifold.

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[**] Contribution No. 3625 from the Gates and Crellin Laboratories of Chemistry.

[1] The importance of vibrational overlap in determining rates of nonradiative decay has been delineated by *G. W. Robinson* and *R. P. Frosch*, J. chem. Physics *37*, 1962; *38*, 1187 (1963).

Most organic molecules contain even numbers of electrons which are spin paired and occupy orbitals that may be classified as localized, delocalized (as in conjugated unsaturated systems), or nonbonding (such as the pairs on oxygen and nitrogen). In addition, organic molecules, which are composed primarily of light atoms, have rigidly defined spin selection rules for electronic transitions. These molecules usually have ground singlet configuration, and display only spin allowed, singlet-singlet transitions in absorption spectra in the absence of strong external perturbation.

Following the rapid deactivation of the initially produced excited-singlet state to the lowest excited-singlet state, what pathways of deactivation do exist for this momentarily "trapped" molecule? Physical processes which degrade singlet states are familiar; fluorescence and nonradiative decay, both to the ground state and crossing to the excited triplet manifold. This latter process, known as intersystem crossing has proved to be of immense importance to photochemistry. The triplet state populated by the intersystem crossing process may also emit light (phosphorescence) or may return to the ground state by nonradiative paths. Events of more interest to photochemists include bond formation or fragmentation in the excited state (chemical quenching), energy transfer to suitable substrates, and formation of excited complexes (exiplexes) having decay characteristics different from those of the excited monomers.

2. The Chemical Quenching of Excited States

Because of the considerable energy possessed by electronically excited states, activation barriers for chemical reactions are frequently easily overcome. Conceptually, the quenching of excited states by bond formation or fragmentation is very simple; in practice the details are often difficult to explore. Two quenching mechanisms of this type have received considerable attention in our laboratories, *i.e.* the photoreduction and photoreactions of ketones and the photodimerization of conjugated dienes.

The photochemical reaction of ketones with alcohols is a familiar method for the production of pinacols [2].

[2] *A. Schönberg* and *A. Mustafa*, Chem. Reviews *40*, 181 (1947).

Until the late 1950's, however, little effort had been directed toward elucidation of the reaction mechanism, although the involvement of free radicals was generally accepted. In 1960, *Bäckstrom* and *Sandros* [3] were able to show compelling evidence for the identification of the reactive species as the triplet state of the ketone. Their results were focused on a study of the energy transfer from benzophenone *(1)* to biacetyl, monitored by the observation of induced phosphorescence from the latter. *Hammond, Moore,* and *Foss* [4] were able to obtain results in substantial agreement with those of *Bäckstrom* and *Sandros*. By using benzhydrol *(2)* as the hydrogen donor the reaction was simplified by virtue of the fact that only a single kind of free radical was produced.

$$\underset{(1)^*}{(C_6H_5)_2CO^*} + \underset{(2)}{(C_6H_5)_2CHOH} \xrightarrow{k_r}$$

$$2\,(C_6H_5)_2\dot{C}OH \rightarrow (C_6H_5)_2COH{-}COH(C_6H_5)_2 \qquad (1)$$

The dependence of the quantum yield of benzophenone disappearance ($\Phi_{-(1)}$) on benzhydrol concentration was explained in terms of the competition of unimolecular decay [reaction (2)] with pinacol formation [reaction (1)]

$$\underset{(1)^*}{(C_6H_5)_2CO^*} \xrightarrow{k_d} \underset{(1)}{(C_6H_5)_2CO} \qquad (2)$$

Treatment of $(C_6H_5)_2CO^*$ as an unstable intermediate led to eq. (3).

$$1/\Phi_{-(1)} = 1/a + k_d/ak_r\,[(2)] \qquad (3)$$

The constant a is the yield of benzophenone *(1)*. Experimental results showed that $a = 1.0$ and that $k_d/k_r = 0.05$ moles/liter. Since k_r cannot be larger than the diffusion-controlled limit, the data demanded the conclusion that the excited state $(C_6H_5)_2CO^*$ be longer lived than the excited singlet state. The hypothesis that the excited state produced by absorption of light by benzophenone undergoes quantitative intersystem crossing to yield a long lived triplet excited state, which is the chemically reactive species, has thus proved durable.

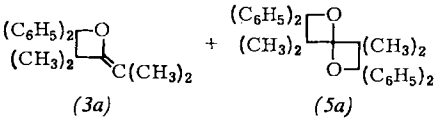
In a subsequent study, *Hammond* and *Leermakers* [5] showed that carbonyl compounds such as naphthaldehyde and acetonaphthone, which possess lowest triplet states of $\pi \rightarrow \pi^*$ rather than $n \rightarrow \pi^*$ configuration, are relatively unreactive in photoreduction. The effect is striking because the lifetimes of $\pi \rightarrow \pi^*$ triplets are longer than those of $n \rightarrow \pi^*$ triplets. The strong dependence of chemical reactivity on electronic configuration of the excited states dispels the vague notion that energy rich, excited molecules are nondiscriminating in their chemical reactivity.

$$R_2CO^* + \gtrless C{=}C \lessgtr \longrightarrow \begin{matrix} R_2C{-}O \\ | \\ \gtrless C{-}C \lessgtr \end{matrix} \quad (3)$$

Other typical photoreactions have also been shown to occur from $n \rightarrow \pi^*$ lowest excited triplet states, including the widely studied oxetane-forming reaction [6, 7].

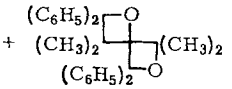
Arnold and *Glick* [8], and *Hammond et al.* [9] have obtained, for example, the oxetane *(3a)* and the two dioxaspiroheptanes *(5a)* and *(5b)* from the allene *(4)* and benzophenone.

$$\underset{(1)}{(C_6H_5)_2CO} + \underset{(4)}{(CH_3)_2C{=}C{=}C(CH_3)_2} \xrightarrow{h\nu}$$



(3a)

(5a)



(5b)

Further data obtained by *Leermakers* and *Hammond* [10] confirmed the supposition that triplet states are involved in the photoreductions and photoreactions of ketones. A number of compounds were found to quench the photoreduction of benzophenone by benzhydrol. Interestingly, many quenchers, such as 2-acetonaphthone, naphthalene, *cis-* and *trans*-1,3-pentadiene, azulene, 1-naphthaldehyde, display remarkably similar quenching efficiencies. Since the compounds above all possess triplet energies lower than that of benzophenone it was inferred that the quenching mechanism must involve energy transfer from benzophenone at close to the same rate for all quenchers, presumably at or near that of a diffusion controlled process. Other quenchers, with triplet energies higher than that of benzophenone, such as cyclohexene, are considerably less efficient.

The use of specific quenchers for triplet states is now a commonplace technique for determining the spin multiplicity of a photoreactive state. An often overlooked criterion for energy transfer, however, is the production of an excited state of the quencher. This is perhaps most easily demonstrated when employing the conjugated dienes as quenchers [10–12].

Irradiation of solutions of conjugated diene and benzophenone (at wavelengths only absorbed by benzophenone) leads to *cis-trans* isomerization in the case of 1,3-pentadiene, and dimerization occurs with many

[3] *H. L. J. Bäckstrom* and *K. Sandros*, Acta chem. scand. *14*, 48 (1960).

[4] *W. M. Moore, G. S. Hammond,* and *R. P. Foss*, J. Amer. chem. Soc. *83*, 2789 (1961).

[5] *G. S. Hammond* and *P. A. Leermakers*, J. Amer. chem. Soc. *84*, 207 (1962).

[6] *N. C. Yang*: Organic Photochemistry. Butterworths, London 1965; Pure appl. Chem. *9*, 591 (1964).

[7] Oxetane formation which proceeds through an excited singlet n, π^* state has recently been reported. See *N. J. Turro, P. Wriede, J. C. Dalton, D. A. Arnold,* and *A. H. Glick*, J. Amer. chem. Soc. *89*, 3950 (1967).

[8] *R. Arnold* and *A. Glick*, Chem. Commun. *1966*, 813.

[9] *H. Gotthardt, R. Steinmetz,* and *G. S. Hammond* Chem. Commun. *1967*, 480; *H. Gotthardt, R. Steinmetz,* and *G. S. Hammond*, J. org. Chemistry, *33*, 2774 (1968).

[10] *P. A. Leermakers* and *G. S. Hammond*, J. physic. Chem. *66*, 1148 (1962).

[11] *G. S. Hammond, J. Turro,* and *P. A. Leermakers*, J. physic. Chem. *66*, 1142 (1962).

[12] This fact coupled with the existence of an unusually large singlet-triplet splitting has made 1,3-pentadiene the "quencher of choice" in many recent photochemical studies.

dienes at high concentrations. Neither reaction proceeds with high efficiency from the excited singlet states of the diene, and the product distribution for dimers in no way resembles that formed from ground state molecules in thermal reactions. The triplet state was thus specifically implicated in the photoreactions of the ketones quenched by the dienes.

Triplet quenchers, such as 1,3-pentadiene, were employed more recently by *Hammond* and *Wagner* [13,14] to prove the reactive character of both singlet and triplet states in Norrish Type II photoelimination. The cyclobutane derivative is usually only a minor product.

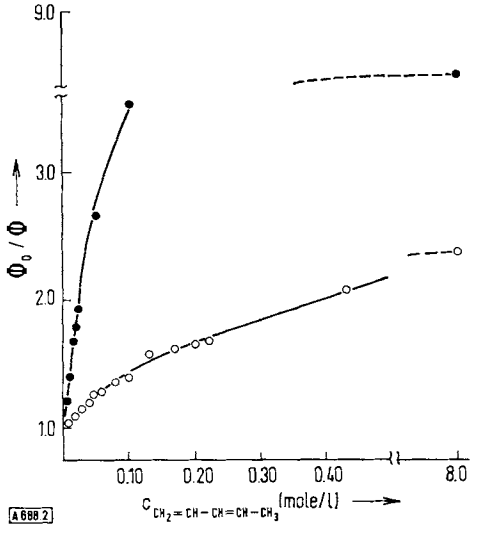
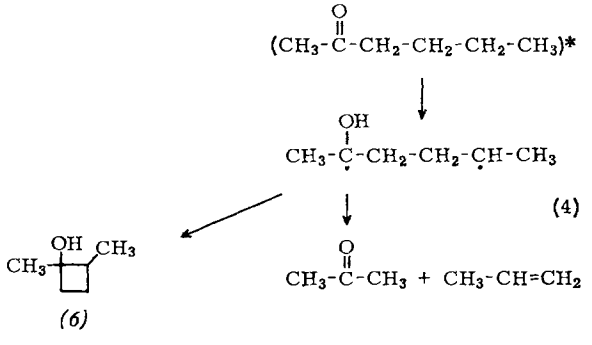


Fig. 2. Ratio (Φ_0/Φ) of quantum yield for disappearance of ketone with no quencher to quantum yield at given quencher concentrations *vs* concentration of quencher (1,3-pentadiene). Φ_0 = quantum yield for disappearance of 2-pentanone (●) and 2-hexanone (○) without quencher; Φ = quantum yield with 1,3-pentadiene as quencher.

Quenching data in Figure 2 show that, even at high pentadiene concentration (8 M), 2-hexanone still gives a significant amount of cleavage [see reaction (4)], and



that a lesser, but still significant portion of the 2-pentanone reaction is unquenched. The most obvious interpretation is that the phototransformations have sizable singlet-state contribution (see Table 1). These results underline the fact that singlet and triplet states

Table 1. Quantum yields (Φ) for disappearance of 2-pentanone and 2-hexanone and appearance of acetone. The 0.20 M ketone solution (with addition of 8 mole/l of 1,3-pentadiene) in hexane was irradiated at 3130 Å.

	−Ketone			+Acetone		
	Φ_0 [a]	Φ_s [b]	$\Phi_t = \Phi_0 - \Phi_s$	Φ_0 [a]	Φ_s [b]	$\Phi_t = \Phi_0 - \Phi_s$
2-Pentanone	0.44	0.05	0.39	0.30	0.04	0.26
2-Hexanone	0.50	0.21	0.29	0.44	0.18	0.26

[a] Quantum yield with no added 1,3-pentadiene. [b] Quantum yield with addition of 1,3-pentadiene.

having the same electronic configuration (*e.g.*, n → π* or π → π*) are likely to show similar chemical reactivities. The importance of the triplet state in photochemistry lies in its lifetime, which is often sufficiently long to allow photochemistry to compete with modes

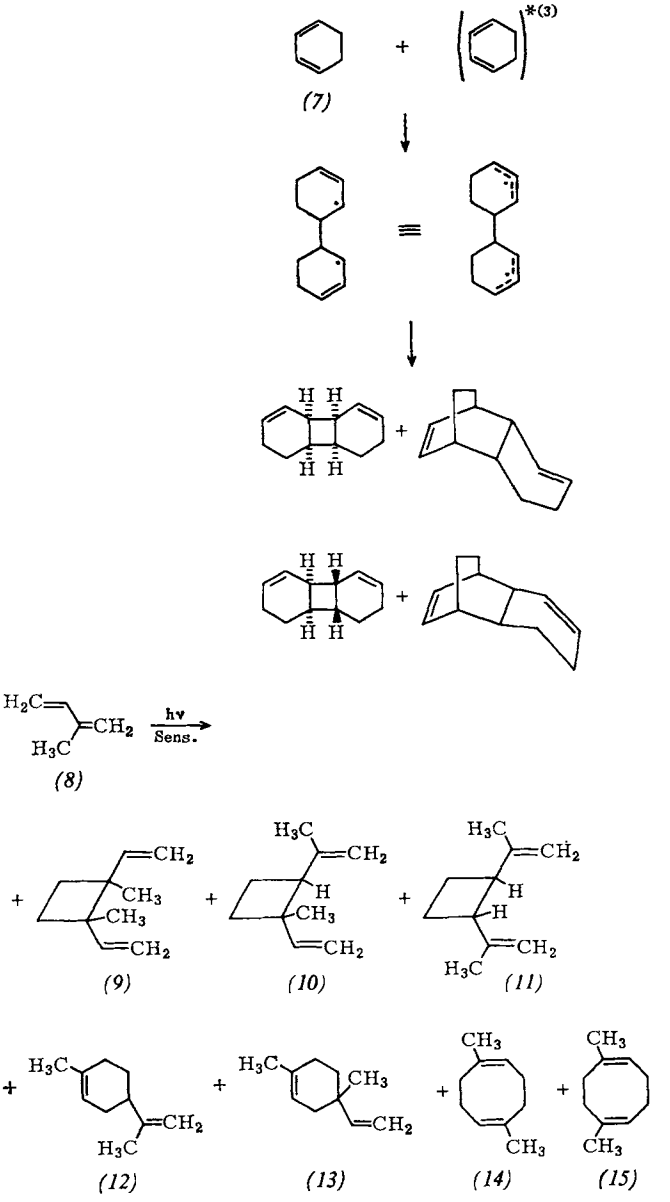


Table 2. Quantum yield (Φ) for formation of isoprene dimers (in 10 M solution).

Sensitizer	Intersystem Crossing Yield	Φ (9)–(15)
benzophenone	1.00	0.40
β-acetonaphthone	0.85	0.25
fluorenone	0.92	0.29

[13] *P. J. Wagner* and *G. S. Hammond*, J. Amer. chem. Soc. *87*, 4009 (1966).

[14] *P. J. Wagner* and *G. S. Hammond*, J. Amer. chem. Soc. *88*, 1245 (1966).

of physical deactivation, whereas corresponding excited singlets decay much more rapidly.

The reaction of conjugated dienes in their ground states with excited triplet states of dienes to produce dimers furnishes our second example of chemical quenching. Dimers are produced smoothly when the excited triplet states are produced *via* energy transfer from benzophenone or other appropriate triplet energy donors.

The dimerization of 1,3-butadiene [15], 1,3-pentadiene and isoprene [16], 1,3-cyclopentadiene [17], and 1,3-cyclohexadiene [18] has been studied in detail. Product mixtures, although complex, could be accounted for by assuming that the addition reaction occurs in two discrete steps, first formation of an intermediate biradical, and then cyclization of the biradical to form the final products. The process is illustrated below for the dimerization of 1,3-cyclohexadiene *(7)* (Table 2) [19] and isoprene *(8)*.

A plot of 1/(yield of dimer) *vs* 1/(diene concentration) in a set of matched samples subjected to equivalent irradiation is linear. Information concerning the lifetime of the diene triplet was obtained by use of azulene quenching. In the presence of a high concentration of diene, small amounts of azulene are not expected to influence the transfer of energy from sensitizer to diene. However, addition of slightly more than 10^{-2} M azulene is capable of quenching the dimerization by more than a factor of 1/2 (see Figure 3). Clearly the

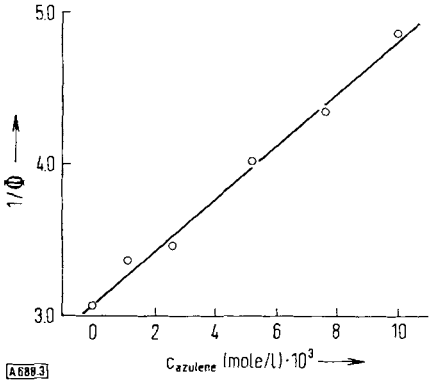


Fig. 3. Quantum yield for dimerization of isoprene in the presence of varying concentrations of azulene.

azulene is capable of quenching the diene triplet state. From the slope of the plot the ratio of the quenching constant to the rate constant for the attack of diene triplet on ground state molecules is found to be 1.2×10^3. This indicates that the rate constant for reaction must be about 2×10^6 liter mole^{-1} sec^{-1} or less; analysis of the dependence of quantum yield on diene concentration gives the ratio of the rate constant for the dimerization reaction to that for radiationless decay of triplets and places a lower limit of 2×10^{-8} sec on the triplet lifetime [20].

Attempts to extend these methods to cross additions of dienes have led, not unexpectedly, to complex mixtures of products. In addition, attempts to add dienes to olefins photochemically have met with little success [21]. It is important to note, however, that bond formation between the excited state and other molecules is an important quenching pathway, even for rather short-lived states, and that high yields of products are obtained from such interactions. This fact will be of importance later in discussions of other quenching phenomena [22] (see Section 4.1).

3. Triplet Energy Transfer in Solution

The transfer of triplet excitation energy from donors to acceptors is an efficient pathway for the quenching of excited states. The photochemical significance of the production of chemically reactive states of the acceptor was illustrated in the previous section. The energy transfer process will now be outlined for the photochemical *cis-trans* isomerization of the stilbenes [24–26].

The following generalized mechanism will prove adequate for discussion. Here S is sensitizer in a singlet, $S^{*(1)}$, or triplet, $S^{*(3)}$, excited state, with c = *cis* olefin, t = *trans* olefin, and T = olefin triplet states [27].

Three types of measurements have been made: quantum yields of sensitized *cis* → *trans* isomerization, measurements of the stationary state composition of the system following prolonged irradiation, and flash spectrophotometric measurement of the rates of decay of sensitizer triplets in the presence of the isomerizable olefins.

[15] *G. S. Hammond, N. J. Turro,* and *A. Fischer,* J. Amer. chem. Soc. *83,* 4674 (1961).

[16] *G. S. Hammond* and *R. S. H. Liu,* J. Amer. chem. Soc. *85,* 477 (1963).

[17] *J. Turro* and *G. S. Hammond,* J. Amer. chem. Soc. *84,* 2841 (1962).

[18] *D. Valentine, N. J. Turro,* and *G. S. Hammond,* J. Amer. chem. Soc. *86,* 5202 (1964).

[19] *R. S. H. Liu, N. J. Turro,* and *G. S. Hammond,* J. Amer. chem. Soc. *87,* 3406 (1965).

[20] This derives from the hypothesis that azulene will quench at (or probably less than) a diffusion controlled rate, estimated at 6×10^9 liters mole^{-1} sec^{-1}. The deactivation of a diene triplet state probably involves a process in which a twisted triplet reverts to a planar ground-state form. Energy transfer requiring a change in geometry of one of the reactions will, in all probability, be slower than the diffusion controlled rate (see Section 3). 1,3-Cyclohexadiene, which has recently been studied by *G. F. Vesley* in these laboratories, appears to be incapable of undergoing very extensive distortion in excited states. Consequently, the high susceptibility of cyclohexadiene to quenching by azulene confirms this viewpoint.

[21] *R. S. H. Liu* and *G. S. Hammond,* J. Amer. chem. Soc. *86,* 1892 (1964).

[22] This also seems to be at the heart of the most satisfying argument against a mechanism for energy transfer involving bonding of the sensitizer and substrate, rather than physical excitation transfer. See references [19] and [23].

[23] *G. O. Schenck* and *R. Steinmetz,* Bull. Soc. chim. Belgique *71,* 781 (1962).

[24] *G. S. Hammond et. al,* J. Amer. chem. Soc. *86,* 3197 (1964), and references cited therein.

[25] *K. A. Muszkat, D. Cegion,* and *E. Fischer,* J. Amer. chem. Soc. *89,* 4814 (1967).

[26] *G. S. Hammond,* Chem. and Ind. chem. (Kagaku to Kogyo) *18,* 1464 (1965).

[27] The mechanism implies that *cisoid, transoid,* and *nonplanar* triplet states of the olefin are indistinguishable or are rapidly interconverting species. Although data indicate that decay to *trans* stilbene becomes slightly more favorable at higher temperature, thus indicating a small barrier to interconversion between *transoid* and *nonplanar* (or *cisoid*) triplet states, no evidence forcing the abandonment of the common triplet hypothesis has been found with α-methyl- or α,α'-dimethyl-stilbenes.

$$S \xrightarrow{h\nu} S^{*(1)} \quad \text{excitation} \quad (5)$$

$$S^{*(1)} \xrightarrow{k_f} S\,(+h\nu) \quad \text{decay to ground state} \quad (6)$$

$$S^{*(1)} \xrightarrow{k_{ic}} S^{*(3)} \quad \text{intersystem crossing} \quad (7)$$

$$S^{*(3)} + c \xrightarrow{k_1} S + T \quad (8)$$

$$S^{*(3)} + t \xrightarrow{k_2} S + T \quad (9)$$

energy transfer to *cis* or *trans* olefin

$$T \xrightarrow{k_c} c \quad (10)$$

$$T \xrightarrow{k_t} t \quad (11)$$

decay of substrate triplet states to *cis* or *trans* ground states

Applying reactions (5)–(11) the stationary state measurements are expected to be determined by the product of two functions, an excitation ratio and a decay ratio [eq. (12)]. From this several predictions can be made regarding the behavior of the photo-

$$[cis]/[trans] = \underbrace{(k_2/k_1)}_{\text{excitation ratio}} \times \underbrace{(k_c/k_t)}_{\text{decay ratio}} \quad (12)$$

stationary state with respect to the sensitizer triplet energy. Barring steric effects, or other unanticipated difficulties, sensitizers with triplet energies greatly in excess of both *cis*- (57 kcal/mole) and *trans*-stilbene (50 kcal/mole)[28] should transfer energy at equal rates to both isomers, and, if the decay ratio is independent of sensitizer, as the mechanism implies, a high energy region of similar photostationary states would be obtained. As the sensitizer energy is varied between $\sim$ 57 and $\sim$ 50 kcal/mole a falloff in transfer rates to *cis* stilbene is expected, thus pumping the system to *cis* rich mixtures. As the sensitizer energy drops below 50 kcal/mole, it is expected that the stationary state will again level off, and with the deficiency made up as activation energy the excitation ratio would assume the value

$$k_2/k_1 = e^{-(57\,000-50\,000)/RT}$$

and lead to an extremely *cis* rich mixture.

Values obtained for the *cis*/*trans* photostationary state ratios of stilbene with varying sensitizer triplet energies agree with these predictions to only a limited extent (Fig. 4). In the high energy region a near "ideal" behavior is noted, but, although rate constants near that of a diffusion controlled reaction are noted, a slightly sloping line cannot be ignored.

Valentine has considered various factors as sources of possible inefficiency in exothermic energy transfer[29]. He concludes that energy transfer to the *cis* isomer is not diffusion controlled and becomes more rapid as the sensitizer energy increases. Steric factors may well be important and it should be noted that the structure of the sensitizer becomes less complex with higher energy.

[28] *D. F. Evans*, J. chem. Soc. (London) *1957*, 1351; from oxygen perturbed singlet-triplet spectrum

[29] *D. Valentine*, Ph.D. Thesis, California Institute of Technology, Pasadena, California, 1966.

In a closely related study, *Herkstroeter, Jones*, and *Hammond*[30] have shown evidence for considerable steric interference in energy transfer from benzophenone derivatives with bulky *ortho* substituents, with transfer rates to *cis*-stilbene being more strongly affected than those to *trans*-stilbene. Figure 4 shows

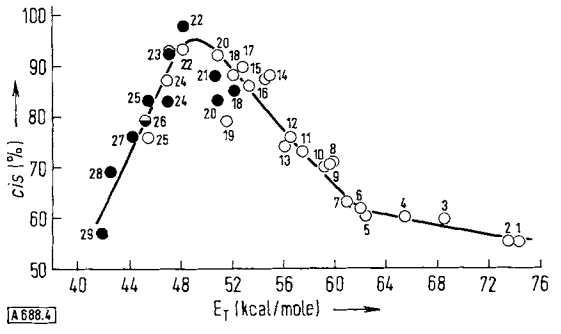
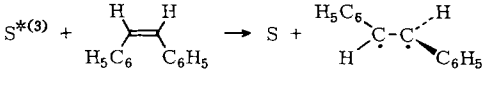


Fig. 4. Photostationary states for the stilbenes, measured (○) and predicted from k_q measurements (●). E_T = triplet energy of sensitizer. Sensitizers: 1, cyclopropyl phenyl ketone. 2, acetophenone. 3, benzophenone. 4, thioxanthone. 5, anthraquinone. 6, flavone. 7, Michler's ketone. 8, 2-naphthyl phenyl ketone. 9, 2-naphthaldehyde. 10, 2-acetonaphthone. 11, 1-naphthyl phenyl ketone. 12, chrysene. 13, 1-naphthaldehyde. 14, biacetyl. 15, 2,3-pentadione. 16, fluorenone. 17, fluoranthrene. 18, dibenz[*a,h*]anthracene. 19, duroquinone. 20. benzil. 21, dibenz[*a,c*]anthracene. 22. pyrene. 23, benz[*a*]anthracene. 24, benzanthrone. 25, 3-acetylpyrene. 26, acridine. 27, 9,10-dimethylbenz[*a*]anthracene. 28, anthracene. 19, benz[*cd*]pyrene.

that as the sensitizer triplet energy drops from $\sim$ 60 kcal/mole to $\sim$ 50 kcal/mole[31] the photostationary states indeed move to *cis*-rich mixtures. At low triplet energies, however, instead of leveling off, the curve again returns to *trans*-rich mixtures, clearly unexpected behavior. This result may be rationalized in two ways; either transfer of energy to *cis*-stilbene is decreasing less rapidly than predicted, or rates of transfer to *trans*-stilbene decrease more rapidly than predicted (or both).

In preliminary communications, *Hammond* and *Saltiel*[32] adopted the former approach. In particular, they suggested that *cis*-stilbene is converted directly to a *transoid* or nonplanar (shown above) excited triplet during energy transfer. The planar *trans* triplet is known to possess a lower energy than the planar *cis*



form and nonplanar triplets are predicted, on the basis of calculations[33,34], to have lower energy. Consequently, transitions from *cis*-stilbene to either the

[30] *W. G. Herkstroeter, L. B. Jones*, and *G. S. Hammond*, J. Amer. chem. Soc. *88*, 4777 (1966).

[31] The 3–5 kcal/mole excess energy needed to obtain efficient transfer is not well understood but is found in many systems, including ones more rapid than stilbene.

[32] *G. S. Hammond* and *J. Saltiel*, J. Amer. chem. Soc. *85*, 2516 (1963).

[33] *D. S. McClure*, Symposium on Photochemistry, California Institute of Technology, Pasadena (1966).

[34] *P. Borrell* and *H. H. Greenwood*, Proc. Roy. Soc. (London) *1967*, 453.

trans, planar, or twisted triplet states should require less energy than excitation to the planar *cis* triplet. This process is not observed spectroscopically (it would violate the Franck-Condon principle) and hence is termed a non-vertical transition or a non-vertical energy transfer. The key postulate is that energy transfer with non-vertical excitation of the acceptor may occur when vertical transitions are forbidden for energetic reasons. The phenomenon is expected to be an important factor only if one or both of the partners is a flexible molecule, *i.e.*, a molecule having significantly different equilibrium geometry in ground and excited states.

Confirmation of this point of view was later obtained by *Hammond* and *Herkstroeter*[35] in a study of these energy transfer rates by kinetic flash spectrophotometry[36]. A solution containing a sensitizer and one of the isomerizable substrates is flashed with a high-intensity light pulse. A significant fraction of the sensitizer molecules are promoted to excited triplet states by light absorption followed by intersystem crossing. Decay of sensitizer triplets is then monitored by absorption spectroscopy. Decay is accelerated in the presence of substances to which the sensitizers can transfer their excitation.

Measurement of the dependence of decay rates on the concentration of the quencher allows evaluation of bimolecular rate constants for the quenching reaction. A number of sensitizers were studied using the isomeric stilbenes and 1,2-diphenylpropenes (α-methyl-

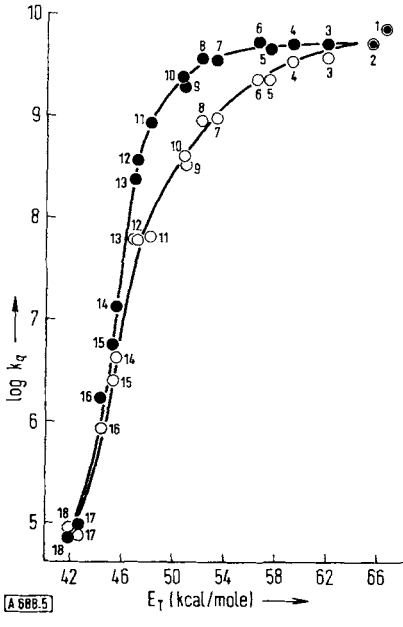


Fig. 5. Rate constants for quenching of sensitizers by *cis*- (○) and *trans*-stilbene (●). k_q = quenching constant. E_T = triplet energy of sensitizer. Sensitizers: 1, triphenylene. 2, thioxanthone. 3, phenanthrene. 4, 2-acetonaphthone. 5, 1-naphthyl phenyl ketone. 6, chrysene. 7, fluorene. 8, dibenz[*a,h*]anthracene. 9, benzil. 10, dibenz[*a,c*]anthracene. 11, pyrene. 12, benz[*a*]anthracene. 13, benzanthrone. 14, 3-acetylpyrene. 15, acridine. 16, 9,10-dimethylbenz[*a*]anthracene. 17, anthracene. 18, benz[*cd*]pyrene.

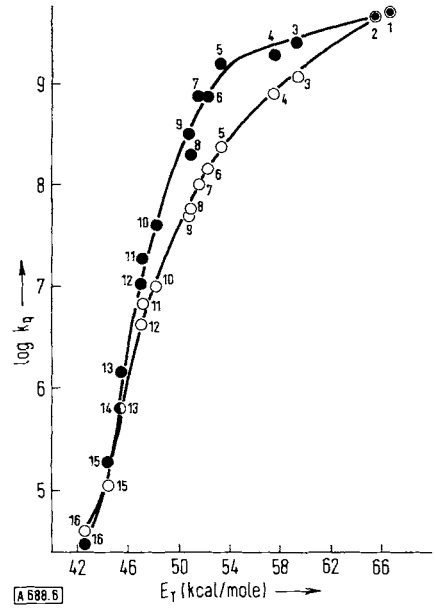


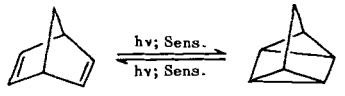
Fig. 6. Rate constants for quenching of sensitizers by *cis*- (○) and *trans*-1,2-diphenylpropene (●). k_q = quenching constant. E_T = triplet energy of sensitizers. Sensitizers: 1, triphenylene. 2, thioxanthone. 3, 2-acetonaphthone. 4, 1-naphthyl phenyl ketone. 5, fluorenone. 6, dibenz[*a,h*]anthracene. 7, duroquinone. 8, benzil. 9, dibenz[*a,c*]anthracene. 10, pyrene. 11, benz[*a*]anthracene. 12, benzanthrone. 13, 3-acetylpyrene. 14, acridine. 15, 9,10-dimethylbenz[*a*]anthracene. 16, anthracene.

stilbenes) as quenchers. Plots of the logarithms of the quenching constants (log k_q) against the triplet energies of the sensitizers (E_T) are shown in Figures 5 and 6. If the energy deficiency for the low energy sensitizers were made up as activation energy, the straight line portion of these figures should follow equation (13).

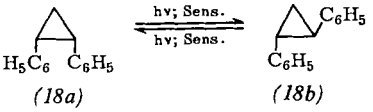
$$\Delta \log k_q/\Delta E_T = -1/(2.303\ RT) \qquad (13)$$

The slope predicted by this equation is observed for *trans*-stilbene. For *cis*-stilbene the rates of energy transfer fall off much more slowly than a classical mechanism would imply. The postulate of nonvertical energy transfer is fully consistent with these results. Nonvertical energy transfer is inferred to be operative with both isomers of α-methylstilbene, since slopes smaller than the classical value are observed with both isomers.

Several other systems have also been discussed in terms of nonvertical energy transfer, among these the photosensitized interconversion of norbornadiene *(16)* and quadricyclene *(17)*[37] and the *cis* → *trans* isomerization of 1,2-diphenylcyclopropane *(18)*[38].



(16) *(17)*



(18a) *(18b)*

[35] *W. G. Herkstroeter* and *G. S. Hammond*, J. Amer. chem. Soc. *88*, 4769 (1966).

[36] Described by *G. Porter* in *S. L. Fress*, *E. S. Lewis*, and *A. Weissburger*: Technique of Organic Chemistry. Interscience, New York 1965, Vol. VIII, Part II, p. 1055.

[37] *G. S. Hammond*, *N. J. Turro*, and *A. Fischer*, J. Amer. chem. Soc. *83*, 4674 (1961).

[38] *G. S. Hammond*, *P. Wyatt*, *C. D. DeBoer*, and *N. J. Turro*, J. Amer. chem. Soc. *86*, 2532 (1964).

The triplet excitation energy of quadricyclene has been measured as 92 kcal mole^{-1} [39] and the vertical excitation energy of diphenylcyclopropane is probably nearly as high as that of benzene. Consequently, it was felt that energy transfer, coupled with bond breakage, could be involved – another example of nonvertical energy transfer. However, recent investigations [40] have shown that the quadricyclene – norbornadiene interconversion involves strong interaction with excited singlet states of the sensitizers in many cases and that triplet energy transfer may not be involved at all.

In similar findings, *Cole* and *Hammond* [41] were able to induce asymmetry into *trans*-diphenylcyclopropane using optically active naphthalene derivatives as sensitizers; once again, singlet state interactions are responsible for the sensitized reaction [40]. Application of the concept of the nonvertical mechanism for triplet energy transfer of these systems was obviously an overenthusiastic application of the theory. However, re-examination of the original cases confirms the utility of the hypothesis in those examples. The scope of the phenomenon is essentially undefined at this time.

An examination of the revised Saltiel plot (Figure 4) shows several interesting features [42].

The chemical response of the system (*e.g.*, the [*cis*]/[*trans*] ratio) changes abruptly as the triplet energy of the donor passes through a point of the energy scale 2–3 kcal/mole higher than that of the acceptor. Note that with the stilbenes the curve begins a steep rise in the region of 60 kcal/mole and a descent in the region of 50 kcal/mole. If the notions of the previous sections concerning energy transfer rates are correct these points should be near the spectroscopic excitation energies of the triplet states of the stilbenes.

The photochemical dimerization of isoprene leads to the compounds *(9)–(15)*, which may be classed as cyclobutanes, cyclohexenes, and cyclooctadienes. Table 3 gives the product distribution with various sensitizers. Five of the compounds, *(9)*, *(10)*, *(11)*, *(14)*, and *(15)*, behave as a unit and their formation is competitive with the production of the two cyclohexenes *(12)* and *(13)*. These trends are shown in

Table 3. Composition of products from photosensitized dimerization of isoprene *(8)*.

No.	Sensitizer [a]	E_T (kcal/mole) [c]	Σ [d]	Distribution of dimers, %					
				(9)	*(10)*	*(11)*	*(12)*	*(13)*	*(14)* and *(15)*
1	Propiophenone	74.6	93	29.7	30.7	9.7	4.4	2.2	23.3
2	Cyclopropyl phenyl ketone	74.4	92	28.0	30.5	8.0	5.4	2.9	25.2
3	Acetophenone	73.6	92	29.0	29.7	8.2	4.8	3.0	25.4
4	1,3,5-Triacetylbenzene	73.3	92	29.5	29.6	6.7	4.6	3.7	25.8
5	Benzaldehyde	71.9	90	28.4	26.1	7.5	6.3	3.4	28.2
6	*o*-Dibenzoylbenzene	68.7	92	29.6	31.2	7.7	4.9	2.8	23.9
7	Benzophenone	68.5	93	29.0	30.1	9.0	4.7	2.1	25.2
8	Thioxanthone [b]	65.5	92	28.6	26.0	8.0	5.2	3.2	28.9
9	2-Acetylfluorene [b]	67.5	91	29.2	30.0	8.0	6.1	3.0	23.8
10	Anthraquinone [b]	62.4	91	28.6	29.5	7.5	6.2	3.2	25.1
11	Flavone [b]	62.0	90	26.2	28.3	5.8	7.8	3.9	28.1
12	Michlers' ketone [b]	61.0	91	27.8	29.5	7.7	5.8	3.3	25.8
13	Acetylbiphenyl	60.6	90	28.6	29.1	8.3	6.8	3.1	24.2
14	β-Naphthyl phenyl ketone	59.6	81	24.4	26.9	8.7	13.7	5.9	21.1
15	β-Acetonaphthone	59.3	81	26.3	27.2	9.3	14.5	4.5	18.2
16	β-Naphthaldehyde	59.5	76	22.1	21.7	6.3	15.9	7.5	26.5
17	α-Naphthyl phenyl ketone	57.5	75	23.2	25.0	5.4	18.7	6.9	20.9
18	α-Acetonaphthone	56.4	66	19.6	19.5	8.7	27.0	7.7	17.4
19	α-Naphthaldehyde	56.3	60	18.3	19.3	5.2	29.2	11.0	16.8
20	Biacetyl	54.9	53	18.8	19.8	4.1	34.6	12.7	10.0
21	2,3-Pentanedione	54.7	49	14.5	14.6	4.9	38.6	12.4	15.4
22	Benzil	53.7	45	13.5	12.4	3.5	38.5	16.9	15.3
23	Fluorenone	53.3	43	12.7	11.7	4.6	42.5	14.6	14.1
24	Dibenz[*a*,*h*]anthracene [b]	52.3	38	11.9	10.0	2.6	43.3	18.6	13.6
25	Pyrene [b]	38.7	36	12.1	12.4	2.1	45.4	18.4	9.5
26	Benzanthrone [b]	47	35	11.9	11.8	2.2	46.6	18.7	8.7
27	3-Acetylpyrene	45	51	13.5	15.5	6.4	36.6	12.3	15.7
28	9,10-Dimethyldibenz[*a*]anthracene [b]	44.4	58	17.5	19.0	5.0	30.3	12.1	16.1
29	Anthracene [b]	42.5	87	27.3	29.8	8.2	8.5	4.9	21.4
30	9,10-Dibromoanthracene [b]	40.2	94	30.8	33.8	7.9	3.6	2.1	21.8

[a] Sensitizer was 0.1 M in neat isoprene unless otherwise stated. [b] Saturated solution of sensitizer in isoprene.
[c] E_T = triplet energy of sensitizer. [d] Sum of percentages of *(9)*, *(10)*, *(11)*, *(14)*, and *(15)*.

4. Applications of Quenching Studies

Apart from yielding some understanding of triplet energy transfer and the behavior of excited states of various substrates, the studies of *cis-trans* isomerization and other modes of chemical deactivation of excited states have pointed to several useful applications.

[39] *P. S. Wei*, Ph.D. Dissertation, California Institute of Technology, Pasadena, California, 1968.

[40] *S. Murov*, *R. S. Cole*, and *G. S. Hammond*, J. Amer. chem. Soc. *90*, 2959 (1968); *S. Murov* and *G. S. Hammond*, J. physic. Chem. *72*, 3797 (1968).

[41] *G. S. Hammond* and *R. S. Cole*, J. Amer. chem. Soc. *87*, 3256 (1965).

[42] Reference [25] gives a Saltiel plot displaying much more fine structure than can be found in Figure 4. Many of the minima responsible for this structure have now been removed. It is found that the isomerization induced by several sensitizers, namely the quinones and the brominated sensitizers such as eosin, proceeds by mechanisms other than energy transfer. It is significant that many of these stationary states are closer to the composition at thermal equilibrium than that mixture induced by normal sensitization. A thorough analysis of this problem is incomplete.

Figure 7 where the sum of the yields of the cyclobutanes *(9)–(11)* and cyclooctadienes *(14)* and *(15)* is plotted against the triplet excitation energies of the sensitizers. The reasonable postulate is made that the

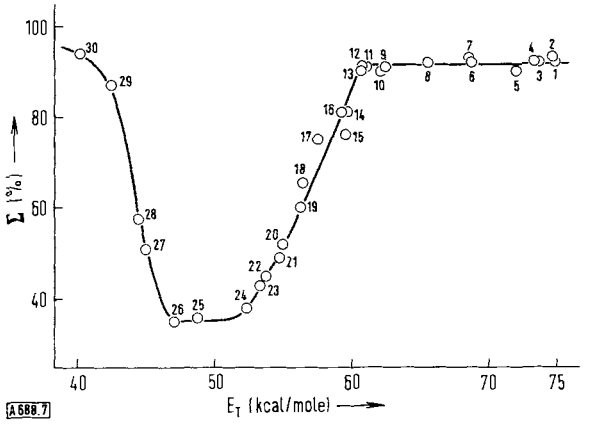
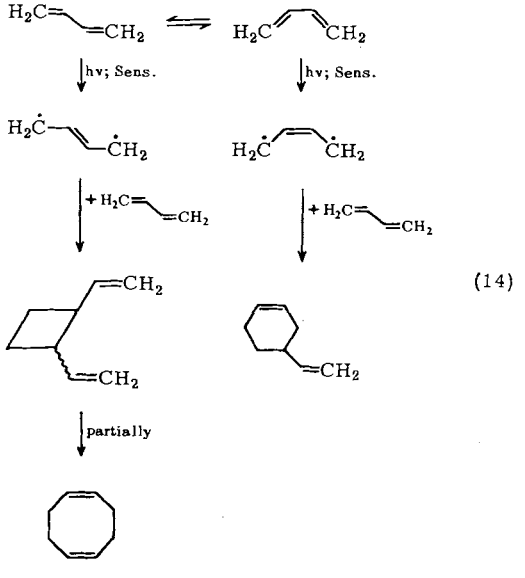


Fig. 7. Dependence of isoprene dimer composition on triplet energy of sensitizer. Σ = sum of *(9)*, *(10)*, *(11)*, *(14)*, and *(15)*. E_T = triplet energy of sensitizer. For sensitizers 1—30, see Table 3.

cyclohexenes are derived from interaction between *transoid* ground states and *cisoid* excited triplet states and that the cyclobutanes are derivable from *transoid* ground and excited states. The cyclooctadienes, while in principle derivable from an interaction between *cisoid* ground- and *cisoid* excited-states, may actually be formed by thermal rearrangement of the *cis*-dimethylcyclobutanes [see reaction (14)].



(14)

If the interpretation of the origin of the products is correct, the first break in the curve should correspond to a decrease in the rate of energy transfer to the *transoid* diene, predominantly present in solution (~ 95% in isoprene at room temperature). Thus the lowest triplet state of the *transoid* olefin was assigned an energy of approximately 60 kcal/mole. The next break in chemical response occurs at ~ 50 kcal/mole and represents a decrease in the rate of energy transfer to the *cisoid* form, whose triplet energy was assigned a value of 50 kcal/mole [43]. Using high pressures of O_2, *Evans* [44] has observed these highly forbidden $S_0 \rightarrow T$ absorptions and places the energy for isoprene triplet (a model *transoid* diene) at 60 kcal/mole and for cyclohexadiene (a model *cisoid* diene) an energy of 53 kcal/mole. Obviously, the method of chemical spectroscopy provides a useful adjunct to optical spectroscopy in this case.

4.2. Quantum Yields of Isomerization. A Method of Triplet Counting

In addition to placing nonvertical energy transfer on a firm experimental basis, the flash spectroscopic results of *Herkstroeter* also demonstrated the insensitivity of the olefin triplet decay ratio to the structure of the sensitizer. Using the triplet decay ratio and the ratio of rate constants for quenching by *cis* and *trans* species, values of expected photostationary state compositions were calculated and found to be in good agreement with experimental values.

Recognizing this fact, *Lamola* and *Hammond* [46] were able to show that the quantum yield for *cis* → *trans* isomerization of an olefin is a function of only three variables; the yield of sensitizer triplets produced by intersystem crossing, the efficiency of energy transfer to the olefin, and the triplet decay ratio of the olefin triplet. In addition, the work of *Herkstroeter* had made it clear that energy transfer rates could compete very favorably with triplet decay rates with all but the very lowest energy sensitizers. Thus, nearly 100% efficiency in triplet energy transfer could be effected in most cases even at relatively low acceptor concentrations.

Preliminary studies with benzophenone confirmed these ideas, since this sensitizer was already known to intersystem cross with unit efficiency (see Table 4).

Table 4. Quantum yields for *cis-trans* olefin isomerization by benzophenone (*c* = *cis*, *t* = *trans*).

Olefin	$\Phi_{c\rightarrow t}$	$\Phi_{t\rightarrow c}$	$\Phi_{c\rightarrow t} + \Phi_{t\rightarrow c}$
α-methylstilbene	0.55 ± 0.01	0.44 ± 0.01	0.99 ± 0.02
1,3-pentadiene	0.44 ± 0.01	0.55 ± 0.01	0.99 ± 0.02
1-phenylpropene	0.51	0.51	1.02

The quantum yield for sensitized, *cis* → *trans* isomerization in the absence of the *trans* isomer is given by Equation (15).

[43] Figure 7 is reminiscent of the Saltiel stilbene curve (Figure 4), and again would seem to demand the postulation of a nonvertical energy transfer. Flash kinetic studies which confirm this feeling even for the relatively rigid 1,3-cyclohexadiene, have been performed by *G. F. Vesley*. However, recent work by *Liu* and *Edman* [45] shows that sensitization with low-energy sensitizers sometimes involves energy transfer from more highly excited triplet states. This phenomenon may have made some contribution to data shown in Figure 7.

[44] *D. F. Evans*, J. chem. Soc. (London), *1960*, 1735.

[45] *R. S. H. Liu* and *J. R. Edman*, J. Amer. chem. Soc. *90*, 213 (1968).

[46] *A. A. Lamola* and *G. S. Hammond*, J. chem. Physics *43*, 2129 (1965).

$$\Phi_{c\to t} = \left(\frac{k_{ic}}{k_f + k_{ic}}\right)\left(\frac{k_1[c]}{k_1[c] + k_d}\right)\left(\frac{k_t}{k_t + k_c}\right) \quad (15)$$

k_{ic} = rate constant for intersystem crossing by the sensitizer.

k_f = rate constant for fluorescence by the sensitizer.

k_1 = rate constant for triplet energy transfer to the *cis* substrate.

k_t, k_c = rate constants for decay of substrate triplets to *trans* and *cis* ground states.

k_d = rate constant for unimolecular decay of sensitizer triplets to the ground state.

If, as with benzophenone, energy transfer is 100% efficient [47], the intersystem crossing yield (Φ_{ic}) of the sensitizer is obtained by merely summing the quantum yields of isomerization.

$$\Phi_{c\to t} = \Phi_{ic}\, k_t/(k_t + k_c) \quad (16)$$

$$\Phi_{t\to c} = \Phi_{ic}\, k_c/(k_t + k_c) \quad (17)$$

$$\Phi_{c\to t} + \Phi_{t\to c} = \Phi_{i.c.} \quad (18)$$

The intersystem crossing yield of a sensitizer is a matter of some practical interest to a photochemist. This measurement, coupled with measurements of fluorescence and phosphorescence yields, allows a complete detailing of the extent of nonradiative decay [1,48,49] from both the singlet and triplet manifolds.

Hammond and *Lamola*, exploiting the method outlined above, were able to develop a simple and accurate method for the measurement of intersystem crossing efficiencies in solution at room temperature. Unfortunately, the highly variable rates of this reaction could not be rationalized in terms of molecular structure, or other obvious parameters. The data seemed to demonstrate the occurrence of some nonradiative decay from the excited singlet state in several systems (notably naphthalene and derivatives, see Section 4.3), in contradiction to the implication of theory [48].

4.3. Complications in the Triplet Counting Scheme; Complex Formation in the Excited State

The necessity for the postulation of nonradiative decay from the first excited-singlet state of aromatic hydrocarbons, as suggested by the data obtained by *Lamola*, has found strong disagreement in the literature. Deuteration has no effect on singlet lifetimes, indicating a lack of nonradiative decay from that state [47]. Furthermore, *Lamola*'s unpublished value for benzene intersystem crossing, 0.24, disagreed sharply with values estimated by *Lim* (0.80 [50]) and *Noyes* and *Ishikawa* (0.78 [51])

The inherent simplicity and usefulness of the method made an investigation of these anomalies desirable. 1,3-Pentadiene, the most widely employed triplet counter because of its high singlet energy and low triplet energy (> 100 and < 60 kcal/mole, respectively), formed the focus of this study. The finding that conjugated dienes are capable of quenching the fluorescence of aromatic hydrocarbons revealed one important source of error in triplet counting experiments [52]. It is further observed that products characteristic of the diene triplet photoreactions do not arise from the singlet quenching.

Figures 8, 9, and 10 show the quenching of naphthalene fluorescence by *cis*-1,3-pentadiene, a Stern-Volmer treatment of the quenching data, and the decreasing *cis* → *trans* quantum yield as the concentration of *cis*-1,3-pentadiene is increased. Data of this type have allowed corrections to be applied to the earlier results obtained by *Lamola* for several aromatic hydrocarbons, in particular naphthalene and derivatives. These data agree closely with those obtained by *Wilkinson* and co-workers [53, 54] who employed a different

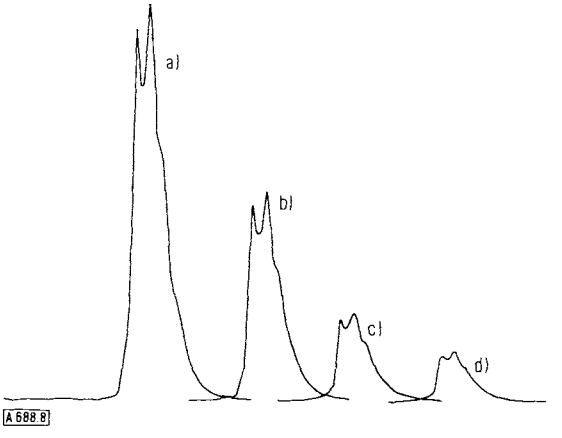


Fig. 8. Naphthalene fluorescence in the presence of a) 0.0, b) 0.1, c) 0.4, d) 0.8 mole/l of *cis*-1,3-pentadiene (relative).

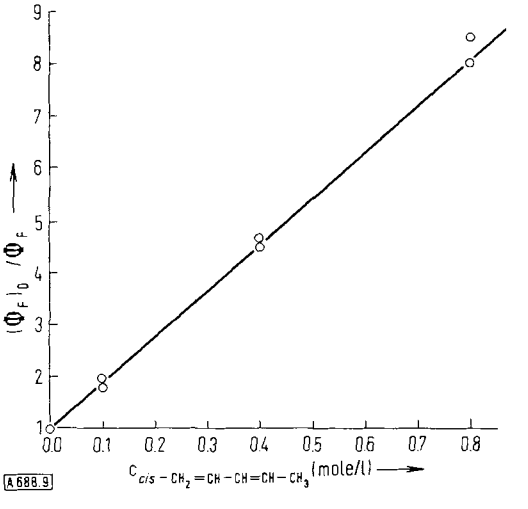


Fig. 9. Stern-Volmer treatment of naphthalene quenching by *cis*-1,3-pentadiene.

[47] This is most easily demonstrated by showing that $\Phi_{c\to t}$ is invariant with increasing olefin concentration.

[48] See, for example, *J. D. Laposa, E. C. Lim*, and *R. E. Kellogg*, J. chem. Physics *42*, 3025 (1965).

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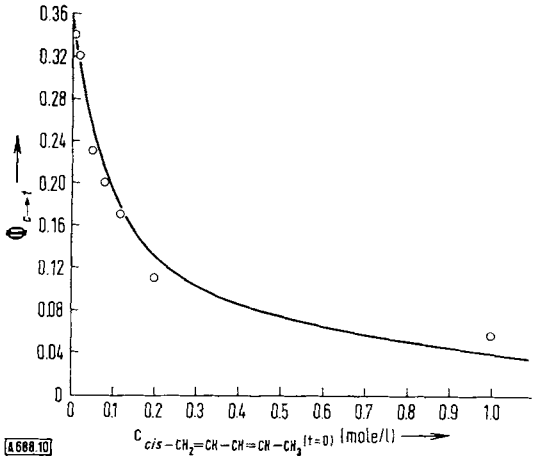


Fig. 10. The *cis-trans* isomerization quantum yield for 1,3-pentadiene sensitized by naphthalene as a function of initial *cis*-1,3-pentadiene concentration.

method of triplet counting. Substantial support is found for the conclusion that, in the absence of specific quenchers, nonradiative decay from the first excited-singlet state of aromatic hydrocarbons is unimportant.

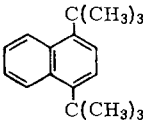
The mechanism of this singlet quenching process is a subject of continuing study. Quenching by conjugated dienes is ineffective in inducing photochemical transformations typical of the diene triplet state. In addition, careful searches have revealed no evidence for products which characteristically arise from excited singlet states of the dienes. In particular, no trace of cyclobutene is produced from 1,3-pentadiene, hexatriene is not formed from cyclohexadiene, nor are any of the several rearrangement products of myrcene found. All processes are known to proceed from the excited singlet following direct irradiation. Adducts are sometimes formed from the aromatic compound and the diene but the quantum yields of such products are far too small to account for more than a small part of the quenching. "Chemical quenching" and transfer of singlet energy are thus eliminated as mechanistic possibilities.

Table 5. Quenching of fluorescence of aromatic hydrocarbons by dienes.

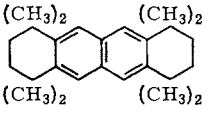
Aromatic	Diene	$c^1/_2$ [a] (mmole/l)	$k_q \times 10^{-9}$ [b] ($l mole^{-1} sec^{-1}$)
Naphthalene	2,5-Dimethyl-2,4-hexadiene	2.63	3.96
Naphthalene	1,3-Cyclohexadiene	3.95	2.50
Naphthalene	4-Methyl-1,3-pentadiene	8.76	1.20
Naphthalene	*trans*-2-*trans*-4-Hexadiene	16.8	0.62
Naphthalene	*trans*-2-*cis*-4-Hexadiene	20.5	0.51
Naphthalene	*cis*-2-*cis*-4-Hexadiene	45.3	0.23
Naphthalene	3-Methylenecyclohexene	61.2	0.17
Naphthalene	*trans*-2-Methyl-1,3-pentadiene	94.2	0.11
Naphthalene	*trans*-1,3-Pentadiene	95.0	0.11
Naphthalene	*cis*-1,3-Pentadiene	113	0.092
Naphthalene	2,3-Dimethyl-1,3-butadiene	680	0.015
1-Methyl-naphthalene	1,3-Cyclohexadiene	12	1.1
Anthracene	1,3-Cyclohexadiene	67	2.96

[a] $c^1/_2$ is the concentration required to quench half the fluorescence.
[b] Calculated assuming τ_S for naphthalene = 77 nanoseconds, as estimated by oxygen quenching.

For the most part, this quenching must be described as a catalysis of the nonradiative decay of the quenchers. The rates observed for naphthalene quenching are shown in Table 5 and do not exceed those expected in diffusion controlled reactions. Results also show [55] that addition of alkyl substituents to naphthalene, as in *(19)* and *(20)*, reduces sensitivity to quenching by 1,3-pentadiene [*(19)*, $k_q = 13 \times 10^6$ l mole^{-1} sec^{-1}; *(20)*, $k_q = 8.7 \times 10^6$ l mole^{-1} sec^{-1}; naphthalene, 140×10^6 l mole^{-1} sec^{-1}].



(19)



(20)

We tentatively conclude that quenching not only requires that the two molecules be in contact but that the contact be sufficiently intimate to be subject to steric hindrance.

A model designed to account for the reactivity relationships has been formulated and assumes that, within a complex formed between excited singlet state quenchee (A) and ground state quencher diene (Q), a small amount of the electronic excitation is delocalized to the quencher.

$$A^*Q \leftrightarrow A \cdot Q^*$$

Since the singlet excitation energies of the dienes are considerably greater than those of the quenchers, the contribution from the second configuration is expected to be small. However, the importance of the A · · Q* structure arises primarily from its effect on the rate of internal conversion, not from its contribution to the binding energy of the complex. This suggests that the weak coupling may allow the excited complex to borrow some of the very rapid, nonradiative decay characteristics of the diene.

This work was supported by the National Science Foundation and the Directorate of Chemical Sciences, Air Force Office of Scientific Research, under Contract No. AF 49 (638)-1479.

Received: March 26, 1968 [A 688 IE]
German version: Angew. Chem. *81*, 279 (1969)

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Organometal Sulfides as Ligands in Pentacarbonylchromium(0) Complexes[**]

By *H. Schumann, O. Stelzer,* and *W. Gick*[*]

Organo-germanium, -tin, and -lead sulfides are astonishingly stable compounds, a fact which is explained in many cases as a result of the participation of the sulfur's lone pair electrons in the metal-sulfur bond in terms of (p → d) π-type multiple bonding[1]. Accordingly, trimethylgermyl- and trimethylstannyl-sulfides ought to exhibit a different complex chemical behavior from dialkyl- or diaryl-sulfides, which occur in a number of complexes as σ-donors[2]. Results of previous investigations[3] showed that in the reactions of transition metal carbonyls and organotin sulfides the tin-sulfur bonds are cleaved; stable complexes with organotin sulfides as ligands could not be prepared.

We have now been able to synthesize for the first time stable carbonylchromium(0) complexes with organometal sulfides as ligands by means of the reaction of bis(trimethyl-germyl)-, bis(trimethylstannyl)-, phenyltrimethylgermyl-, or phenyltrimethylstannyl sulfide with hexacarbonylchromium under UV irradiation in tetrahydrofuran (THF) at room temperature[4].

$$(CH_3)_3M\text{-}S\text{-}M(CH_3)_3 + Cr(CO)_6 \xrightarrow{h\nu} \begin{matrix}(CH_3)_3M\\ \diagdown\\ \quad S\text{-}Cr(CO)_5\\ \diagup\\ (CH_3)_3M\end{matrix}\ \textit{(1)} + CO$$

$$(CH_3)_3M\text{-}SC_6H_5 + Cr(CO)_6 \xrightarrow{h\nu} \begin{matrix}(CH_3)_3M\\ \diagdown\\ \quad S\text{-}Cr(CO)_5\\ \diagup\\ C_6H_5\end{matrix}\ \textit{(2)} + CO$$

(M = Ge, Sn)

The choice of solvent in this reaction is particularly important. If pentane is used as solvent instead of THF then the rate of reaction is slowed down considerably; this may be due, on the one hand, to the difference in solubility of the hexacarbonylchromium in these solvents and on the other to the part played by THF in the course of the reaction[5]. Compounds *(1)* and *(2)* are sensitive to atmospheric oxygen and to water; they are essentially less stable thermally than are the corresponding organometal-phosphine complexes[6].

As a result of removal of the degeneracy of the E_1 vibration under the influence of the asymmetrical ligands[7], the IR spectra show four CO-stretching vibrations for the $Cr(CO)_5$ skeleton whose positions are only slightly dependent on the complex partner. Further, there is only a trivial change in the frequencies of the CrS- and MS-stretching vibrations within the series. In the case of all four compounds an absorption band, corresponding to their yellow color, is to be observed in the region of 250–800 nm which is shifted into the long-wave region on going from M = Ge to M = Sn.

Cpd. M =	Decomp. pt. (°C)	νCO (cm^{-1})	δCH₃ [a] (Hz)	νCrS (cm^{-1})	νMS (cm^{-1})	νMS [b] (cm^{-1})	λ (nm)
(1a), Ge	70	2066 1984 1930 1912	−49	449	383 360	414 366	420 ε = 895
(1b), Sn	95	2087 2004 1956 1937	−45	447	325 348	366 321	435 ε = 816
(2a), Ge	45	2079 1996 1949 1930	−46	446	367	374	413 ε = 774
(2b), Sn	45	2074 1996 1949 1926	−44	451	342	342	417 ε = 1200

[a] 5% solution in $CDCl_3$, TMS as external standard.
[b] In the free organometal sulfide.

From the remarkable stability of *(1)* and *(2)* it follows that the blocking of a lone electron pair of the sulfur in organometal sulfides by complex formation does not necessarily lead to the cleavage of the metal-sulfur bond and that consequently organogermanium- and organotin-sulfides can occur as σ-donors in transition metal complexes in the same way as do dialkyl- or diaryl sulfides.

Experimental:

12 mmoles of organometal sulfide and 12 mmoles (2.6 g) of hexacarbonylchromium are dissolved in 50 ml of THF (previously dried over CaH_2) in an irradiation apparatus. The solution is stirred with a magnetic stirrer and irradiated with a high pressure mercury vapor lamp[4]. A slightly reduced pressure in the gasometer that is used for the measurement of the CO evolved favors the reaction, which is complete after a period of 2 h irradiation; the solution turns orange yellow in color. The solvent is removed under vacuum and the reaction products (in all cases a pale yellow powder; yields quantitative) can be recrystallized from pentane at −40 °C. The products can be further purified by sublimation at 30–75 °C/10^{-5} torr.

Received: September 3, 1968 [Z 913 IE]
German version: Angew. Chem. *81*, 256 (1969)

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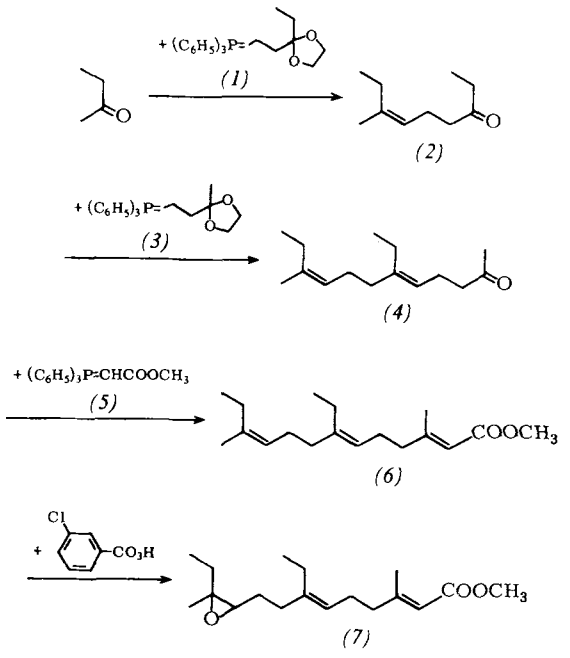
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Synthesis of the (±)-Juvenile Hormone of the Giant Silkworm Moth *Hyalophora cecropia* L.

By *H. Schulz* and *I. Sprung*[*]

The *H. cecropia* juvenile hormone was identified by *Röller et al.*[1,2] as methyl *cis*-10,11-epoxy-7-ethyl-3,11-dimethyl-*trans*-2,*trans*-6-tridecadienoate *(7)*. Since then several syntheses of this insect hormone have been published[3–6]. *Corey*[4], *Johnson*[6], and *Zurflüh*[8] report highly stereospecific reactions, of which the synthesis by *Zurflüh et al.* leads only to 6-ethyl-10-methyl-*trans*-5,*cis*-9-dien-2-one *(4)*. These very elegant procedures, however, require a very considerable number of steps.

We now describe a new synthesis based on the construction scheme $C_4 + C_6 + C_5 + C_2$.



Our synthesis involves three steps for building the C_{17} skeleton, permits the preparation of all eight possible pairs of isomers, and allows variations to be introduced at C-3, C-7, and C-11 of the juvenile hormone. Stereospecific syntheses, on the other hand, do not, of course, allow preparation of the other isomer pairs, nor can other substituents be introduced at all the positions named above.

Our synthesis starts from simple materials. From γ-butyrolactone and ethyl acetate or propionate are prepared two α-acyl-γ-butyrolactones which give the ω-bromo ketones on ketone fission in the presence of hydrogen bromide. The carbonyl group is then protected as ethylene ketal, and the bromo ketals are treated with triphenylphosphine, which gives the triphenylphosphonium salts needed for the first two carbonyl-olefinations.

The phosphorane *(1)* is obtained from the phosphonium bromide and sodamide in liquid ammonia and gives a 69% yield in the Wittig reaction with 2-butanone. According to gas-chromatographic analysis the resulting mixture of *cis-trans*-isomers of the ethylene ketal contains 63% of the *cis*- and 37% of the *trans*-compound; 42% of the *cis*-C_{10} ketal was obtained by distillation through a 100-cm Teflon spinning band column and on hydrolysis with 3 N perchloric acid in tetrahydrofuran and subsequent column chromatography on silica afforded the unsaturated ketone *(2)* in 96% yield.

Treating this ketone with the phosphorane *(3)* [7] in a second Wittig reaction led to a 74% yield of the mixture of C_{15} ethylene ketal isomers, containing equal parts of the *cis-cis*- and the *trans-cis*-compound. Distillation separated 29% of the *trans-cis*-isomer and this was hydrolyzed by perchloric acid in water-tetrahydrofuran to the ketone [8], which was isolated in 92% yield on column chromatography on silica.

On treating the phosphorane *(5)* with the ketone *(4)* in a bomb tube at 175 °C for 17 h [9] under nitrogen we obtained a 76% yield of the C_{17} methyl ester which contained 54% of the desired *trans-trans-cis*-compound *(6)*; 52% [calculated on the isomer mixture *(6)*] of this isomer was isolated on distillation through a spinning band column. Finally the C_{17} ester *(6)* was epoxidized by *m*-chloroperbenzoic acid in ethylene dichloride at 0 °C, whereafter chromatography afforded the juvenile hormone in 43% yield.

The intermediates *(2)*, *(4)*, and *(6)*, and the compound *(7)*, gave correct elemental analyses; their structures were confirmed by IR and NMR spectra and their purity was ascertained by gas chromatography. The structure of *(7)* was also confirmed by its mass spectrum.

In a biological test on *Tenebrio molitor* [10] our material showed activity comparable with that of a sample obtained from *Röller et al.* [11].

Received: January 2, 1969; revised: February 5, 1969 [Z 942 IE]
German version: Angew. Chem. *81*, 258 (1969)

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A New Mode of Formation of Sulfur-Containing Heterocycles

By *M. G. Voronkov* and *A. N. Pereferkovich* [*]

Aryl halogenoalkanes can react with sulfur at 200–250 °C to give various types of sulfur-containing heterocycles [1]. We have now found that bromo and iodo derivatives of aromatic hydrocarbons also react with sulfur at temperatures above 180 °C to form primarily diaryl polysulfides:

$$2\,ArX + n\,S \xrightarrow[-X_2]{} Ar\,S_n\,Ar \quad (X = Br, I;\ n \geqslant 2)$$

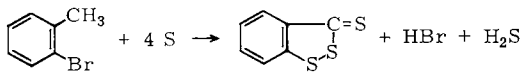
The di- and trisulfides isolated by vacuum distillation are probably partially formed by decomposition of the higher polysulfides.

In a few cases copper(II) sulfide, which does not react with aryl halides under the reaction conditions, was used for fixation of the liberated halogen. The presence of free halogen or SBr_2 lowers the yield of diaryl polysulfides.

A mixture of 20.4 g (0.1 mole) of iodobenzene, 1.6 g (0.05 g-atom) of sulfur, and 4.8 g (≈ 0.05 mole) of CuS is boiled (190–200 °C) and stirred for 25 h. The reaction mixture is then diluted with benzene, filtered, and the residue left after removal of the solvent is distilled under vacuum. In addition to 7.5 g of unchanged iodobenzene, 5.0 g of an oily product is obtained which crystallizes out on standing and has a thiophenol-like smell. After recrystallization from *n*-hexane the yield of diphenyl disulfide (m.p. 60–61 °C) is 3.0 g (44% yield referred to reacted iodobenzene).

When a mixture of *p*-bromotoluene (17.1 g, 0.1 mole), sulfur (1.6 g, 0.05 g-atom), and CuS (4.8 g, ≈ 0.05 mole) is boiled for 25 h, di-*p*-tolyl disulfide (m.p. 44–45 °C; lit. [2] m.p. 45 to 48 °C) is obtained. If double the amount of sulfur is added, di-*p*-tolyl trisulfide (m.p. 80–81 °C; lit. [2] m.p. 82 °C) can be isolated from the reaction product.

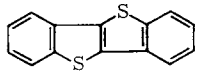
Sulfuration of *o*-bromotoluene (without CuS) leads to the formation of 3*H*-benzo[*c*]-[1,2]-dithiole-3-thione *(1)*. The



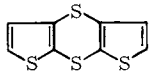
(1)

latter is prepared by boiling a solution of *o*-bromotoluene (17.1 g, 0.1 mole) in *o*-dichlorobenzene (30 ml) with sulfur (32.0 g, 1 g-atom) in the presence of dimorpholine disulfide (0.01 g) for 30 hours. The sulfur that precipitates out when the reaction mixture is cooled is filtered off and the residue left after removal of solvent from the filtrate is distilled under vacuum. An oil, which crystallizes out on standing and has a boiling range 170–210 °C/2 torr, distills over. This is mixed with dimethylformamide and then filtered; the red crystals [2.7 g (15%) of crude substance, m.p. 88–89 °C] obtained after removal of dimethylformamide from the filtrate are then washed with ether. After purification, the crystals melt at 95–96 °C (lit.[2] m.p. 95–98 °C). The intermediate formation of di-*o*-tolyl polysulfides was verified by thin layer chromatography and confirmed by sulfuration of di-*o*-tolyl disulfide, which afforded *(1)* in 7% yield.

Dropwise addition of *o*-bromotoluene to a boiling (230 °C) mixture of sulfur and *o*-chlorobenzene leads to the formation of *(1)* (1%) and of dibenzothieno[3,2-*b*]thiophene *(2)*, which occurs on pyrolysis of *(1)*[3]. After heating compound *(1)* for 5 hours at 260–280 °C, the presence of *(2)* and sulfur could be detected by thin layer chromatography.



(2)



(3)

2-Iodothiophene also reacts with sulfur; however, in this case di-2-thienyl sulfide is apparently formed as primary product alongside the hitherto unknown dithieno[2,3-*b*,3′,2′-*e*]-[1,4]-dithiine *(3)* (m.p. 88–89 °C, *m/e* 228).

Received: January 27, 1969 [Z 940 IE]
German version: Angew. Chem. *81*, 257 (1969)

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[1] *M. G. Voronkov*, *V. E. Udre*, and *T. V. Lapina*, 2nd Organic Sulphur Symposium, Groningen 1966, Abstract of Papers, p. 38; Chim. geterocikličeskich Soedinenij *1965*, 683; *1966*, 527; *1967*, 633, 1003; *1968*, 43, 49.

[2] *E. E. Reid*: Organic Chemistry of Bivalent Sulfur, Vol. III, Chemical Publishing Co, New York 1960, pp. 100, 398, 412.

[3] *B. Böttcher* and *A. Lüttringhaus*, Liebigs Ann. Chem. *557*, 89 (1947).

Nitroacetylenes[1]

By *V. Jäger* and *H. G. Viehe*[*]

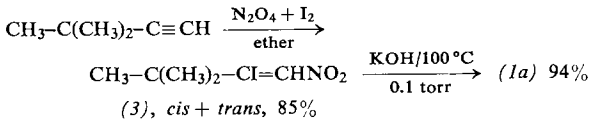
The synthesis of *tert*-butylnitroacetylene [3,3-dimethyl-1-nitro-1-butyne] *(1a)* described in this communication affords, to the best of our knowledge, and contrary to earlier claims[2], the first representative of this class of compounds. In nitroacetylenes, the triple bond is polarized in the opposite sense to that in the reactive ynamines *(2)*[3]. Compound *(1a)* is a greenish-yellow, volatile, lachrimatory liquid having m.p. ~ −3 °C and b.p. ~ 55 °C/15 torr.



(1) *(2)*

(1a), R = $C(CH_3)_3$

The nitroacetylenes *(1)* promise to be highly reactive as electrophiles, and also as dienophiles and dipolarophiles. Moreover, the combination of an electronegative sp-hybridized carbon with a nitro group suggests such high ground state energy[3] that the thermal stability of these compounds should be limited. Nevertheless, *(1a)* is readily isolable, and can be detonated neither by shock, nor by heating, nor by a glowing wire. Pure *(1a)*, which has a half-life of 2–3 days at room temperature, was synthesized in the gas phase by elimination of hydrogen iodide from 2-iodo-3,3-dimethyl-1-nitro-1-butene *(3)* over solid KOH.

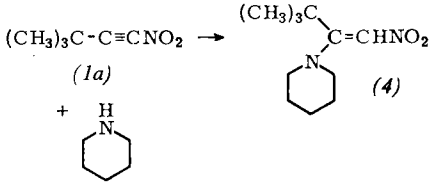


(3), *cis* + *trans*, 85% *(1a)* 94%

Like the main isomer *(3a)*, the mixture of isomers of *(3)* (15:85) obtained in the above reaction (analogous to the case in ref.[4]) gives analytically pure *tert*-butylnitroacetylene *(1a)*[5]. Its IR spectrum is highly characteristic: The strongest bands correspond to the nitro group (ν_{as} = 1512 cm^{-1}, ν_{sym} = 1350 cm^{-1}) and the CC triple bond (ν = 2231 cm^{-1} with a shoulder at 2270 cm^{-1}). NMR signals appear at δ = 1.34 and 0.75 ppm in CCl_4 and in C_6D_6, respectively (TMS as internal reference).

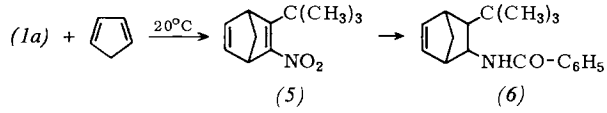
Chemical evidence for the structure *(1a)* comes from the smooth reduction by $LiAlH_4$ in ether to the known compound 3,3-dimethylbutylamine[6].

In spite of its relatively high stability in the pure state, *(1a)* reacts readily with bases; primary and secondary amines add rapidly in dilute solution to give nitro-enamines, and triethylamine forms products of higher molecular weight. In the absence of a solvent this reaction proceeds explosively, the mixture bursting into flames. Piperidine in ether converts *(1a)* into a single isomer of the monoadduct *(4)* [orange-yellow crystals having m.p. 59.5–60 °C] in an exothermic reaction. The latter compound can be reduced by $LiAlH_4$ in ether to the amine, which was isolated as benzamide.



(1a) *(4)*

The exceptional reactivity of *(1a)* as a dienophile – compared to ethyl *tert*-butylacetylenecarboxylate and the corresponding nitrile – is apparent in its reaction with cyclopentadiene. Whereas the other two *tert*-butylacetylene derivatives do not react even over a period of several days, according to gas-chromatographic analysis, *(1a)* yields the norbornadiene derivative *(5)* (yellow liquid, b.p. ~ 50 °C/0.1 torr) quantitatively within two hours. Reduction with $LiAlH_4$ and benzoylation gives the benzamide derivative *(6)*.



(5) *(6)*

On repetition of earlier attempts to synthesize nitroacetylenes[2] bearing ethyl, propyl, and phenyl substituents by removal of HBr from α-bromonitroolefins with primary and secondary amines, we obtained dark, decomposable oils in agreement with the literature. Unlike *(1a)*, however, these products showed no C≡C absorption in their IR spectra and at least four components were detected by thin-layer chromatography. Although elemental analysis gave approxi-

mately fitting results for nitrogen, those found for the other elements deviated strongly from the correct values. Further, our experience with *(1a)* shows that primary or secondary amines cannot be used for the preparation of nitroacetylenes, since they add immediately to the triple bond.

Spectroscopic evidence for the existence of nitroacetylenes having R = C_6H_5 and *n*-C_4H_9 was obtained from attempts at their synthesis.

3,3-Dimethyl-1-nitro-1-butyne (1a)

Compound *(3)* (5.0 g) is distilled slowly (*ca.* 1 g/h), in a manner similar to that employed in a bulb-tube distillation, under a pressure of 0.1 torr through a glass tube (length 30 cm, i.d. 1.5 cm) containing KOH and heated to 100 °C. The contents of the receiver, which is cooled with acetone/Dry Ice, are dissolved in *n*-pentane. The solution is dried over Na_2SO_4 and the solvent is drawn off, leaving 2.35 g (94%) of a pale yellowish green, volatile, strongly lachrimatory liquid having m.p. ~ −3 °C and b.p. ~ 55 °C/15 torr. The NMR spectrum shows a signal at 1.34 (CCl_4) and 0.75 ppm (C_6D_6), and the IR spectrum contains bands at 2967, 2874, 2270, 2231, 1512, 1368, 1350 cm^{-1}. UV spectrum: $\lambda_{max}^{n\text{-hexane}}$ = 238 nm (log ε = 3.9).

Received: December 5, 1968 [Z 944 IE]
German version: Angew. Chem. *81*, 259 (1969)
Publication delayed at the authors' request

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[1] Part 21 of Heterosubstituted Acetylenes. – Part 20: *R. Buijle* and *H. G. Viehe*, Tetrahedron *24*, 4217 (1968).

[2] *J. Loevenich, J. Koch*, and *U. Pucknat*, Chem. Ber. *63*, 636 (1930); *J. Loevenich* and *H. Gerber*, *ibid. 63*, 1707 (1930).

[3] For a review see *H. G. Viehe*, Angew. Chem. *79*, 744 (1967); Angew. Chem. internat. Edit. *6*, 767 (1967).

[4] *T. E. Stevens* and *W. D. Emmons*, J. Amer. chem. Soc. *80*, 338 (1958).

[5] All the compounds mentioned gave correct elemental analyses and molecular weights.

[6] *A. P. Howe* and *H. B. Hass*, Ind. Engng. Chem. *38*, 252 (1946).

A New Cyclophane Synthesis[1, 2]

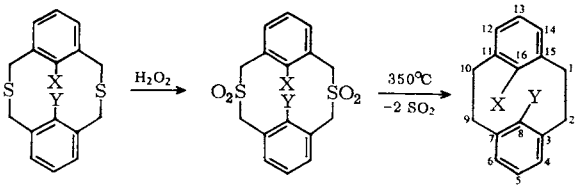
By *F. Vögtle*[*]

During ^{1}H–NMR investigations of 1,10-dithia[2.2]metacyclophanes[3] and 1,10-dithia-16-aza[2.2]metacyclophanes[4] carrying substituents in the interior of the ten-membered ring it appeared desirable to compare these compounds with the hitherto unknown [2.2]metacyclophanes of type *(3)*[5], X ≠ Y, that are substituted in an analogous fashion and contain no sulfur. The usual Wurtz synthesis[6] is not suitable for their preparation, since it inevitably affords mixtures of products in the case of unsymmetrical cyclophanes.

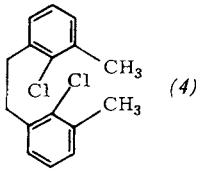
We obtained compounds *(3a)–(3d)* as almost colorless distillates that crystallize on solidification by pyrolysis (1–5 h, 350 °C[7]; yield 15–20%[8]) of the disulfones *(2)* prepared from the 2,11-dithia[3.3]metacyclophanes *(1)* and H_2O_2.

It was not possible to detect a monosulfone in which the C–C linkage had already been formed on one side. It is remarkable that only the unsymmetrical [2.2]metacyclophanes *(3b)* and *(3d)* are formed from the unsymmetrical sulfones *(2b)* and *(2d)*; in both cases symmetrical products could not be detected, even in traces (mass spectrometry). Linkage of the fragments therefore occurs exclusively by an intramolecular process.

The [2.2]metacyclophane structure was established for compounds *(3b)–(3d)* by mass spectrometry and proton magnetic resonance. In the ^{1}H–NMR spectrum, both the methylene



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



(4)

	X	Y	*(3)*, M. p. (°C)
(a)	H	H	132–133
(b)	H	F	108–109
(c)	F	F	158–159
(d)	H	Cl	126–127
(e)	Cl	Cl	see text

groups [AA'BB' system for *(3c)*, ABCD system for *(3b)* and *(3d)*] and the internal aromatic protons of *(3b)* and *(3d)* [τ = 5.63 and 6.06, respectively; *(3a)*: $\tau_{H(8)}$ = 5.71; in $CDCl_3$] absorb at characteristically high field strengths.

Under similar conditions, pyrolysis of *(2e)* does not afford 8,16-dichloro[2.2]metacyclophane but leads to a mixture of crystalline products – apparently owing to the mutual steric hindrance of the two "internal" chlorine atoms. The main component of the mixture was shown by mass spectrometry to be compound *(4)*, in which linkage has occurred only on one side; some pyrene was also detected by UV spectroscopy.

The symmetrical starting compounds *(1a)*[9], *(1c)*, and *(1e)* were prepared by reaction of the ω,ω'-dibromo-*m*-xylenes with sodium sulfide in accordance with the dilution principle; the unsymmetrical representatives *(1b)* and *(1d)* are obtained from the disodium salt of ω,ω'-dimercapto-*m*-xylene and ω,ω'-dibromo-2-fluoro- or -chloro-*m*-xylene, respectively, also at high dilution[10].

By means of this ring-contraction method we were able to prepare a number of other sterically hindered or strained ring systems, *e.g.* 2,2''-ethano-*m*-terphenyl[11], [2.2]metaparacyclophane[12], [2.2]paracyclophane, and [2.2.0]metacyclophane.

Received: January 20, 1969; revised: February 21, 1969 [Z 943 IE]
German version: Angew. Chem. *81*, 258 (1969)

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[1] Part 8 of Steric Interactions of Inner Atoms in Cyclic Compounds. – Part 7: *F. Vögtle* and *L. Schunder*, Chem. Ber., in press.

[2] These investigations were supported by the Deutsche Forschungsgemeinschaft.

[3] *F. Vögtle*, Tetrahedron Letters *1968*, 3623.

[4] *F. Vögtle* and *A. H. Effler*, Chem. Ber., in press.

[5] After these investigations had been completed, another method for the preparation of unsymmetrical cyclophanes came to our notice: *T. Hylton* and *V. Boekelheide*, J. Amer. chem. Soc. *90*, 6887 (1968).

[6] Cf. *B. H. Smith*: Bridged Aromatic Compounds. Academic Press, New York 1964, p. 88ff.

[7] At this temperature the crystalline sulfones *(2)* "decompose" without melting and with vigorous evolution of SO_2.

[8] No impurities are apparent from the ^{1}H–NMR spectrum of the distillates.

[9] Compounds *(1a)* and *(2a)* have recently also been prepared by *T. Sato, M. Wakabayashi, M. Kainosho*, and *K. Hata*, Tetrahedron Letters *1968*, 4185.

[10] Cf. *F. Vögtle* and *L. Schunder*, Chem. Ber., in press.

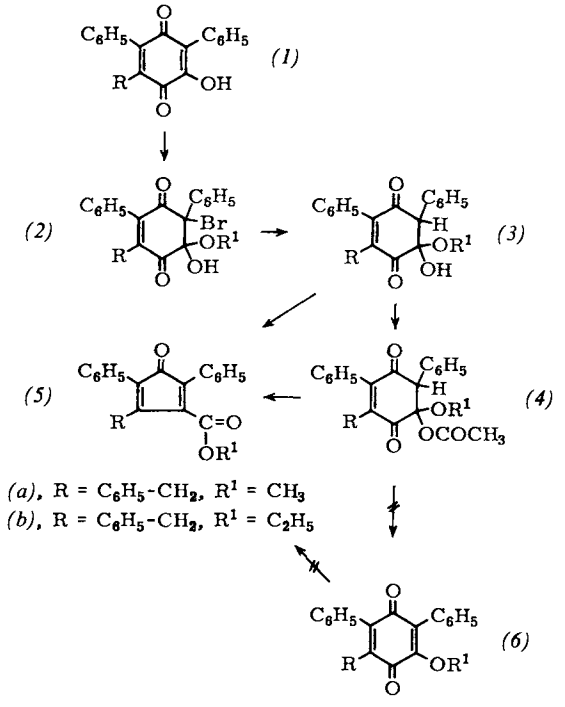
[11] *F. Vögtle*, Chem. Ber., in press. The compound is formed in quantitative yield.

[12] Pyrolysis of the sulfone is probably the most convenient method of preparation for [2.2]metaparacyclophane at least.

Synthesis of Substituted Cyclopentadienones by Ring Contraction

By *W. Ried, W. Kunkel,* and *P. B. Olschewski*[*]

In attempts to convert 5-alkoxy-3-benzyl-5-hydroxy-2,6-diphenyl-2-cyclohexene-1,4-diones *(3a)* and *(3b)* by an excess of acetic anhydride into the acetyl compounds *(4a)* and *(4b)* and thence by loss of acetic acid into the alkoxy quinones *(6a)* and *(6b)*[1], respectively, gave, not only the expected compound *(4a)* or *(4b)*, but also surprisingly the new, deep red 5-benzyl-3-oxo-2,4-diphenyl-1,4-cyclopentadiene-1-carboxylates *(5a)* [m.p. 158 °C (from methanol); IR spectrum, ν_{CO} = 1720 cm^{-1}; ^1H–NMR spectrum (in $CDCl_3$)[2], τ = 2.5–3.0 (15 H), D; τ = 5.9 (2 H), S; τ = 6.65 (3 H), S] and *(5b)* [m.p. 105 °C (from methanol or ethanol); IR spectrum, ν_{CO} = 1720 cm^{-1}]. Compound *(3a)* or *(3b)* (2.5 mmoles) was heated with acetic anhydride (60 ml), the initial colorless solution becoming deep red; the hot mixture was poured into water.



The mixed products were separated by chromatography on silica gel with benzene as eluant. The yields of *(5a)* and *(5b)* increased monotonically with increasing reaction time. After 6-hours' heating of *(3a)* or *(3b)* in acetic anhydride the yields obtained were 10% of *(5a)* with 64% of *(4a)* [m.p. 168 °C (from light petroleum); ν_{CO} = 1710, 1740 cm^{-1}] or 16.5% of *(5b)* with 61% of *(4b)* [m.p. 127 °C (from light petroleum); ν_{CO} = 1710, 1730 cm^{-1}].

The acetyl compounds *(4a)* and *(4b)* can also be converted into the esters *(5a)* and *(5b)*, respectively, and are thus apparently intermediates. However, it is unlikely that the alkoxy quinones *(6)* are intermediates in production of the five-membered ring compounds as the known compound *(6a)*[1] is not converted into *(5a)* under the above reaction conditions.

For synthesis of the starting materials *(3a)* [m.p. 136 °C (from methanol or light petroleum; ν_{CO} = 1730 cm^{-1}] and *(3b)* [m.p. 150 °C (from ethanol or light petroleum); ν_{CO} = 1720, 1740 cm^{-1}], 3-benzyl-5-hydroxy-2,6-diphenyl-1,4-benzoquinone *(1a)*[1] was converted into *(2a)* [m.p. 149 °C (from methanol); ν_{CO} = 1740, 1750 cm^{-1}] and *(2b)* [m.p. 127 °C (from ethanol); ν_{CO} = 1740, 1750 cm^{-1}], respectively, by bromine or *N*-bromosuccinimide in the presence of methanol or ethanol, respectively, and then debrominated catalytically by hydrogen or by treatment with zinc in glacial acetic acid.

The structures of the esters *(5a)* and *(5b)* were proved by elemental analyses, by IR, ^1H–NMR, and mass spectra, and also chemically, by decarbonylation of the dimethyl acetylenedicarboxylate Diels-Alder adduct[3] of *(5a)* to give trimethyl 6'-benzyl-*p*-terphenyl-2',3',5'-tricarboxylate and by reduction[4] of *(5a)* with zinc and glacial acetic acid to methyl 5-benzyl-3-oxo-2,4-diphenyl-2-cyclopentenecarboxylate.

Received: January 2, 1969; revised: January 24, 1969 [Z 945 IE]
German version: Angew. Chem. *81*, 260 (1969)

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[1] *W. Ried* and *W. Kunkel*, Liebigs Ann. Chem. *717*, 54 (1968).

[2] The IR spectra were measured on a Perkin-Elmer grating spectrometer 337 and the NMR spectra on a Varian A-60 instrument with tetramethylsilane as internal standard.

[3] *M. A. Ogliaruso, M. G. Romanelli,* and *E. I. Becker*, Chem. Reviews *65*, 261 (1965).

[4] *D. A. Brown, J. P. Hargaden, C. M. McMullin, N. Gogan,* and *H. Sloan*, J. chem. Soc. (London) *1963*, 4914; *N. O. V. Sonntag, S. Linder, E. I. Becker,* and *P. E. Spoerri*, J. Amer. chem. Soc. *75*, 2283 (1953).

Alkali-Metal Tetraorganylborates from Triorganylboranes

By *M. A. Grassberger* and *R. Köster*[*]

Tetraorganylborates are of importance for the preparation of organic and organometallic compounds and as analytical reagents[1]. We have found that the alkali-metal tetraorganylborates *(2)–(9)* can be prepared from alkali-metal tetraethylborates *(1)* and triorganylboranes at 130–180 °C in accordance with reaction (a) (cf. Table 1). Presence of solvent is not usually necessary.

$$3\ MB(C_2H_5)_4 + 4\ BR_3 \rightleftharpoons 3\ MBR_4 + 4\ B(C_2H_5)_3 \qquad (a)$$

(1a), M = Li — *(2)–(9)*

(1b), M = Na

Table 1. Alkali-metal tetraorganylborates MBR_4.

	M	R	Temp. (°C)	Yield (%)	M.p. (°C) [c]
(2b)	Na	Butyloxy	140	100	>350
(3b)	Na	Allyloxy	130	77	>350
(4b)	Na	Crotyl	140	86	130
(5b)	Na	Methallyl	135	85	166
(6b)	Na	[a]	140	91	30
(7a)	Li	Phenyl	180	92 [b]	>350
(8a)	Li	Benzyl	160	70	198
(8b)	Na	Benzyl	140	95	200
(9b)	Na	Pyrrolyl	145	81	>350

[a] *cis-trans* mixture of isomers. See eq. (c) for formula.
[b] Obtained with a 50% excess of BR_3.
[c] All compounds except *(6b)* decompose on melting.

In solution, an equilibrium always sets in. For example, compound *(5b)* reacts with an equimolar amount of triethylborane in dimethyl sulfoxide at room temperature to give trimethallylborane and sodium triethylmethallylborate.

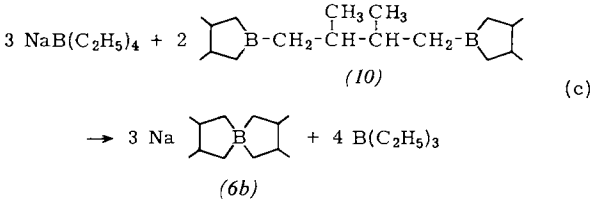
The hitherto unreported sodium tetraallylborates *(4b)* and *(5b)*, as well as sodium tetrabenzylborate *(8b)*, can, in particular, be obtained in good yields from the easily accessible[2] sodium tetraethylborate *(1b)* (m.p. 144 °C). The alkali-metal tetraethylborate can be recovered by reaction of alkali-metal hydride and ethylene with the triethylborane formed at the same time in reaction (a)[2].

Lithium tetraethylborate *(1a)* reacts much more rapidly than does the sodium salt *(1b)*. Whilst, for example, lithium tetraphenylborate *(7a)* can be obtained in good yields by reaction of *(1a)* with excess triphenylborane at 180 °C, reaction with *(1a)* under similar conditions yields practically pure sodium ethyltriphenylborate. In boiling xylene, however, exchange of the last ethyl group for the phenyl residue takes place when the sodium salt is used in the reaction.

With trialkylboranes BR_3 (where $R > C_2H_5$) dehydroboration cannot always be avoided. For example, in the preparation of sodium tetrabutylborate in boiling toluene, compounds with B–H bonds are formed.

$$3\ NaB(C_2H_5)_4 + 4\ B(n\text{-}C_4H_9)_3 \xrightarrow{110\,^\circ C}$$
$$3\ NaB(n\text{-}C_4H_9)_{4-x}H_x + 4\ B(C_2H_5)_3 + 3\ x\ C_4H_8 \qquad (b)$$

With tricyclohexylborane, dehydroboration is the main reaction. In contrast, the borolanyl derivative *(10)* reacts smoothly with *(1b)* to form 2,3,7,8-tetramethyl-5-boraspiro-[4.4]nonane *(6b)* [3].



(5b) is hydrolyzed quantitatively by water. Sodium tetrabenzylborate is stable towards air and water; the slightly soluble potassium tetrabenzylborate precipitates out when $K^{\oplus}$ ions are added in aqueous solution.

Sodium tetrabenzylborate (8b)

On heating 14.2 g (50 mmole) of tribenzylborane and 5.68 g (37.8 mmole) of compound *(1b)* to 140 °C triethylborane (3.6 g) distills off. The residue is boiled in 30 ml of anhydrous benzene and then filtered. 13.65 g of *(8b)* is recovered as residue; the filtrate is then concentrated to *ca.* 5 ml whereupon a further 0.6 g of *(8b)* is precipitated. 14.25 g (95%) of pure *(8b)* is obtained. ^1H–NMR spectrum (dimethyl sulfoxide, *ca.* 30%): τ = 2.95 ppm (S), 8.49 ppm (Q, $J_{11_{B,H}}$ = 5.5 Hz), in the intensity ratio 5:2.

Received: January 17, 1969 [Z 946 IE]
German version: Angew. Chem. *81*, 261 (1969)

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[1] *M. F. Lappert* in *E. L. Muetterties*: The Chemistry of Boron and its Compounds. Wiley, New York 1967, p. 451 ff., and further literature cited there.

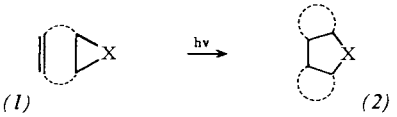
[2] *R. Köster*, US-Pat. 3163679 (Nov. 15, 1960), *K. Ziegler*; Chem. Abstr. *58*, 10236e (1963); *J. B. Honeycutt jr.* and *J. M. Riddle*, J. Amer. chem. Soc. *83*, 369 (1961).

[3] *R. Köster*, Advances in Organometallic Chemistry *2*, 302 (1964); cf. *L. Weber*, Dissertation, Technische Hochschule Aachen, 1967.

Photochemical Olefin-Oxirane Cyclodimerization[1]

By *H. Prinzbach* and *M. Klaus* [*]

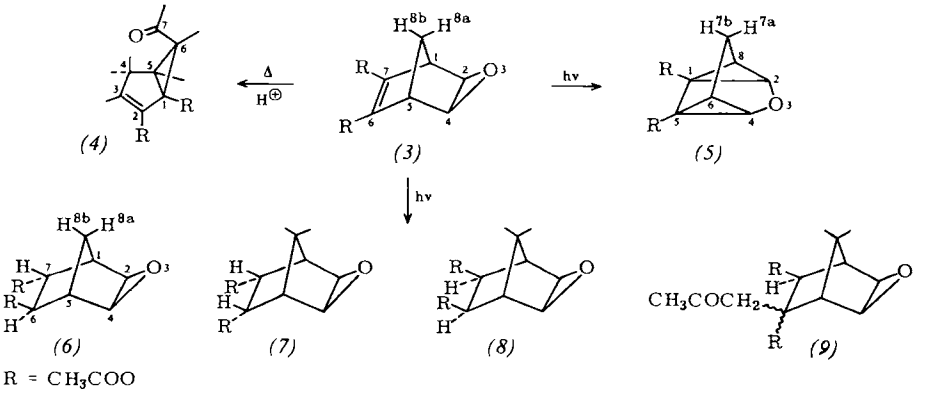
Intramolecular ($2\pi + 2\sigma$) cycloadditions between ethylene and cyclopropane units to give cyclopentane derivatives [*(1a)* → *(2a)*] have been accomplished both photochemically [2] and thermally [3]. Taking compound *(3)* as an example, we shall now show that a corresponding valence isomerization between a CC double bond and an oxirane ring [*(1b)* → *(2b)*] can also be achieved photochemically [4].



(a), X = CH_2, CR_2
(b), X = O

The double bond and the three-membered ring in the *exo*-epoxynorbornene system *(3)*, which is stabilized by the ester groups R [5] and which preferentially undergoes thermal or proton-catalyzed isomerization upon C–O scission to bicyclo[3.1.0]hexenecarbaldehyde *(4)*, are arranged favorably for the valence isomerization *(1b)* → *(2b)* [2b]. On UV irradiation (Hanovia 450 W high pressure mercury lamp, Vycor filter) of an oxygen-free solution of *(3)* in CH_3CN (5.0 g of *(3)* that has been purified by crystallization [6] / 500 ml CH_3CN, −20 °C), the intensity of the absorption maximum at 254 nm decreases only very slowly; after removal of the solvent from the reaction solution obtained on irradiation for about 14 h, 1.4–1.5 g (28–30%) of a mixture of *(5)*, *(6)*, and *(8)* could be isolated by distillation (10^{-3} torr, *ca.* 120 °C). Colorless crystals of *(5)* are obtained when the mixture is seeded with a sample that has been purified by gas chromatography (0.8–1.0 g; 16–20%).

No *(5)* is formed in ether or cyclohexane; a very rapid reaction takes place (5 g/2 h) yielding a mixture (48–52%) of the dihydro compounds *(6)*, *(7)*, and *(8)*, in addition to polymeric material. Nor can *(5)* be detected after irradiation in acetone (Pyrex filter). *(6)* and *(8)* as well as the addition compound *(9)* can be distilled off from the polymeric residue in a total yield of 55%.



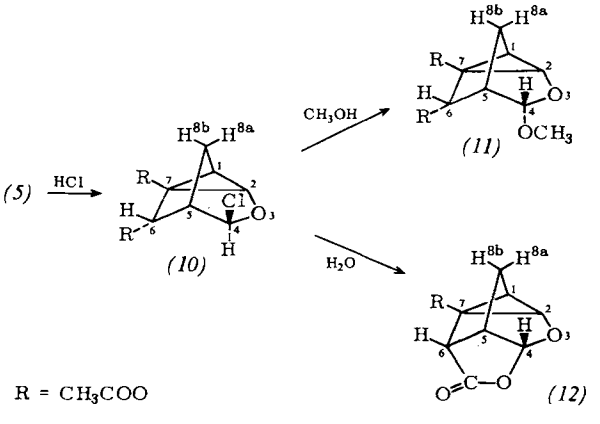
R = CH_3COO

Cpd. [a] M.p. (°C) (B.p. (°C/10^{-3}Torr))	UV [b] λ_{max} (nm, ε)	NMR [c] (τ); J (Hz)									Molecular ion at *m/e*
		H^1	H^2	H^3	H^4	H^5	H^6	H^7 a | b	H^8 a | b	CO_2CH_3	
(3) 46	254(3800)	6.7 (M)	6.4 (S)		6.4 (S)	6.7 (M)			8.2(dT) | 8.5(dM) $J^{8a,8b}=9$ $J^{1,8a}=J^{5,8a}=1.2$	6.2	224
(4) (102)	224(≈4000) $\varepsilon_{300}\approx120$			3.4 (M)	6.9—7.7 (M)	6.9—7.7 (M)	6.9—7.7 (M)	0.8 (D) $J^{6,7}=3.6$		6.3	—
(5) 68—69	$\varepsilon_{210}=1400$		5.6 (dD) $J^{2,8}=6.2$ $J^{2,7b}=1.0$		5.6 (dD) $J^{4,6}=6.2$ $J^{4,7b}=1.0$		7.9 (dD) $J^{6,7b}=4.5$ $J^{4,6}=6.2$	8.1 (D) | 7.8 (dT) $J^{7a,7b}=11.5$ $J^{6,7b}=J^{8,7b}=4.5$	7.9 (dD) $J^{8,7b}=4.5$ $J^{2,8}=6.2$	6.3	224
(6) (≈110)	$\varepsilon_{210}=340$	7.1—7.3 (M)	6.9 (AB) $J^{2,4}=4.0$		6.9 (AB) $J^{4,2}=4.0$	7.1—7.3 (M)	7.3 (dD) $J^{6,7}=4.5$ $J^{6,8a}=1.5$	6.7 (dD) $J^{6,7}\sim J^{1,7}=4.5$	8.7 (M) | 9.0 (M) $J^{8a,8b}=10.5$ $J^{6,8a}=1.5$	6.3	226
(7) (≈110)	$\varepsilon_{210}=640$	7.0 (br.S)	6.3 (S)		6.3 (S)	7.0 (br.S)	7.4 (D) $J^{5,6}=2.0$	7.4 (D) $J^{1,7}=2.0$	≈8.7 (AB) $J^{8a,8b}\approx10$	6.3 (6.4)	—
(8) (≈110)		7.0 (br.S)	6.3 (S)		6.3 (S)	7.0 (br.S)	7.3 (M)	7.3 (M)	≈8.7 (AB) $J^{8a,8b}\approx10$	6.4 (6.3)	—
(9) [d] 171—172	272(27) $\varepsilon_{210}=208$	7.4 (M) (7.6)	7.1 (D) (6.8) $J^{2,4}=3.5$		6.8 (dD) (7.1) $J^{2,4}=3.5$ $J^{4,8b}=1.5$	7.6 (M) (7.4)		6.5 (D) [e]	8.6 (dQ) | 8.4 (dM) $J^{8a,8b}=11.0$ $J^{7,8a}=1.5$ $J^{4,8b}=1.5$	6.3 6.5	—
(10)		7.8—8.2 (M)	5.7 (D) $J^{1,2}=6.8$		4.2 (dD) $J^{4,5}=2.5$ $J^{4,8b}=1.5$	7.1—7.5 (M)	6.5 (D) $J^{5,6}=5.1$		7.3 (D) | 7.8—8.2 (M) $J^{8a,8b}=11.5$	6.3 6.4	—
(11) (≈120)	$\varepsilon_{210}=1000$	8.0—8.5 (M)	5.9 (D) $J^{1,2}=6.8$		5.7 (D) $J^{4,5}=2.5$	~7.6 (M)	≈6.7 [f]		7.6 (D) | 8.0—8.5 (M) $J^{8a,8b}=11.5$	6.3 6.4	—
(12)		7.7—8.0 (M)	5.7 (D) $J^{1,2}=6.0$		4.6 (D) $J^{4,5}=4.0$	6.7—7.1 (M)	6.7—7.1 (M)		7.7—7.8 (M)	6.2	—

[a] Satisfactory elemental analyses were obtained. [b] In ethanol. [c] In CCl_4. [d] NMR spectrum in $CDCl_3$, acetonyl group: τ = 8.0 (S) (3 H), τ = 6.6, 6.9 (AB, J = 18 Hz) (2 H). [e] Partly masked by ester signals; when recorded in $CDCl_3/C_6D_6$, H^7 clearly lies at τ = 6.3 (D) ($J^{7,8a}$ = 1.5 Hz). [f] Partly masked by CH_3O signal (τ = 6.7); when recorded in C_6D_6/CCl_4, H^6 clearly lies at τ = 6.7 (D) ($J^{5,6}$ = 5.8 Hz).

Like the isocyclic system[2b], the tetracyclic ether *(5)* is thermally very stable and does not react with dimethyl acetylenedicarboxylate below 200 °C. When HCl gas is passed into a solution of *(5)* in CCl_4 (0 °C) stereospecific addition of HCl occurs to give *(10)*.

The highly water-sensitive α-halogeno ether *(10)* is converted into the stable acetal *(11)* on treatment with methanol; with water *(10)* immediately forms the lactone *(12)*.



The *exo* position of the epoxide ring in *(3)* is evidenced by $J^{1,2}=J^{4,5}\sim0$ Hz and by the difference in δH^{8a} and δH^{8b} [7]. The photoisomer is shown to have the structure *(5)* by spectroscopic data and by its reaction to form *(10)*, *(11)*, and *(12)*: end absorption in the electronic spectrum; disappearance of the C=C– band (1610 cm^{-1}) and the epoxide band (855 cm^{-1})[8] in the IR spectrum; NMR signals in the intensity ratio 2:2:1:1 (retention of the plane of symmetry) having chemical shifts and coupling constants that agree well with those measured for model compounds[2b,9].

The stereochemistry of the addition of HCl is apparent from $J^{5,6}$ [10], $J^{4,5}$, and from the M-coupling $J^{4,8b}$ in the spectrum of *(10)*. The absence of this M-coupling in the spectrum of *(11)* and the formation of the lactone *(12)* confirm that inversion occurs during substitution to form *(11)*. The structures of the co-products *(6)*, *(7)*, *(8)*, and *(9)* were determined mainly from NMR data; in the case of compound *(9)* the stereochemistry at C-6 is not clear.

Received: January 24, 1969 [Z 948 IE]
German version: Angew. Chem. *81*, 289 (1969)

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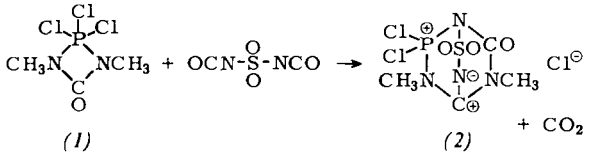
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Synthesis of a Derivative of 6-Thia-2-phosphonia-1,3,5,8-tetraazabicyclo[2.2.2]oct-4(5)-ene Chloride[1]

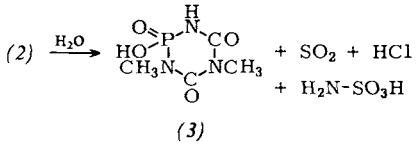
By *H. P. Latscha* and *W. Klein*[*]

During our investigations of the reactions of phosphorus compounds with isocyanates, we have synthesized the compound 2,2-dichloro-3,8-dimethyl-6,6,7-trioxo-6-thia-2-phosphonia-1,3,5,8-tetraazabicyclo[2.2.2]oct-4(5)-ene chloride *(2)* from 1,1,1-trichloro-2,4-dimethyl-1,2,4-phospha(v)-diazetidin-3-one *(1)* and sulfuryl diisocyanate.

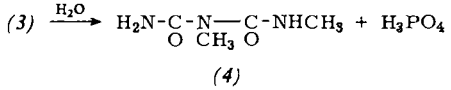


(1) *(2)*

Compound *(2)* is colorless, extremely sensitive to water, and decomposes above 132 °C with evolution of gas. It is soluble in cold nitromethane, from which it may be precipitated in well formed crystals by addition of anhydrous benzene. The ^{31}P–NMR spectrum of a nitromethane solution of *(2)* contains a signal at −44.5 ppm (85% aqueous H_3PO_4 as external reference). The ^1H–NMR spectrum consists of a singlet (δ = 3.81 ppm) and a doublet (δ = 3.56 ppm), in the intensity ratio 1:1, that can be assigned to two nonequivalent methyl groups. The splitting of the doublet is caused by the coupling of the protons of a methyl group with the phosphorus nucleus (J_{PH} = 11.1 ± 0.2 Hz).



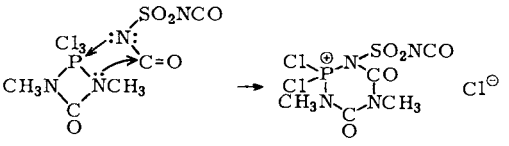
(3)



(4)

Compound *(2)* reacts with water to give 1-hydroxy-2,4-dimethylperhydro-1,2,4,6-phospha(v)-triazine-1,3,5-trione *(3)* and 1,3-dimethylbiuret *(4)*, which were both characterized by their mass numbers.

During the formation of *(2)*, the isocyanate molecule is observed to react in two different ways: one isocyanate group of the sulfuryl diisocyanate reacts with *(1)* to give the non-isolable species *(2a)*. Previous experiments have shown that the isocyanate group is inserted between the phosphorus atom and the nitrogen atom[3,4].



(1) *(2a)*

The formation of a phosphonium salt is indicated by the negative value of the chemical shift of the phosphorus nucleus[3,5].

The second isocyanate group of the sulfuryl diisocyanate reacts with the carbonyl group of *(1)* with elimination of CO_2.

Preparation of compound (2)

A solution of sulfuryl diisocyanate[7] (15 g, 0.1 mole) in benzene is added dropwise, with stirring, to an ice-cooled solution of *(1)*[6] (22.5 g, 0.1 mole) in anhydrous benzene; an exothermic reaction soon sets in with vigorous evolution of gas. After about 2 hours' stirring at room temperature, a white crystalline precipitate of *(2)* is formed in almost quantitative yield. The product can be purified by recrystallization from nitromethane/benzene.

Received: January 17, 1969 [Z 949 IE]
German version: Angew. Chem. *81*, 291 (1969)

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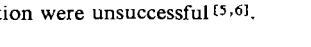
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A New Synthesis of Thioformamide

By *R. Tull* and *L. M. Weinstock*[*]

We wish to report the synthesis of thioformamide *(1)* from hydrogen cyanide and hydrogen sulfide. This versatile intermediate for the synthesis of thiazoles has been prepared heretofore by the reaction of formamide with phosphorous pentasulfide[1,2] and by treatment of dithioformic acid with ammonia[3], methods which have not achieved economic significance. Many higher homologs of thioformamide have been prepared from the corresponding nitriles and hydrogen sulfide[2,4], but there is no record of the application of this reaction to hydrogen cyanide, the simplest member of the series. Indeed, previous attempts to effect this reaction in the gas phase or in aqueous solution were unsuccessful[5,6].



(1)

The use of ammonia and tertiary amines has provided yields of thioformamide in the range of 50–70%. No thioformamide was detectable when strong base catalysts such as sodium methoxide were employed, presumably because of the more rapid polymerization of hydrogen cyanide under these conditions. The reaction of hydrogen cyanide and hydrogen sulfide can be conducted in either nonaqueous protic or aprotic solvents under 13–17 atm hydrogen sulfide pressure at room temperature or at 50 °C. The simplicity of the reaction allows the synthesis of thiazoles without isolation of thioformamide.

For example, hydrogen cyanide (4.0 ml, 0.1 mole) and then triethylamine (0.7 ml, 0.005 mole) are added to 30 ml of benzene at 5–10 °C. The mixture is saturated with hydrogen sulfide at 13–17 atm in a bomb and shaken for 16 h at 20 °C. The mixture can be assayed by removal of the benzene and measurement of the thioformamide content by UV spectroscopy [λ_{max} (CH_3OH) = 263 nm (ε = 12500)]. In the above example the yield by assay is 50%. When 0.1 mole of triethylamine is used the yield by assay is 70%.

Treatment of the benzene solution with 10 ml (0.12 mole) of chloroacetone (after removal of the hydrogen sulfide by partial evaporation) under reflux for one hour provided 4-methylthiazole in 53% yield.

Thioformamide could be isolated in 40% yield from a reaction of hydrogen cyanide (0.1 mole) and an excess of hydrogen sulfide in presence of 0.1 mole of ammonia in methanol solution. The isolated thioamide was converted into 4-methylthiazole in 85% yield.

Received: February 28, 1969 [Z 951 IE]
German version: Angew. Chem. *81*, 291 (1969)

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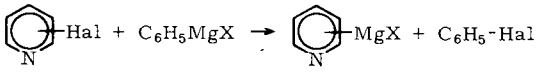
[6] The reaction of potassium cyanide with hydrogen sulfide in aqueous solution forms 5-aminothiazole-2-thiocarboxamide [5] (chrysean). We have repeated this reaction and have confirmed the proposed structure of chrysean.

A New Method for the Preparation of Organomagnesium Compounds of Pyridine[1]

By *H. H. Paradies* and *M. Görbing* [*]

Pyridylmagnesium compounds may be prepared by simultaneous addition of ethyl bromide and halogenopyridine to magnesium[2]; they react analogously to Grignard compounds[3,4].

In order to elucidate the reaction mechanism and the structure[5] of this class of compounds we treated halogen derivatives of pyridine with phenylmagnesium bromide or iodide in anhydrous polar solvents.



The reaction that occurs proceeds neither by a normal addition-elimination mechanism[6,7] in the case of 2-bromopyridine, nor by an elimination-addition mechanism[7,8] in the case of 3-halogenopyridine. Gas chromatography of the hydrolysis products of the pyridylmagnesium bromide or iodide, which is formed in high yield during the reaction, failed to establish the presence of 2-phenylpyridine or 3- or 4-phenylpyridine. It is essential for the success of the new preparation that the products be insoluble in the organic solvents.

Typical procedure for the preparation of 2-pyridylmagnesium bromide:

3-Chloropyridine (2 mmole) is dissolved in anhydrous ether (THF) (30 ml) under purified nitrogen. An ethereal (or THF) solution of phenylmagnesium bromide (10 ml, 40%) is then added over a period of 10 min. Reaction starts immediately and is complete within 15 min. The finely crystalline product is collected on a glass filter (1 G 2), dried over $CaCl_2$ in a stream of N_2, and stored under N_2. The corresponding reactions with phenylmagnesium iodide do not give such good yields:

Hal-C_5H_4N	Yield (%) [9] X = Br	I	Solvent X = Br	I
2-Cl-	85	60	ether	
3-Cl-	80	60	ether	
4-Cl-	63	40	THF	
2-Br-	90	60	THF	THF, ether
3-Br-	95	60	THF	THF, ether
4-Br-	70	31	THF	

In contrast to the products obtained according to ref.[3], the white crystalline pyridylmagnesium bromides and iodides prepared by the above procedure are odorless. They do not melt below 350 °C and are insoluble in anhydrous solvents. The substances react with benzaldehyde to give the corresponding secondary alcohols which were characterized by their melting points.

The *d* values calculated from Guinier photographs and results of analysis clearly show that the compounds prepared in the above manner are identical with those synthesized by the method of *Proost* and *Wibaut*[4].

Received: January 8, 1969 [Z 955 IE]
German version: Angew. Chem. *81*, 293 (1969)

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Heptavalent Plutonium

By *C. Keller* and *H. Seiffert* [*]

Krot and *Gel'man*[1] recently obtained evidence for the existence of heptavalent neptunium by oxidation of Np^{VI} with ozone in alkaline solution and were later able to confirm this finding by use of other oxidizing agents[2]; we then succeeded in preparing Li_5NpO_6, the first crystalline compound containing Np^{VII}[3]. Similar investigations also pro-

vided indication of the existence of plutonium having oxidation numbers in excess of +6[3]. We have now been able to obtain pure pentalithiumplutonium(VII) hexoxide, Li_5PuO_6.

Preparation of Li_5PuO_6:

A finely powdered mixture of Li_2O and PuO_2 (*ca.* 3:1; an excess of Li_2O has been found necessary) is heated slowly ($\approx$ 6 °C/min) in a stream of pure oxygen to 430 ± 10 °C and kept at this temperature until no further increase in weight can be detected (*ca.* 2 h); regarding the weighing procedure see reference[4]. Typical quantities: 83.51 mg Li_2O + 252.46 mg PuO_2 (Li:Pu = 5.95:1) ——Δm at 430 °C (*ca.* 2 h, $p(O_2)$ = 1 atm): 22.40 ± 0.1 mg; these data afford a valency of 6.98 ± 0.02 for the plutonium.

The X-ray diffraction pattern of the greenish-black Li_5PuO_6 shows the lattice to be hexagonal with $a = 5.19 \pm 0.02$ Å and $c = 14.48 \pm 0.02$ Å [space group $R\bar{3}$ (?), $d_{X\text{-ray}}$ for $Li_5{}^{239}PuO_6$ = 3.53 g/cm³]. Li_5PuO_6 is isotypic with the analogous compounds of Np^{VII}[3], Tc^{VII}[5], and Re^{VII}[6]. The ternary oxides $Li_6M^{VI}O_6$, $Li_7M^{V}O_6$, $Li_8M^{IV}O_6$ probably also have the same crystal structure, as was first established by *Scholder*[7]. However, plutonium is the first element to occur in all four types of compounds[8–10]. It is therefore not surprising that only one phase, *i.e.* a solid solution of Li_6PuO_6 and Li_5PuO_6, is observed with partially oxidized samples in which the plutonium has a mean oxidation number between +6 and +7 (cf. ref.[8,9]). An accurate crystal-structure determination of compounds of the type Li_xMO_6 has been carried out by *Trömel* and *Hauck* with Li_8SnO_6[11].

Since both Re^{VII} and Tc^{VII} form ternary oxides with alkali and alkaline-earth metals, corresponding compounds of heptavalent plutonium should also be preparable. This is indicated qualitatively, *e.g.*, by the fact that the products of the reaction $Na_2O_2 + PuO_2 + O_2$ (400 °C) show the typical absorption spectrum of Pu^{VII} on dissolution in water.

Li_5PuO_6 dissolves in water and in LiOH solutions to give a green coloration. Such solutions are not stable and are quantitatively converted into yellow solutions of Pu^{VI} within 2–3 min, the rate of reaction being inversely proportional to the concentration of LiOH. It may be concluded from qualitative observations on plutonium in dilute LiOH solution[8] that two absorption bands at 400–410 nm and 620–630 nm, respectively, are to be assigned to Pu^{VII}. Oxidation of Pu^{VI} to Pu^{VII} in LiOH solution can be performed by addition of $K_2S_2O_8$ to the hot solution. Like Np^{VII}, Pu^{VII} is stable only in alkaline solution; reduction to Pu^{VI} occurs immediately on acidification.

Received: December 20, 1968 [Z 956 IE]
German version: Angew. Chem. *81*, 294 (1969)

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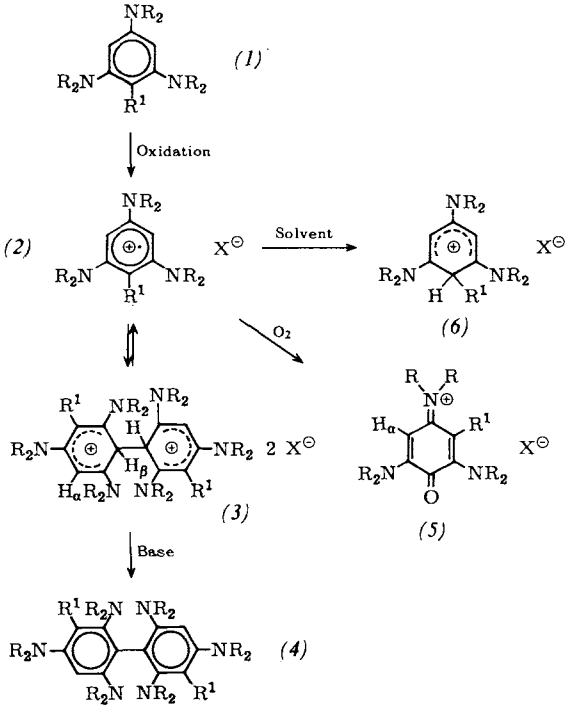
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Mechanism of Oxidative Dimerization of Aminobenzenes[1]

By *F. Effenberger, W. D. Stohrer*, and *A. Steinbach*[*]

Compounds of type *(3)*, which hitherto have not been isolated[2], are postulated as intermediates in the oxidative dimerization of *N,N*-disubstituted anilines.

We have been able to prepare the red σ-complexes *(3)* in the crystalline state [UV absorption of *(3a)* in C_2H_5OH: λ_{max} = 431 nm, ε = 12800; λ_{max} = 346 nm, ε = 41000] by oxidation of symmetrical triaminobenzenes *(1)*[3]; on reaction with bases, these complexes afford the hexaaminobiphenyls *(4)*.



	—R—R—	R^1	X	(3) M.p. (°C)	(3) Yield (%)	(5) M.p. (°C)	(5) Yield (%)
(a)	$-(CH_2)_4-$	H	CBr_5	177–178	33	—	—
(b)	$-(CH_2)_4-$	H	ClO_4	254–256	91	200 to 201	93
(c)	$-(CH_2)_4-$	CH_3	ClO_4	158–159	82	—	—
(d)	$-(CH_2)_4-$	C_2H_5	ClO_4	123–127	96	—	—
(e)	$-(CH_2)_5-$	H	ClO_4	215–216	56	—	—
(f)	$-(CH_2)_2-O-(CH_2)_2-$	H	I_3	140–145	2.5	—	—

The oxidation was carried out at room temperature with silver salts in dimethylformamide and with tetrahalogenomethanes, cyanogen halides, or halogens in dichloromethane. The salts *(3)*, whose structure has been established by elemental analysis, molecular-weight determinations and ^{1}H-NMR spectra [*(3b)* in liquid SO_2: H_α = singlet at τ = 5.03, H_β = singlet at τ = 5.67] are obtained in good yields.

Noteworthy is the occurrence of a stable $CBr_5^\ominus$ anion in the reaction of 1,3,5-tripyrrolidinobenzene with CBr_4 in dichloromethane. No CBr_4 is liberated from *(3a)* by extraction with ether for several days. Compound *(3a)* is formed smoothly from *(3b)* by treatment with alcoholic sodium perchlorate solution. The structure of $CBR_5^\ominus$ is at present being investigated.

On warming or on being allowed to stand in polar solvents the dimers *(3)* dissociate into the radical cations *(2)*, which abstract H from the solvent to form compounds *(6)*[4,5]. The tendency to dissociate is far greater in the case of the alkyl-substituted derivatives *(3c)* and *(3d)* than in the case of *(3b)*.

The radical cations *(2)*, which are obviously not very stable, cannot be detected by ESR spectroscopy[6]. Evidence of their intermediate formation is, for example, formation of a green salt in the oxidation of *(1)*, R–R = $(CH_2)_4$, R^1 = H, in the presence of atmospheric oxygen to which we ascribe the structure *(5)* on the basis of elemental analysis, molecular-weight determination, and spectroscopic data [UV absorption in CH_3OH: λ_{max} = 627 nm, ε = 3300, λ_{max} = 431 nm, ε = 10680; ^{1}H-NMR spectrum in $CDCl_3$: H_α = singlet at τ = 4.69; IR absorption: ν(C=O) = 1700 cm^{-1}. Chemical proof of the structure of *(5)* has yet to be carried out.

Experimental:

a) *1,1'-Bi(2,4,6-tripyrrolidinocyclohexadienylium) pentabromocarbonate (3a)*

CBr_4 (19.9 g) is added to a solution of 1,3,5-tripyrrolidinobenzene (8.56 g) in dichloromethane (50 ml) cooled to −5 °C. The reaction mixture immediately turns deep red. The solvent is subsequently distilled off under vacuum, and the oily residue is dissolved in 30 ml of hot chloroform and filtered. After a short time 6.8 g (33%) of brick-red crystals, m.p. 176–177 °C, precipitate, which can be recrystallized (m.p. 177–178 °C) from chloroform.

b) *1,1'-Bi(2,4,6-tripyrrolidinocyclohexadienylium) perchlorate (3b)*

Pulverized $AgNO_3$ (1.7 g) is added with stirring to a suspension of 1,3,5-tripyrrolidinobenzene (2.85 g) in dimethylformamide (15 ml) under pure nitrogen at −5 °C. The deep-red reaction mixture is stirred for 10 min, filtered, and the filtrate added dropwise to 100 ml of ether. An oil separates which crystallizes on rubbing. The crystalline paste is filtered by suction, and the recovered solids are dissolved in 100 ml methanol and treated with 20 ml of a saturated aqueous $NaClO_4$ solution. Compound *(3b)* precipitates as brick-red crystals (yield 3.5 g (91%); m.p. 254–256 °C).

Received: February 5, 1969 [Z 947 IE]
German version: Angew. Chem. *81*, 261 (1969)

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Investigation of Superadditivity in Photographic Development by Current-Voltage Curves at a Silver Electrode

By *M. Brezina, W. Jaenicke*, and *H. Raithel*[*]

Mixtures of certain developers give rise to higher rates of development than the pure components (referred to the same overall molar concentration). This phenomenon, which is called superadditivity, has hitherto been investigated on the basis of measurements of the increase in density with time during the development; a complete elucidation has not yet been presented.

Since the effect also occurs on physical development of silver grains[1,2], to which the electrode theory of photographic development applies, an investigation by electrochemical methods should be possible[2]. We have studied the systems hydroquinone/1-phenyl-3-pyrazolidone (Phenidone®) and hydroquinone/*p*-methylaminophenol (metol)[3] at a stationary silver disk electrode in phosphate-, borate-, or carbonate-buffered solution in the pH range between 8 and 11.3 with and without the addition of sulfite. The current-voltage curves were recorded with a Radiometer PO4 polarograph at 400 mV/min from negative to positive potential and also in the reverse direction.

Phenidone is found to be an almost reversible redox system with a transfer of one electron per molecule, also in the presence of SO_3^{2-}. Hydroquinone is oxidized irreversibly, its overvoltage being dependent on electrode pretreatment; it decreases with the pH and increases considerably in the presence of sulfite and/or gelatine (up to 200 mV). Even the addition of very small amounts (1%) of phenidone to hydroquinone reduces the overvoltage. The height of the wave is therefore increased until hydroquinone behaves almost reversibly as the amount of phenidone increases. Even with very small concentrations of phenidone no kinetic wave of phenidone occurs. Regeneration of phenidone by hydroquinone in homogeneous phase can therefore be excluded as a cause of superadditivity. The catalytic activity of the additive must therefore be due to a heterogeneous process. Perhaps specifically adsorbed phenidone is acting as electron-transferring agent.

Metol behaves similarly to phenidone.

Acceleration of development by phenidone by addition of hydroquinone cannot be interpreted in terms of such a process. In this case it should be borne in mind that whereas phenidone is oxidized in a one-electron step, hydroquinone in the presence of sulfite can contribute four electrons per molecule; consequently, acceleration can also be observed here when phenidone is partially replaced by equimolar quantities of hydroquinone.

Received: January 2, 1969 [Z 957 IE]
German version: Angew. Chem. *81*, 293 (1969)

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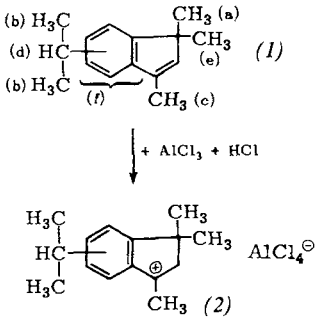
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1,1,3-Trimethylisopropylindenium Tetrachloroaluminate

By *M. Strohmeyer, K. H. Hiller*, and *K. Witte*[*]

In the propylation of a technical aromatic mixture in the presence of $AlCl_3$/HCl we have obtained 1,1,3-trimethylisopropylindene *(1)*[1] which forms 1,1,3-trimethylisopropylindenium tetrachloroaluminate *(2)* on reaction with $AlCl_3$ and HCl.

The structural determination of *(1)* and *(2)* has been largely confirmed by the NMR spectrum, from which, however, the



position of the isopropyl groups cannot be established [*(1)*: δ = 1.60 (H_a), S; 1.60 (H_b), D (J_{bd} = 7 Hz); 2.35 (H_c), D (J_{ce} = 1.4 Hz); 3.25 (H_d), sept.; 6.22 (H_e), Q; 7.42 ppm (H_f), S; *(2)*: δ = 2.10 (H_a), S; 1.97 (H_b), D; 3.96 (H_c), S; $\approx$3.8 (H_d), M; 4.42 (H_e), S; 8.42 (H_f), M; 9.13 ppm (H_f), D (J_{vic} = 9 Hz), (TMS external standard)]. Oxidation of *(1)* with chromic acid, however, leads to the formation, among other things, of terephthalic acid[2] provided that *(1)* is substituted in the *p*-position (*i.e.* on C-5 or C-6).

Reaction of indene with $AlCl_3$ and HCl does not lead to a definite complex but to polymers only. Assuming that the isopropyl group occupies position 6 in *(2)*, the formation of polymers is ascribed to the positive charge in both important boundary forms being localized on the tertiary C-atom, whilst an indenium ion shows secondary C-atoms in the corresponding positions. Moreover, the substituents can take on partial charges.

The complex *(2)* is extraordinarily stable and exhibits interesting properties as a Friedel-Crafts catalyst. We have investigated the transalkylation and the isopropylation in the presence of $AlCl_3$/HCl as well as of *(2)* at 25 °C. 99% 1,2,4-triisopropylbenzene was used for the transalkylation which, with benzene (molar ratio 1:2) mainly disproportionates to cumene, *m*- and *p*-diisopropylbenzene, as well as to 1,3,5-triisopropylbenzene. The concentration of free $AlCl_3$ and of that present in *(2)* is 0.75%.

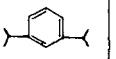
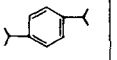
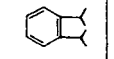
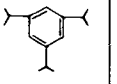
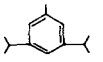
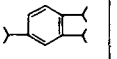
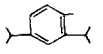
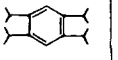
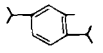
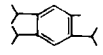
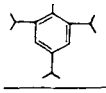
In contrast to $AlCl_3$/HCl, which consumes 1,2,4-triisopropylbenzene within an hour, the complex *(2)* shows practically no transalkylation properties. In the isopropylation of toluene and cumene under normal conditions (Table 1) the isomeric distribution of the main product is very much different in the presence of each of the two catalysts.

In experiments 1 and 3, as well as in 2 and 4, however, the *para- : meta-* ratio agrees very well. Further, it is worthy of note that we could not obtain essentially higher *p*-diisopropylbenzene and *o*-cymene values in other catalyst systems with degrees of propylation of 0.27 or 1.26. The results show that *(2)* is a much weaker isomerization catalyst than $AlCl_3$/HCl on account of its lower acidity.

1,1,3-Trimethylisopropylindenium tetrachloroaluminate (2)

8 parts by weight of propene and 30 parts by volume of HCl are added to 215 parts by weight of a technical aromatic mixture (benzene 8 parts, cumene 78 parts, *m*-diisopropylbenzene 8 parts, *p*-diisopropylbenzene 4 parts, triisopropylbenzene 2 parts) at 50–70 °C in presence of 0.5 parts by weight of $AlCl_3$. 200 g of the lower phase of the reaction mixture is treated with water; the fraction boiling below 240 °C is distilled from the organic phase. The residue is cooled to 0 °C and the crystals which separate out are filtered off and dissolved in 120 g of methanol with warming. On cooling 52 g of *(1)* (m.p. 50–51 °C) separates out. – 60 g (0.3 mole) of *(1)* is dissolved in 250 g of hexane. About 15 l of HCl is introduced per hour and 40 g (0.3 mole) of sublimed $AlCl_3$ is added slowly with vigorous stirring within 75 min at a temperature of 35–40 °C. On completion of reaction, 109 g (88%) of compound *(2)* (m.p. 78–80 °C) crystallizes out.

Table 1. Experimental conditions and results of the isopropylation.

	1	2		3	4
Aromatic cpd.	Toluene 325 g	Toluene 325 g		Cumene 239 g	Cumene 239 g
Catalyst	$AlCl_3$	*(2)*		$AlCl_3$	*(2)*
[a]	2.4 g	6.6 g		1.8 g	4.85 g
Propene (l/h)	14	14		11	11
n [b]	0.28	0.27		1.28	1.26
Composition of the propylation mixture (%)					
Propene	0.52	0.59	Propene	0.41	0.57
?	0.08	0.11	2-Methyl-pentane	–	0.20
Toluene	65.99	67.93	Benzene	1.02	–
	0.72	0.68	Cumene	64.62	73.12
	10.94	4.82		14.78	5.58
	10.50	7.75		14.02	9.18
	5.10	10.69		0.24	2.82
	trace	0.79		4.66	2.43
	3.81	2.47		0.25	3.39
	1.34	2.24		–	2.71
	0.97	0.70			
?	–	0.22			
	–	0.75			
	–	0.56			
Isomeric distribution (%) of the cymene fraction			of the diisopropylbenzene fraction		
o-	19.22	45.96	*o*-	0.82	16.04
m-	41.22	20.72	*m*-	50.89	31.74
p-	39.56	33.32	*p*-	48.27	52.21
p/m	0.96	1.61	*p/m*	0.95	1.64

[a] Corresponds to 0.75% $AlCl_3$, based on the aromatic compounds.
[b] *n* = degree of propylation = ispropyl groups per benzene nucleus.

Received: January 2, 1969 [Z 953 IE]
German version: Angew. Chem. *81*, 292 (1969)

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Coordination Chemistry

The first part of the Eleventh International Conference on Coordination Chemistry, which was sponsored by IUPAC, took place at Haifa (Israel) on September 8–12, 1968. For the first time, various selected topics were treated in plenary symposia. In this way specialized branches of research were introduced to a relatively large number of participants. An introductory lecture was followed by four papers concerned with characteristic facets of the subject, thus providing a basis for a general discussion amongst the 450 scientists (representing 30 countries) who were present.

1. Coordination Compounds in Homogeneous Catalysis

Complex compounds of transition metals occur as catalytically active intermediates in numerous processes, including some of considerable technical importance (*e.g.* hydrogenation, oxidation, polymerization, carbonylation). A number of factors responsible for the versatility of such catalyst systems were indicated in an introductory lecture by *J. Halpern* (Chicago, USA). Thus, the central metal atom may be capable of stabilizing reactive intermediates inside the coordination sphere. By way of contrast, stable molecules can be "promoted to an excited state" by coordinative bonding to the metal: an activation of this kind is assumed to occur, for example, with σ-bonded hydride or alkyl ligands, as well as with π-bonded olefins, allyl systems, or aromatic compounds. Pre-orientation of ligands in a manner specific for a particular reaction or rearrangement can occur within the coordination shell of the metal. Moreover, the metals of Group VIII are also capable of alternately adopting different oxidation numbers and of varying their number of coordinatively bound ligands.

L. Vaska (Potsdam, N.Y., USA) reported on the reversible activation of covalent molecules (H_2, O_2, SO_2, CO, C_2H_4) by addition to *trans*-$[P(C_6H_5)_3]_2Ir(CO)Cl$. The kinetic and thermodynamic data for this reversible addition in a homogeneous phase differ characteristically from those for the adsorption of a gas onto solid metal surfaces. – According to *P. Heimbach* (Mülheim/Ruhr, Germany), the central metal atom can also serve as a "template" in organic synthesis. Coupling of two butadiene molecules within the coordination sphere of nickel(0) leads to a C_8 chain, bound to nickel, which can be converted into *cis,cis*-1,5-cyclooctadiene or 1,3,7-octatriene, depending on the reaction conditions and on the concentration of additional donor ligands (amines, tertiary phosphines, or phosphites), or into 10- or 12-membered ring systems by addition of further unsaturated hydrocarbons.

The significance of homogeneous catalysis in biochemical systems was referred to by *G. L. Eichhorn* (Baltimore, USA). Biological macromolecules (proteins, porphyrin systems, nucleic acids) surround the metal ion, functioning as multidentate ligands, and often induce a high and specific reactivity at a particular coordination position of the complex.

The investigation of homogeneous hydrogenation continues to occupy a focal point of catalyst research, and a number of new catalyst systems for this reaction were presented at Haifa. Decarbonylation of organic carbonyl compounds (aldehydes, acid chlorides, acid anhydrides) by means of rhodium(I) compounds of the kind $[P(C_6H_5)_3]_3RhCl$ is becoming more and more important. Papers dealing with molecular nitrogen as a ligand in transition metal complexes were received with particular interest. *A. D. Allen* (Toronto, Canada) gave a review of metal compounds containing the grouping M–N≡N. It appears that the ruthenium(II)-pentammine system is particularly able to take up molecular nitrogen; however, N_2 complexes of Fe, Co, Ni, Os, and Ir have also been prepared. Since the coordinatively bound nitrogen cannot simply be reduced to NH_3, the technically interesting conversion of atmospheric nitrogen into ammonia remains distant music in spite of the biological example of nitrogen-reducing enzymes. According to *J. Chatt* (Brighton, England), experiments with isotope-enriched nitrogen show that even in the case of the "classical" example $[Ru(NH_3)_5N_2]^{2+}$ the hitherto assumed partial hydrogenation of the N_2 ligands by tetrahydridoborates cannot be reproduced.

2. Photochemistry in Coordination Compounds

A. W. Adamson (Los Angeles, USA) listed the possible reactions of photochemically excited complex molecules. Irradiation in the frequency range of ligand-field transitions (d→d) generally leads to substitution processes within the coordination shell, without any change in the type of complex or in the oxidation number of the central metal atom. On the other hand, excitation of the intense charge-transfer transitions in the near ultraviolet often promotes a redox process between the metal and ligand system, as for example with Co^{III} or Cr^{III}. In addition, spin-forbidden transitions can also play a role; it often appears that one and the same reaction can start from more than one excited state.

A. D. Kirk (Victoria, Canada) reported the influence of Cr^{III} complexes on the formation of I_3^- during photolysis of iodide solutions. In the reaction, the coordination compound undergoes intermediate reduction to Cr^{II} by acceptance of a hydrated electron; the actual oxidizing agent for the iodide ion is dissolved oxygen, which acts *via* secondary formation of chromium peroxide compounds or H_2O_2. *L. E. Orgel* (San Diego, USA) presented a model system in which $[Fe(CN)_6]^{4-}$ first oxidizes to $[Fe(CN)_6]^{3-}$ on ultraviolet irradiation and then is cleaved to 1/2 $(CN)_2$ and $[Fe(CN)_5(H_2O)]^{3-}$ in the presence of visible light; the resulting cyanogen may play a role in the phosphorylation of nucleosides. – Finally, *D. Valentine jr.* (Princeton, USA) described the photolytic cleavage of paramagnetic μ-peroxodicobalt(III) compounds of the type $[(NH_3)_5Co{-}O_2{-}Co(NH_3)_5]^{5+}$ and $[(NH_3)_4Co{-}(O_2, NH_2){-}Co(NH_3)_4]^{4+}$. These dinuclear complexes disproportionate in ultraviolet light to give O_2 and an equimolar mixture of octahedral Co(II) and Co(III), coordinatively unsaturated fragments such as $[Co(NH_3)_5]^{3+}$ being formulated as intermediates.

3. Kinetics and Mechanism of Reactions of Coordination Compounds

The last of the "Plenary Symposia" was opened by *M. Eigen* (Göttingen, Germany) with a lecture on the stability and dynamics of many complexes involving ions of the main groups in inert-gas configurations, which play a part in biological mechanisms of transport and activation. The competing complex formation of these ions often shows specific differences in formation- and rate constants, which are exploited in Nature, as, for example, with the pairs Mg^{2+}/Ca^{2+} and Na^+/K^+. *G. Schwarzenbach* (Zürich, Switzerland) went into investigations on the deprotonation of hydrated metal cations and subsequent condensation to multinuclear complexes which characterize the first steps of a neutralization reaction (with NaOH). It proved possible to obtain excellent pK_1 values in a number of cases (Be^{2+}, Cr^{3+}) by means of rapid pH measurements. – The rate of chelate formation

with diamine ligands, the subject of the paper presented by *J. Bjerrum* (Copenhagen, Denmark), was also determined with the aid of pH measurements. In the *trans*-$[(NH_3)-PtCl_2-NH_2(CH_2)_nNH_2]$ system, the stable five-membered ring incorporating ethylenediamine ($n = 2$) is formed about 100 times as fast as the corresponding six-membered ring with trimethylenediamine ($n = 3$).

M. Anbar (Rehovot, Israel) reported on the reaction of a large number of transition metal complexes with hydrated electrons. The rate of this process depends on the nature and on the oxidation number of the central metal atom, as well as on the ligands; in many cases the process is diffusion controlled. Since the activation energy invariably lies below 4 kcal/mole, a tunnel mechanism was suggested for the transfer of the electron to the central metal atom.

The second part of the Eleventh ICCC took place on September 16–18, 1968, at Jerusalem. The subjects dealt with were: Coordination compounds in solvent extraction (in conjunction with the 5th International Conference on Solvent Extraction Chemistry), and coordination compounds in non-aqueous solvents.

4. Coordination Compounds in Non-aqueous Solvents

A. I. Popov (East Lansing, Mich., USA) reported on IR-spectroscopic investigations of alkali metal and ammonium salts in various solvents (dialkyl sulfoxides, 2-pyrrolidone derivatives, tributyl phosphate, pyridine). In all cases a band was observed between 450 and 200 cm^{-1} whose frequency is characteristic of the cation and of the solvent but not of the anion. The extinction of this band is proportional to the concentration of the cation and independent of the concentration of anions. Solid solvates of alkali metal salts with dimethyl sulfoxide (DMSO) of various stoichiometric ratios (1–4 moles of DMSO per metal ion) exhibit spectra similar to those of the corresponding solutions. It is concluded that the observed band is due to the vibration of the solvated cation in the solvent cage. NMR investigations on lithium salt solutions in DMSO indicate the existence of a definite solvate $Li(DMSO)_2^+$ whilst in the case of sodium and ammonium salts, although there is considerable interaction with the solvent, no definite stoichiometry is indicated.

The donor number (DN) introduced by *V. Gutmann* (Wien, Austria) affords a measure of the solvent properties of a donor solvent. It is defined as the negative reaction enthalpy for the reaction between a donor solvent and antimony pentachloride in the gas phase. The ability of the solvent to ionize dissolved salts increases with increasing donor number, while the formation of complex compounds with competing ligands becomes more difficult. This relationship has been studied by means of the formation of halogeno- and pseudohalogeno complexes of divalent cobalt of the type $[CoX_4]^{2-}$ ($X^- = Cl^-$, Br^-, I^-, NCS^-, N_3^-) in various solvents.

The formation of mixed cadmium-nitrate-halide complexes by addition of a cadmium halide to a eutectic lithium nitrate/potassium nitrate melt was discussed by *M. Zangen* (Yavne, Israel) who studied the distribution of cadmium between the salt melt and a eutectic polyphenyl mixture at 150 to 200 °C. From the measurements it was concluded that the melt contained all the species of the type $[CdX_n(NO_3)_{4-n}]^{2-}$ (X = Cl, Br, I; $n = 0,1,..,4$), of which only the dihalide ($n = 2$) – after loss of the two nitrate ions – can distribute between the two phases. Further, it was shown that the complex $[CdXX'(NO_3)_2]^{2-}$ which forms on addition of two halide ions is considerably more stable than the corresponding zinc or mercury complex.

5. Solvent Extraction: Fundamental Studies

Extraction of metals by organic compounds has frequently been used to gain information concerning the complexes present in the aqueous or in the organic phase. In such investigations the dependence of the distribution coefficient on the concentration of the extractant and of the anions in the aqueous phase is followed. However, a lecture by *Y. Marcus* (Jerusalem, Israel) on "mass action law and non-ideality in solvent extraction systems" pointed out that much care is needed in the interpretation of such data. For example cryoscopic and osmometric studies show that dialkyl hydrogen phosphates, $(RO)_2P(O)OH$, dimerize in organic solvents *via* hydrogen bonding. In the case of sulfonic acids, such as dinonylnaphthalenesulfonic acid, association to even higher aggregates is observed. Long chain alkylammonium salts are likewise associated in nonpolar organic solvents, and to some extent dimerization is even observed with neutral phosphoric acid esters such as tributyl phosphate. An increase in the concentration of the extractant often leads to a change in the polarity of the organic phase. Variation of the composition of the aqueous phase can lead to a change in the water activity and as a consequence to a change in the concentration of the water extracted into the organic phase. The same is true for the extraction of acids by the extractant. In view of these many deviations from ideal behavior the question which now in fact remains open is: why does the partition coefficient so frequently vary with an integral power of the concentration?

A number of communications were concerned with studies on the association of long chain alkylammonium salts in nonpolar solvents. *E. Högfeldt* has employed the two-phase EMF titration for the computer calculation of association constants. *O. Levy* (Jerusalem, Israel) reported on measurements of the dielectric constants of tertiary and quaternary ammonium salts in benzene. The dipole moments of the monomeric salts and the dimerization constants were calculated using the equations by *Fuoss et al.* and by *Bange et al.* The association constants obtained by these two methods were in good agreement but were lower than those calculated from vapor-pressure measurements. *G. Scibona* (Rome, Italy) has investigated the extraction of zinc chloride with trilaurylammonium chloride/benzene solutions. The association constants of the species occurring in the organic phase can be calculated from partition data and from parallel measurements of the vapor pressure lowering. *D. Gourisse* (Fontenay-aux-Roses, France) has studied third phase formation in the extraction of nitric acid and of thorium nitrate with trilaurylamine. Light scattering measurements showed that in both cases the particle size greatly increases shortly before third phase formation starts. In many systems a splitting into two phases was observed after 5 hours' ultracentrifugation at an average gravitational field of 10^5 g, whereas no third phase appeared under normal gravitation. It is assumed that the formation of the second organic phase is due to the coalescence of amine salt micelles.

A comprehensive report on the coordination compounds which are responsible for synergistic effects was given by *T. V. Healy* (Harwell, England). The word "synergism" denotes the enhancement of metal extraction by a mixture of two extractants compared with extraction by each of the extractants alone. The effect was first observed in the extraction of uranium by mixtures of dialkyl hydrogen phosphates and trialkyl phosphates and was later confirmed with numerous other tetra- and trivalent metals with such extraction systems. Here the synergism is due to the formation of an adduct of the neutral donor molecule with the metal dialkyl phosphate complex in the organic phase. Another mechanism was observed in the extraction of alkali metals by bis(2-ethylhexyl) hydrogen phosphate (HDEHP) in the presence of substituted phenols (S). In the synergistic complex $MS_4(DEHP)$ the phenol molecule occupies the first coordination sphere; the $DEHP^-$ anion is presumably bound to a phenol. In the extraction of numerous metals with β-diketones, such as thenoyltrifluoroacetone (TTA), synergistic effects were observed with donor molecules such as trialkylphosphates, ketones, amides, and alcohols. In many cases the donor molecule is bound directly to the metal, often with substitution of water molecules. In the case of alcohols, however, there is indication of bonding to the β-diketone.

F. Baumgärtner (Karlsruhe, Germany) reported on the kinetics of extraction and back-extraction of uranium(VI) and plutonium(IV) by tributyl phosphate (TBP). Contrary to the older view that the kinetics of extraction is controlled by diffusion, measurements on drops showed the participation of one or more "interfacial complexes" in the rate-determining step. The formation of such a complex at the interface between the two liquid phases can be described by the Langmuir adsorption-desorption theory if one considers that adsorption and desorption may take place from both sides of the interface. From the kinetic data the following picture of the extraction mechanism may be drawn: As soon as the metal enters the interface in ionic or neutral form it belongs to the interfacial complex; the latter successively adds TBP molecules from the organic phase and NO_3^- ions from the aqueous phase, there being no indication of the sequence of this addition. When the coordination shell of the complex is complete, the complex can be desorbed into the organic phase. However, since all the steps taking place at the interface are reversible, it is also possible that the interfacial complex is re-desorbed into the aqueous phase. Furthermore, exchange reactions can take place between the interfacial complexes. Back-extraction from the organic into the aqueous phase can be described in an analogous fashion.

6. Solvent Extraction: Technical Applications

The most important application of liquid-liquid extraction in recent years has been the processing of spent nuclear fuels in which uranium and plutonium are separated from fission products by extraction with tributyl phosphate (TBP) from nitric acid solution (Purex process). In the processing of fuels with high plutonium concentrations (in particular those from fast breeder reactors), the concentrations of uranium and plutonium change in each stage of the multi-stage Purex process, and since each of the two metals influences the extraction of other, the distribution coefficients are also altered in each stage. Consequently, optimization of the process by calculation is difficult. *W. Ochsenfeld* (Karlsruhe, Germany) now reported on the development of empirical functions for the calculation of the distribution coefficients in the system $Pu(NO_3)_4$–$UO_2(NO_3)_2$–HNO_3–TBP–*n*-dodecane. The equilibrium "constants" for the extraction equilibrium

$$M^{n+} + n\,NO_3^- + a\,TBP \rightleftharpoons M(NO_3)_n\,(TBP)_a$$

$$\tilde{K}_M = \frac{[M(NO_3)_n\,(TBP)_a]}{[M^{n+}]\,[NO_3^-]^n\,[TBP]^a}$$

was expressed as a function of the total ionic strength μ:

$$\tilde{K}_{Pu} = 12.163 - 9.033\,\mu + 2.230\,\mu^2 - 0.163\,\mu^3$$

$$\tilde{K}_U = 8.791 + 6.071\,\mu - 6.176\,\mu^2 + 1.579\,\mu^3$$

These functions describe the extraction in the concentration range 20–30 vol-% TBP, 0.1–0.6 mole/l U^{VI}, 0.01–0.2 mole/l Pu^{IV}, 0.6–3.0 mole/l HNO_3 with good accuracy.

The extractant TBP suffers considerable radiation damage, particularly in the processing of highly burnt fuels. Zirconium is particularly well extracted by the degradation products of the TBP, so that the decontamination factors for this fission product are strongly reduced. As *P. Faugeras* (Fontenay-aux-Roses, France) pointed out, the coextraction of zirconium can be suppressed by addition of small amounts (10^{-3} to 10^{-2} mole/l) of fluoride ions. The separation of the fission product ruthenium was also improved at the same time. In this way, decontamination factors of $> 10^5$ for Zr and $> 10^4$ for Ru could be demonstrated with solutions containing up to 10^3 Ci/l fission product activity.

In the extraction of the lanthanides by TBP, the distribution coefficient is not a monotonic function of the atomic number, but deviations occur in the Gd-Dy region. *D. G. Karracker* (Aiken, S.C., USA) showed, by spectroscopic investigations, that this is due to a change in the coordination number of the extracted complexes $Ln(NO_3)_3(TBP)_3$ (Ln = lanthanide). The band shape of the hypersensitive transitions in these $Ln(NO_3)_3(TBP)_3$ complexes suggests a coordination number of 8 for Nd^{3+}, 6 for Er^{3+}, and 6 or 7 for Ho^{3+}. Corresponding results were obtained with different trialkyl phosphates and with tri-*n*-amylphosphine oxide as ligands. ^{31}P- and ^1H-NMR spectra strongly confirm these conclusions, while the Raman spectra seem to indicate bidentate bonding of the nitrate ions, also in the case of the heavy lanthanides.

Ce^{III}, like all trivalent lanthanides, is extracted by bis(2-ethylhexyl) hydrogen phosphate (HDEHP). As *L. A. Bray* (Richmond, Wash., USA) has observed, Ce^{III} is oxidized to Ce^{IV} during washing of the organic phase with a concentrated (6 to 7 M) nitrate solution. Likewise, Ce^{III} is oxidized to Ce^{IV} when it is extracted from concentrated nitrate solutions. Oxidation is complete within 30 sec and proceeds equally fast both in air and in an argon atmosphere. However, if a nitrite "scavenger" such as sulfamic acid is added, the rate of oxidation is considerably reduced. Evidently the nitrous acid (or one of its reaction products) acts as a catalyst in the oxidation. The above effect is significant in the separation of cerium from the other lanthanides.

A flow scheme for the isolation of the transplutonium elements americium and curium from highly radioactive Purex waste solutions was developed by *G. Koch* (Karlsruhe, Germany). Americium, curium, and the lanthanides are extracted by HDEHP from the citrate-complexed aqueous phase. Americium and curium are partitioned away from the rare earths by selective back-extraction of the actinides by an aqueous solution, which is 1 M in lactic acid and 0.05 M in sodium diethylenetriaminepentaacetate and is adjusted to a pH of *ca.* 3. The flow sheet was tested with weakly active synthetic solutions and gave good decontamination factors for lanthanides, zirconium, niobium, ruthenium, and iron. Kinetic experiments showed that in the case of several elements, the extraction kinetics plays a dominant role in the purification effect. For example, on the basis of equilibrium distribution coefficients iron(III) would be expected to accompany the actinides, but since the extraction as well as the back-extraction are slow, a good separation from iron is accomplished in the countercurrent process.

The extraction of lanthanides as tartrate or malonate complexes by long chain primary amines has been studied by *D. Kuiper* (Delft, Netherlands). Tartaric and malonic acid (H_2L) are extracted by the amine (A) as $(AH)_2L$ at lower acid concentrations and as (AH)HL at higher acid concentrations. The distribution coefficients of the lanthanides increase with increasing $(AH)_2L$ concentration and decrease in the presence of (AH)HL. By a series of different experiments the composition of the extracted complexes was found to be $(AH)_5LnL_4$.

German version: Angew. Chem. *81*, 262 (1969) [VB 187 IE]

Metabolic Transformation of Antimalarial Drugs as a Basis for the Development of New Active Substances

By *P. Nickel* [*]

The last 20 years have seen considerable progress in malaria therapy; nevertheless, the disease still presents a very serious problem in many tropical countries. The increasing occurrence of cases of therapy-resistant malaria in South America, and above all in Southeast Asia, in recent years has provided new impetus to the search for effective antimalarials.

During metabolism, the chinchona alkaloids are hydroxylated at C-2 of the quinoline ring, thereby losing their antimalarial

activity. This hydroxylation is hindered and the activity of the alkaloids increased by the presence of substituents, especially phenyl. Owing to toxic side-effects, however, no representative of this much-investigated class of compounds has yet found application in therapy.

The activity of Plasmochin® [8-(4-diethylamino-1-methylbutylamino)-6-methoxyquinoline] must be due to a metabolite since the substance itself is inactive *in vitro*. As long ago as 1942, *Schönhöfer* suspected that quinoid forms were responsible for the activity, which was later confirmed by the discovery of the highly effective metabolite 8-(4-diethylamino-1-methylbutylamino)-5,6-dihydroquinoline-5,6-dione.

The assumption that a similar mode of action could apply to the 6-aminoquinolines led to the discovery of the extremely effective, yet highly toxic, 6-(4-diethylamino-1-methylbutylamino)-5,8-dimethoxyquinoline (*Schönhöfer* and *Schulemann*, 1961). Our investigations of the effects of substituents on the antimalarial activity of this compound indicate a certain similarity to the state of affairs with 8-aminoquinolines.

Proguanil [N^1-(*p*-chlorophenyl)-N^5-isopropylbiguanide] is also inactive *in vitro*; 2,4-diamino-5-(*p*-chlorophenyl)-6,6-dimethyl-5,6-dihydro-1,3,5-triazine (known as cycloguanil) was isolated as active metabolite in this case. Since this compound is rapidly excreted, it is not very effective in humans. However, an intramuscular injection of a difficultly soluble salt of the metabolite does provide protection against infection for a period of several months. Its activity is attributed to inhibition of dihydrofolic acid reductase.

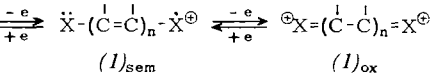
Lecture at Erlangen on January 17, 1969 [VB 189 IE]
German version: Angew. Chem. *81*, 295 (1969)

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Reversible Redox Systems with Stable Radical Cations

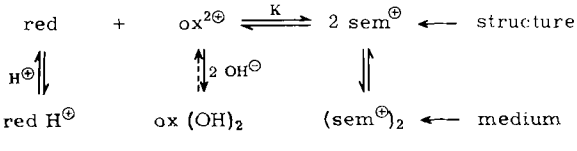
By *S. Hünig* [*]

In principle, compounds of the general formula *(1)* can exist in three oxidation states that are related by two one-electron transfers [1]. Whether the radical ion $(1)_{sem}$ can be detected

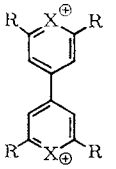


$(1)_{red}$ $(1)_{sem}$ $(1)_{ox}$

or isolated depends both on its thermodynamic stability, which can be expressed as $K = [sem^{\oplus}]^2/[red]\,[ox^{2\oplus}]$, and on the reactivity of each of the three components towards the medium.



K is determined polarographically from the redox potentials and in the cases studied amounts to $\sim 10^3$–10^9, depending on the structure of the compound *(1)*. This lecture was confined to compounds of the Weitz type *(2)* (X = N–CH_3) [2] and variations thereof. For example, introduction of *O (3)* or *S (4)* both lead to stable radical ions which have fully resolved EPR spectra and dimerize reversibly at higher concentrations in CH_2Cl_2. Nucleophiles remove $ox^{2\oplus}$ irreversibly, so that complete disproportionation occurs. The systems *(5)* to *(7)* show the same value $\sim 10^3$ for *K*. However, with the

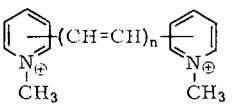


R = H, CH_3, C_6H_5

(2)$_{ox}$, X = N–CH_3

(3)$_{ox}$, X = O

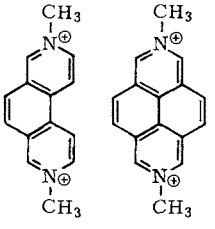
(4)$_{ox}$, X = S



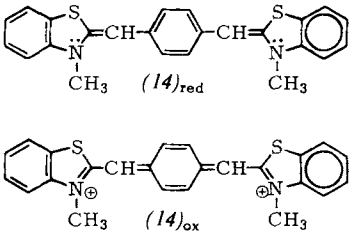
n = 1: *(5)*, 2,2'; *(6)*, 2,4'; *(7)*, 4,4'; *(8)*, 2,3'; *(9)*, 4,3'; *(10)*, 3,3'

n = 3: *(11)*, 4,4'

'*meta*'-derivatives *(8)*–*(10)* the second reduction step is irreversible. Prolongation of the vinylene chain as in *(11)* rapidly reduces *K*, but the vinylene bridges in *(12)* and *(13)* have hardly any influence. The methine groups in *(1)* can be partly or wholly replaced by phenylene groups or N atoms;

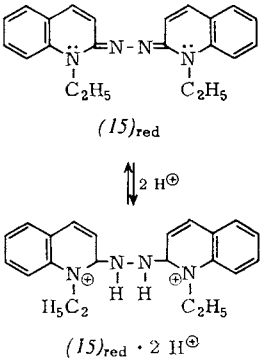


(12)$_{ox}$ *(13)*$_{ox}$



(14)$_{red}$ *(14)*$_{ox}$

for example, the species *(14)* that is known [3] in the reduced and the oxidized form, comproportionates to the stable green radical ion $(14)_{sem}$. The system *(15)*, which can also be isolated in all three oxidation states, forms a very stable radical ion, which disappears reversibly on addition of acid owing to disproportionation to $(15)_{ox}$ and $(15)_{red} \cdot 2\,H^{\oplus}$.



(15)$_{red}$

(15)$_{red} \cdot 2\,H^{\oplus}$

Lecture at Münster (Germany) on January 13, 1969
German version: Angew. Chem. *81*, 295 (1969) [VB 186 IE]

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[1] *S. Hünig*, Liebigs Ann. Chem. *676*, 32 (1964); Pure appl. Chem. *15*, 109 (1967).

[2] Only the formula of the compound introduced in the experiment is reproduced.

[3] *A. J. Kiprianov* and *M. Yu. Kornilov*, Ž. obšč. Chim. *31*, 1699 (1961).

Physical and Chemical Probes for Enzyme Conformation

By *G. K. Radda*

The response of bovine liver glutamate dehydrogenase (GDH) to allosteric inhibitors has been examined by a variety of methods.

8-Anilino-1-naphthalenesulfonate is a convenient probe for the conformational equilibria in the enzyme, which depend on the allosteric ligand GTP and coenzyme NADH, since the fluorescence of the bound dye is sensitive to the physical state of the protein[1]. The same system has been used to measure the rates of allosteric transitions. By fast reaction techniques these were shown to be biphasic, each phase representing some structural transitions in the enzyme with half-lives of 20 and 200 msec[3].

GDH can be desensitized by the modification of one tyrosine residue per subunit (M.W. 52000) without any effect on its activity. The same results are obtained when modification involves nitration by tetranitromethane or *O*-acetylation by *N*-acetyl imidazole.

The reaction of GDH with 2,4,6-trinitrobenzenesulfonate has been analyzed in terms of reaction rates of amino groups of different reactivities[3] of which one group per subunit reacts particularly fast and is involved both in the catalytic and allosteric properties of the enzyme. When this group reacts the allosteric response is lost considerably faster than is the catalytic activity[4]. This phenomenon is more clearly demonstrated when the enzyme is inactivated by an active site directed irreversible inhibitor [4-(iodoacetamido)salicylic acid]. Amino acid analysis and spectral and fluorescence data show that this inhibitor reacts with up to 5.4 SH groups per oligomer (M.W. 310000).

A mathematical theory (based on the binomial theorem) is proposed which accounts for the observations[5] in terms of the response of individual subunits to GTP by the sequential model of *Koshland et al.*[6]. All these observations were incorporated into a physical model for the regulatory properties of GDH which required conformational changes in the subunits followed by a rearrangement of the subunits into a different geometry. Further support for this model was obtained from electron microscopic studies of the two forms of GDH.

Lecture at Konstanz (Germany) on November 21, 1968
German version: Angew. Chem. *81*, 296 (1968) [VB 190 IE]

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[1] *G. H. Dodd* and *G. K. Radda*, Biochem. biophys. Res. Commun. *27*, 500 (1967).

[2] *G. H. Dodd* and *G. K. Radda*, Biochem. J. *108*, 5P (1968).

[3] *R. B. Freedman* and *G. K. Radda*, Biochem. J. *108*, 383 (1968).

[4] *R. B. Freedman* and *G. K. Radda*, Biochem. J. *108*, 5P (1968).

[5] *A. D. B. Malcolm* and *G. K. Radda*, Nature *219*, 947 (1968).

[6] *D. E. Koshland jr.*, *G. Nemethy*, and *D. Filmer*, Biochemistry *5*, 365 (1966).

Transmitter Mechanisms in Isolated Neurons

By *E. Giacobini*[*]

New quantitative microchemical techniques for the measurement of enzyme activity, metabolites, and transmitters in single nerve cells have become available recently. Several enzymes related to the metabolism of transmitters can now be studied with high precision and accuracy in individual neurons.

The cell population in the L7 ganglion of the cat has been used as a model to study the correlation between chemistry and pharmacology of autonomic neurons. Both cholinergic fibers (sweat secretor and vasodilator) and adrenergic fibers (vasoconstrictor) originate from this ganglion. The activity of several enzymes [acetylcholinesterase (AChE), cholineacetylase (ChAc), and monoamine oxidase (MAO)] as well as monoamines have been studied in the total ganglion, in single cells, and in subcellular fractions.

The results obtained by these analyses show that the sympathetic ganglia of the cat contain two distinct cell populations; firstly, a "cholinergic" population, representing in L7 about 10–15% of the ganglion cells. This population is characterized by the presence of ChAc, high concentrations of AChE, and the absence of monoamine fluorescence and MAO activity. The second is an "adrenergic" population, about 72–88% of the ganglion cells. It exhibits fluorescence for noradrenaline and MAO activity and contains low or moderate AChE activity and no measurable ChAc activity.

In the sympathetic ganglia of the cat the level of AChE and ChAc is well correlated when the ganglion is regarded as a whole; however, the AChE-containing neurons are much more numerous than the ChAc-containing neurons. ChAc is localized mostly preganglionically in the nerve terminals whereas AChE is localized both pre- and postganglionically. The postganglionically localized AChE is present not only in the postsynaptic membrane but in the cell body and in the postganglionic fibers as well. These enzymes are also highly concentrated in the postsynaptic terminals. AChE therefore has a more "diffuse" distribution than ChAc. Actually AChE is present also in "adrenergic" neurons while ChAc is probably restricted to "cholinergic" neurons. The presence of AChE in the neuron does therefore not represent an indication that the neuron is "cholinergic".

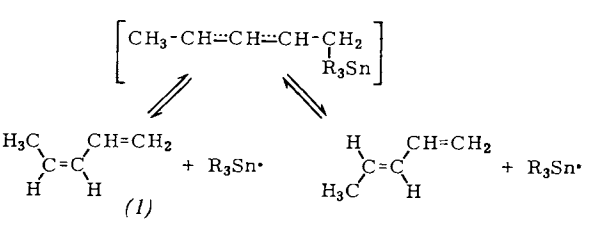
Lecture at Göttingen (Germany) on November 18, 1968
German version: Angew. Chem. *81*, 296 (1969) [VB 191 IE]

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Reactions of Organotin Radicals

By *W. P. Neumann*[*]

The first synthesis of an organotin compound, which was carried out as long ago as 1849 by *E. Frankland*, who prepared $(C_2H_5)_2SnI_2$ from C_2H_5I and elemental zinc, obviously involved a free-radical reaction. 100 years were to pass, however, before renewed interest was directed toward organotin radicals[1]. Much more accurate information about such radical reactions was afforded by investigations on the course of the free-radical hydrostannation of olefins. Depending on the type of olefin, the first step can be reversible as *e.g.* is shown in the case of pure *cis*-piperylene (1,3-pentadiene) *(1)*.



(1)

From experiments, three generally valid conclusions can be drawn:

1. Organotin radicals are formed easily by abstraction of hydrogen from organotin hydrides. The Sn–H group is an unusually strong radical scavenger and in all cases investigated (C-, alkoxy-, acyloxy-radicals) is superior to radical scavengers such as thiols and far superior to hydroquinone.

2. Organotin radicals are very useful and very mild reagents. They add selectively to unsaturated systems such as C=C-, C≡C-, or N=N groups, enter into numerous free-radical reactions, and are of great use in the elucidation of free-

radical reaction mechanisms *e.g.* in peroxides and azo compounds[2]. They are strongly nucleophilic.

3. In the absence of other reaction partners at temperatures below 150 °C, the organotin radicals $R_3Sn^{\bullet}$ (R = CH_3, C_2H_5) do not usually decompose but rather dimerize irreversibly to hexaalkyl distannane.

Discussion of further possibilities of occurrence and reaction of organotin radicals requires a knowledge of the dissociation energies of covalent bonds to the tetrahedral tin atoms; only few such values are as yet known (Ref.[1,3] and recent results obtained in our laboratory by partial calculation from known mass spectrometric appearance potentials of $R_3Sn^{\oplus}$) and are given in Table 1.

Table 1. Dissociation energies, *D*, of $(CH_3)_3Sn-X$

X	*D* (kcal/mole)
CH_3	55
C_2H_5	50
$CH=CH_2$	60
$CH_2-CH=CH_2$	≈37
$CH_2=C_6H_5$	39
C_6H_5	63
$Sn(CH_3)_3$	57
H	≈35
NR_2	(≈65 to 70)
O–COR′	≈95
Cl	≈85
Br	76
I	62

Not only Sn–H but also Sn–C bonds are cleaved under the influence of light of $\lambda \leqq 400$ nm ($\geqq 70$ kcal) and can thereby initiate such reactions. Sensitizers are, of course, necessary since most organotin compounds only absorb measurably below 250 nm. These values are of significance in the photochemistry of organotin compounds, a topic that is still in its infancy.

Lecture at Frankfurt/Main on November 14, 1968
German version: Angew. Chem. *81*, 296 (1969) [VB 188a IE]

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[1] For a review see: *W. P. Neumann*: Die Organische Chemie des Zinns. Enke-Verlag, Stuttgart 1967.

[2] *W. P. Neumann, K. Rübsamen, Ra. Sommer*, and *U. Frommer*, Chem. Ber., in press; *W. P. Neumann, H. Lind*, and *G. Alester*, *ibid. 101*, 2845 (1968); further literature cited therein.

[3] *H. A. Skinner*, Advances Organometallic Chem. *2*, 49 (1964).

X-Ray Structural Analysis of Alkylthiostannic Acids (Monoalkyl Sesquisulfides)

By *C. Dörfelt, E. F. Paulus*, and *H. Scherer*

Alkylthiostannic acids are obtained by the reaction

$$n\ RSnCl_3 + 1.5\ n\ Na_2S \rightarrow (RSnS_{1.5})_n + 3n\ NaCl.$$

The empirical formula $(RSn)_2S_3$[1] and the structural formula R–Sn(S)–S–Sn(S)–R[2] are given in the literature. We, and other research workers[3], have suggested double the molecular weight.

In order to clarify the problem we have carried out a three-dimensional X-ray structural analysis[4] on the methyl compound.

The methyl compound crystallizes monoclinically with $a = 9.768$ Å; $b = 17.39$ Å; $c = 10.96$ Å; $\beta = 109°$. Systematic extinctions yield the space group C2/c or Cc. Four units having the empirical formula $(CH_3Sn)_4S_6$ are present in the unit cell (1767 Å^3). Symmetry properties of the Patterson synthesis calculated on the basis of 1424 reflections permit only the space group C2/c: The molecule has a two-fold symmetry axis; the tin atoms, whose coordination was obtained from the Patterson synthesis, occupy a normal position; the empirical formula $(CH_3Sn)_4S_6$ is confirmed.

Successive Fourier syntheses furnished also the positions of the sulfur and the carbon atoms. Further refinement of the results by the least squares method has not yet been carried out. Methylthiostannic acid has an adamantane-like structure, in which the adamantane skeleton is made up of tin and sulfur atoms. The tin atoms occupy the corners of the tetrahedron, the sulfur atoms the corner of an octahedron including the tin tetrahedrons, and the carbon atoms of the methyl group are situated on the corners of a tetrahedron that surrounds the sulfur octahedrons. The tin-tin bond length is 3.8 Å, the tin-sulfur bond length 2.35 Å, and the tin-carbon bond length 2.1 Å.

Contrary to former representations of the structure we suggest a single bond rather than a double bond to be present between the tin and sulfur

Lecture at Frankfurt/Main on November 14, 1968
German version: Angew. Chem. *81*, 297 (1969) [VB 188b IE]

[*] Dr. C. Dörfelt, Dr. E. F. Paulus, and Dr. H. Scherer
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[1] *P. Pfeiffer* and *R. Lehnardt*, Ber. dtsch. chem. Ges. *36*, 3027 (1903).

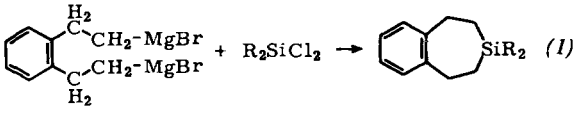
[2] *A. Tchakirian* and *P. Bevillard*, Bull. Soc. chim. France *1950*, 1300.

[3] *M. Komura* and *R. Okawara*, Inorg. nuclear Chem. Letters *2*, 93 (1966).

[4] *C. Dörfelt, A. Janeck, D. Kobelt, E. F. Paulus*, and *H. Scherer*, J. organometallic Chem. *14*, P22 (1968).

SELECTED ABSTRACTS

6,7,8,9-Tetrahydro-5*H*-benzo[*d*]silepins *(1)*, a new class of compounds, have been synthesized by *L. Birkofer* and *E. Krämer*. 7,7-Disubstituted members of this series were obtained by reaction of the Grignard compound derived from



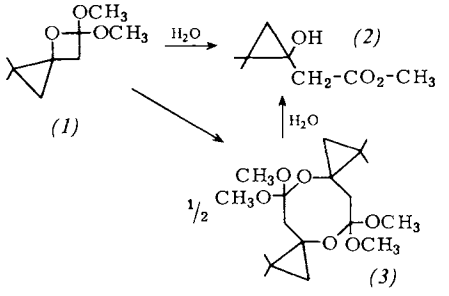
(1)

1,2-bis(β-bromoethyl)benzene with disubstituted dichlorosilanes. Bromination of the 7,7-dimethyl derivative with *N*-bromosuccinimide led by way of hetero-ring opening to 1,2-divinylbenzene, whereas reduction of the 7,7-dichloro derivative by $LiAlH_4$ afforded the parent compound *(1)*, R = H (b.p. 104 °C/12 torr, m.p. 9–10 °C). / Chem. Ber. *102*, 427 (1969) / –Ma. [Rd 970 IE]

The reaction of acetylenes with difluoroamine has been studied by *K. Baum*. 3-Hexyne was found to give 3-hexanone, 3,3-bis-(difluoroamino)hexane, 3-difluoroamino-3-fluorohexane, and *N*-(α-difluoroaminopropyl)propionamide when the reaction was catalyzed by the BF_3 complex of phosphoric acid. Similarly, 1-hexyne afforded 2-hexanone, 2,2-bis(difluoroamino)-hexane, 2-difluoroamino-2-fluorohexane, and *N*-(difluoroaminomethyl)valeramide. When H_2SO_4 was used as catalyst, 3-hexyne, 1-hexyne, and propargyl chloride yielded 3,3-, 2,2-

bis(difluoroamino)hexane, and 1-chloro-2,2-bis(difluoroamino)propane, respectively. The reactions were carried out at the boiling temperature of difluoroamine, *i.e.* −23 °C; they probably proceed *via* vinyldifluoroamine compounds. / J. Amer. chem. Soc. *90*, 7089 (1968) / −Ma. [Rd 973 IE]

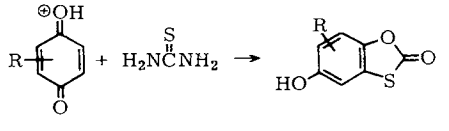
Reaction of 2,2-dimethylcyclopropanone and 1,1-dimethoxyethylene leads, according to *N. J. Turro* and *J. R. Williams*, to the formation of a novel ortho ester *(1)*, the first of its kind containing a four-membered ring (yield 90%). Treatment of *(1)* with water gives *(2)*. Both compounds decompose on



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

standing for several hours. If compound *(1)* is kept in hexane for two weeks, an unusual dimerization occurs to yield compound *(3)* (yield 39%). Compound *(3)* also affords *(2)* on treatment with water. / Tetrahedron Letters *1969*, 321 / −Ma. [Rd 974 IE]

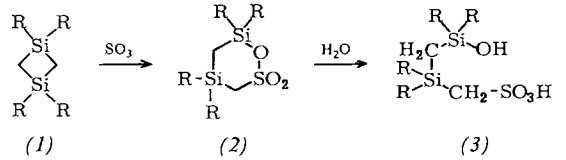
A single-step synthesis of 5-hydroxybenz[*d*]—[1,3]oxathiol-2-ones *(2)* is reported by *P. T. S. Lau* and *M. Kestner*. A large variety of derivatives of *(2)* can be prepared in excellent yields from quinones and an excess of thiourea on heating in aqueous HCl and acetic acid. Good results are also obtained with H_2SO_4 or trifluoroacetic acid. The reaction probably proceeds *via* addition of thiourea to the protonated quinone *(1)*,



(1) *(2)*

thus forming an *S*-(2,5-dihydroxyaryl)thiuronium salt, which cyclizes to 5-hydroxybenz[*d*]-[1,3]oxathiol-2-imine; hydrolysis of this compound affords compounds *(2)*. / J. org. Chemistry *33*, 4426 (1968) / −Ma. [Rd 975 IE]

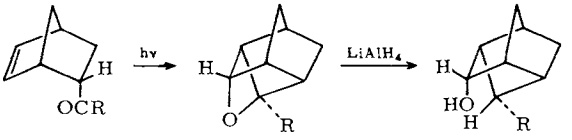
Ring expansion by insertion of SO_3 has been observed by H. *Schmidbauer*, *L. Sechser*, and *M. Schmidt* for 1,1,3,3-tetramethyl-1,3-disilacyclobutane *(1)*, which is converted into 2,2,4,4-tetramethyl-1-oxa-2,4-disila-6-thiacyclohexane 6,6-dioxide *(2)*, m.p. 35–37 °C, yield 96%, in the process. Insertion



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

of SO_3 into metal-carbon bonds is already known. Compound *(2)* is decomposed to a hydroxysilylsulfonic acid *(3)* on treatment with water. / Chem. Ber. *102*, 376 (1969) / −Kr. [Rd 983 IE]

The photocyclization of 5-acylnorbornenes is the subject of a report by *R. R. Sauers*, *W. Schinski*, and *M. M. Mason*. On irradiation in oxygen-free benzene, the *endo*-isomer *(1)*, like other γ,δ-unsaturated ketones, is converted into the tricyclic "oxetane" *(2)*, whereas the *exo*-isomer resinifies instead of undergoing the expected sigmatropic rearrangement. Reductive cleavage of *(2)* yields the secondary alcohol tricyclo-

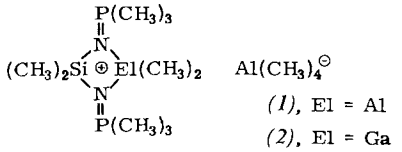


(1) *(2)* *(3)*

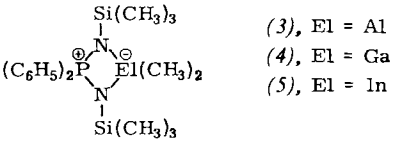
[3.3.0.0^{3,7}]octan-2-ol *(3)* which is readily converted into the ketone and other derivatives. Examples: *(2)*, R = CH_3, b.p. 60 °C/10 torr; *(2)*, R = $C_6H_5CH_2$, b.p. 89–91 °C/0.75 torr; *(3)*, R = H, m.p. 134–135 °C; *(3)*, R = α-naphthol, m.p. 174–175 °C./Tetrahedron Letters *1969*, 79 / −Kr. [Rd 984 IE]

Esters of fluorosulfinic acid with lower alcohols (alkyl fluorosulfites) FS(O)OR have been prepared by *F. Seel*, *J. Boudier*, and *W. Gombler* by distillation of the corresponding ester of chlorosulfinic acid with potassium fluorosulfite in an apparatus made of materials resistant to fluorosulfinic esters (*e.g.* polytetrafluoroethylene). *Zappel*[1] had already used this method (using glass apparatus) to prepare the 1-ethoxycarbonylethyl ester of fluorosulfinic acid. The esters have an unpleasant odor, are thermally highly stable, and react with water to give HF, SO_2, and ROH. Methyl fluorosulfite reacts with trimethylamine to give $[N(CH_3)_4]SO_2F$ and with Lewis acids such as BF_3 to give $[OSOCH_3]^{\oplus}[BF_4]^{\ominus}$, which decomposes to SO_2, CH_3F, and BF_3. Methyl fluorosulfite decomposes powdered glass to give, *inter alia*, SiF_4, $SO(OCH_3)_2$, SO_2, CH_3F. Examples: FSO_2CH_3, b.p. 46.5 °C, yield 75%; $FSO_2-CH_2-CH(CH_3)_2$, b.p. 99 °C, yield 40%. / Chem. Ber. *102*, 443 (1969) / −Kr. [Rd 985 IE]

New four-membered inorganic ring systems have been described by *H. Schmidbaur*, *W. Wolfsberger*, *K. Schwirten*, and *H.-H. Pickel*. Salts such as *(1)* or *(2)* were obtained from bis(trialkylphosphoranylideneamino)dialkylsilanes and trialkylaluminum or trialkylgallium. In contrast, trimethylindium gave only an open chain product. In competition experiments – reaction of the silicon compound with the aluminum and the gallium compound – only compound *(1)* is



(1), El = Al
(2), El = Ga



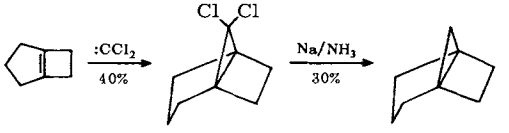
(3), El = Al
(4), El = Ga
(5), El = In

formed. The zwitterions *(3)–(5)* could be prepared from trimethylsilylaminotrimethylsilyliminodiphenylphosphorane and the trimethyl compounds of Al, Ga, and In. *(1)–(5)* are colorless compounds that are extremely sensitive to water and

[1] *A. Zappel*, Chem. Ber. *94*, 873 (1961).

to oxygen. *(1)* and *(2)* decompose without melting, and *(3)–(5)* melt at 114–116 °C, 78–80 °C, and 62–65 °C, respectively. / Chem. Ber. *102*, 556, 564 (1969) / –Kr.
[Rd 986 IE]

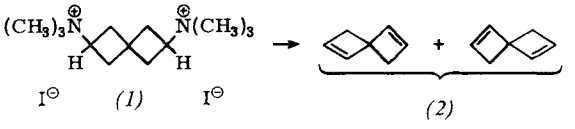
Tricyclo[3.2.1.$0^{1,5}$]octane *(3)* has been prepared by *K. B. Wiberg* and *G. J. Burgmaier* by addition of dichlorocarbene to *(1)* and removal of the chlorine. The structure of *(3)* was



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

proved by NMR spectroscopy and by reaction with acetic acid – a reaction in which *(3)* is converted exclusively into bicyclo[3.2.1]oct-1-yl acetate. *(3)* is remarkably thermally stable; its half-life at 195 °C is more than 20 h. / Tetrahedron Letters 1969, 317 / –Kr.
[Rd 987 IE]

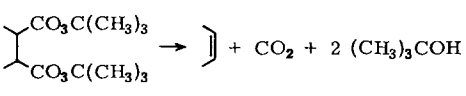
The synthesis of spiro[3.3]hepta-1,5-diene *(2)* has been described by *J. P. H. Houbiers, L. A. Hulshof*, and *H. Wynberg*. Reaction of an aqueous suspension of Ag_2O on the spiran derivative *(1)* and pyrolysis at 150–160 °C/50 torr leads to the formation of *(2)* in *ca.* 27% yield. The compound can be purified by gas chromatography; b.p. 71.6 °C/762 torr. *(2)* has a rigid unsymmetrical 1,4-diene system similar



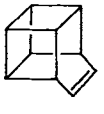
(1) *(2)*

to 5-methylenebicyclo[2.2.1]hept-2-ene and must exist in two optically active forms which have not, as yet, been isolated. / Chem. Commun. *1969*, 91 / –Ma.
[Rd 988 IE]

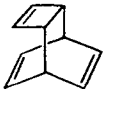
A new synthesis of alkenes from *vic*-dicarboxylic acids by decomposition of peresters of the latter has been reported by *E. N. Cain, R. Vukov*, and *S. Masamune*. Reaction of *tert*-butyl peroxide on dicarboxylic acid dichlorides in neutral non-aqueous solution leads to the formation of the di-*tert*-butyl peresters *(1)*, which decompose to the alkenes either thermally, *e.g.* in *tert*-butyl benzene on heating to 110 to 135 °C in a stream of N_2, or photolytically at room temperature in O_2-free benzene on irradiation with a medium-pressure mercury vapor lamp. Cyclohexene was obtained thermally in 38% yield, norbornene thermally in 34% and photolytically in 30% yield. The hydrocarbon *(2)* occurred



(1)



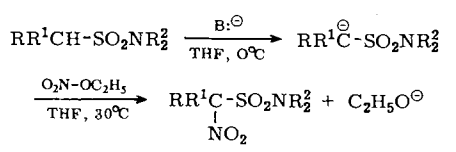
(2)



(3)

photolytically in 40% yield, whilst in the thermolysis of the corresponding perester it isomerized to *(3)*. / Chem. Commun. *1969*, 98 / –Ma.
[Rd 989 IE]

The base-induced α-nitration of sulfonamides has been described by *W. E. Truce* and *L. W. Christensen*. Benzylsulfonamides and many *N,N*-dialkylalkanesulfonamides can be converted, with bases, into a stabilized sulfonamide carbanion, which reacts with alkyl nitrate to form α-nitrosulfonamide. In the case of benzyl derivatives, potassium *tert*-butoxide is suitable as base for the formation of the anion



while *n*-butyllithium is required in the case of aliphatic sulfonamides. The yields are between 21 and 66%. α-Nitrosulfonamides with free α-hydrogen can be easily brominated./ Tetrahedron *25*, 181 (1969) / –Ma.
[Rd 990 IE]

The crystal structure and atomic radius of metallic radium have been determined by *F. Weigel* and *A. Trinkl* on samples of metallic radium obtained in the following manner: A mixture of RaO and aluminum was heated inductively to 1100 to 1200 °C at $< 10^{-6}$ torr in micro crucibles placed in the lower ends of quartz X-ray capillaries; the micro crucibles were manufactured from iron having a low carbon content. The radium metal formed in accordance with the reaction

$$3\ RaO + 2\ Al \rightarrow 3\ Ra + Al_2O_3$$

sublimes directly onto the air-cooled walls of the capillaries above the crucibles as a dull gray metallic mirror. When reaction is complete the capillaries are sealed by a microburner and the reaction product is recrystallized by repeated heating under an IR lamp and cooling with liquid nitrogen. After such recrystallization the radium metal mirror becomes bright and silvery and gives an easily interpretable X-ray diagram. Evaluation of the latter gives a cubic space-centered lattice with $a_0 = 5.148 \pm 0.015$ Å and with two atoms in each unit cell, isotypic with barium metal. From the lattice constant it can be calculated that with two atoms in the unit cell, the density is 5.50 g cm^{-3} and the atomic radius is 2.32 ± 0.02 Å. / Radiochim. Acta *10*, 78 (1968) / –FW. [Rd 991 IE]

Californium(III) oxide fluoride, CfOF, in the form of a bright green single crystal has been obtained by *J. R. Peterson* and *J. M. Burns* during attempts to prepare californium(III) fluoride; its parameters could be measured on a computerized X-ray diffractometer. CfOF crystallizes with the fluorite type structure, space group Fm3m, with statistical distribution of the O and F atoms. The lattice constant has the value $a_0 = 5.561 \pm 0.004$ Å; the Cf–(O,F) distance is 2.408 Å. / J. inorg. nuclear Chem. *30*, 2955 (1968) / –FW.
[Rd 992 IE]

The solid-state reaction of zinc oxide with iron(III) oxide has been investigated by *R. Parker, C. J. Rigden*, and *C. J. Tinsley* by means of thermogravimetric and magnetic measurements. Owing to the diamagnetic character of the Zn^{2+} ion the results of such measurements permit conclusions to be drawn regarding the nature of the intermediates. If a mixture of ZnO and Fe_2O_3 powder is heated to 400 °C and over, the Fe_2O_3 releases oxygen and a spinel lattice is established at a grain boundary. Zinc ions can diffuse through this lattice

with relative ease; if reoxidation is hindered, diffusion of zinc continues until a homogeneous spinel phase is established in which the zinc/iron ratio is determined only by the oxygen deficiency. Subsequent oxidation affords zinc ferrite and γ-iron(III) oxide containing 21% of zinc in solid solution. The last named phase decomposes above 515 °C into zinc ferrite and α-iron(III) oxide. / Trans. Faraday Soc. *65*, 219 (1969) / –Hz. [Rd 993 IE]

Space-charge layers in surface-proximate regions of single crystals of zinc oxide have been investigated by *B. Hoffmann* using electroreflection. The technique is based on the periodic changes in the reflecting power of the surface of the crystal for light in the region of the ground state lattice absorption (near ultraviolet) on application of an alternating electric field oriented perpendicular to the surface of the crystal. Comparison of the phase of the external field and the alternating component of the reflecting power affords the sign of the space charge in the proximity of the surface. By raising the partial pressure of oxygen in the environment of the crystal it proved possible to observe the change from an excess layer (electronic transition gas-crystal) to a depletion layer (electronic transition crystal-gas). The partial pressure of oxygen at which this change takes place depends on the intensity of irradiation and on the concentration of mobile charge carriers in the crystal. / Z. Physik. *219*, 354 (1969) / –Hz. [Rd 994 IE]

The molecular geometry of thiirane *S*-oxide was determined by *W. F. White* and *J. E. Wollrab* from the rotation spectrum, paying particular attention to the orientation of the SO bond relative to the C_2S ring. As is also evident from NMR and Raman data, the molecule belongs to the symmetry group C_s (only one plane of symmetry). Values for the CS bond length (1.821 Å) and the angles CSC (48.47°) and CCS (65.76°) were taken from thiirane, the CH bond length was set at 1.09 Å and the angle HCH at 110.0°; it was further assumed that the HCH plane bisects the CCS angle. The bond lengths CC and SO were thus calculated as 1.494 ± 0.003 Å and 1.473 ± 0.005 Å, respectively. The angle α between the SO bond and the plane of the ring (or the bisector of the CSC angle) is 67.3 ± 0.4°. The bond lengths CC and SO correspond within the limits of accuracy to those in thiirane and dimethyl sulfoxide respectively; the considerable widening of the angle α compared with dimethyl sulfoxide ($\alpha \approx 45°$) is attributed to the decrease of the CSC angle owing to ring formation. The dipole moment of thiirane *S*-oxide is 3.66 D. / Chem. Physics. Letters *3*, 25 (1969) / –Hz. [Rd 995 IE]

Isolation of protease inhibitors with water-insoluble enzyme resins has been described by *H. Fritz et al.* A technique was used in which enzymes (trypsin and plasmin) are bound to copolymers of maleic anhydride. The resulting polyanionic enzyme resins are suitable for isolation of inhibitors having isoelectric points above 4–5. Polyamphoteric resins, which are formed when bis(methylamino)ethane is bonded to the intact anhydride groups of the enzyme resin, exhibit a considerably higher specific binding capacity towards inhibitors and are also suitable for isolation of inhibitors having low isoelectric points. Moreover, such inhibitors are released at considerably higher pH values from polyamphoteric resins than from the corresponding polyanionic resins. The binding capacity of the resins remains constant over several months of storage between 0 and 4 °C in the presence of chloroform or phenol. The following inhibitors were isolated: trypsin inhibitors from pig pancreas, sheep pancreas, guinea-pig seminal vesicles, soya beans; trypsin-kallikrein inhibitor from bovine lung. / Hoppe-Seylers Z. physiol. Chem. *350*, 129 (1969) / –He. [Rd 996 IE]

Various molds produce Aflatoxin B on foodstuffs, as has been shown by *E. Hanssen*. Since Aflatoxin B shows hepatotoxic and lethal effects in human beings and other animals, and also has a carcinogenic action on human liver cells, consumption of foodstuffs affected by mold should be avoided. Even after excision of the mycelium such foodstuffs cannot be consumed without risk since the poisons are capable of migration. They could be detected at a considerable distance from the mycelium. / Naturwissenschaften *56*, 90 (1969) / –He. [Rd 997 IE]

The characterization of t-RNA and of aminoacyl-t-RNA synthetase has been achieved by *V. Neuhoff et al.* by analysis of picomolar quantities of dansyl amino acids using two dimensional chromatography. By means of this method it is possible to determine 10^{-12} to 10^{-13} mole of dansylated amino acid (radioactively labeled) both quantitatively and qualitatively. Of the many applications of this method may be mentioned: The characterization of t-RNA and aminoacyl t-RNA synthetase; the testing of purity of specific t-RNA (a minimum of 5% of each of the desired t-RNA's can be obtained from a specific t-RNA preparation) and of commercial radioactively labeled amino acid preparations. / Hoppe-Seylers Z. physiol. Chem. *350*, 121 (1969) / –He. [Rd 998 IE]

BOOK REVIEWS

Arzneimittel. Entwicklung, Wirkung, Darstellung (Drugs. Their Development, Action, Preparation). By *G. Ehrhart* and *H. Ruschig*. Verlag Chemie GmbH, Weinheim/Bergstrasse 1968. 1st Edit., 2 vols. totalling xii, 1921 pp., 90 illustrations, 277 tables. Linen DM 248.–.

It is no longer possible to treat problems of drug chemistry without comprehensive information from the literature. Thus it is as essential nowadays for the chemist to know the principles and methods of pharmacology and medicine as it is for the physician and the pharmacologist to know those of chemistry and biochemistry. So it is a difficult task to conceive and to bring about a review of the comprehensive information about drugs. That may be why there has hitherto been no such a work in modern German literature; to undertake this task it was first necessary to find a team of experienced industrial scientists who had all the necessary tools of industrial and information science. *G. Ehrhart* and *H. Ruschig*, both of them schooled for ten years in leading positions in a large research team, set themselves this task, and it may be stated at once that they have met it with great success. Their reference work is in two volumes, the first devoted to pharmacodynamics and the second to chemotherapy.

The subject matter is divided uniformly in the two volumes, into 29 chapters each with four sections, according to scientific and medical interests.

An *introduction* describes the historical development of the various groups of drugs, together with the general practical and theoretical principles; it contributes considerably to an understanding of the detail that follows, and awakens the

interest and curiosity of the layman. In parts this introduction is very detailed and informative; for instance, chapter 10, on psychopharmacy, is divided into the following subsections: 10.11 Types of psychopathological condition; 10.12 Historical background of psychiatric therapy; 10.13 Clinical types of psychopharmacy; 10.14 Applications of psychopharmacy; and 10.15 Clinical pharmacodynamic aspects. The material is well chosen; its arrangement is didactically apt and clarified by representative tables and illustrations.

The next section, on *pharmacological and chemotherapeutic tests*, is particularly valuable for the chemist and biochemist. That it includes recent developments is illustrated, for example, by chapter 13 on coronary vasodilators where attempts to measure sympathoinhibitory action are described as well as the current methods of determining coronary circulation. Further, the division of sympatholytics into α- and β-groups and their pharmacological recognition are treated in detail in chapter 3. It must, however, be clearly recognized that it can be no object of the present treatise to describe pharmacological methods in detail; the pharmacological section serves rather to give the reader a rapid survey whilst inducing him to study the specialist literature.

The *development* of groups of medicaments is described in the third section. This section begins, in general, with the history of drugs and their constituents, leading on to synthetic compounds in chronological series. In this way the evolution of relationships is described, and all who are interested in relations between structure and activity will find much of interest therein. Here also are recorded the metabolism and toxicity of many of the compounds.

The last section is devoted to the *preparation of drugs*. The authors seem to have been remarkably successful in choosing the most important of the usually numerous alternative synthetic methods, and they have documented them mainly by reference to patents. Confusion by an excess of material has been happily avoided. Those concerned with drug synthesis are sufficiently served by wide-ranging references to the literature.

A chapter on "The structure and mode of function of the nervous system" and an appendix on "The route and behavior of drugs in the organism" contribute considerably to an understanding of the division into 29 chapters.

The impressive success of this book was confirmed for the reviewer soon after its appearance: in his Institute, where research on drugs is carried out, it is already one of the sources of information that is in greatest use and most frequent demand. The picture that it gives of the relations between experiment and medical and scientific theories gives it an appeal to all, whether it be to chemists, biochemists, pharmacologists, bacteriologists, biologists, or physicians. It can also be recommended to students who are interested in drug research and wish to choose this field for their life's work.

Inevitably there are some mistakes, but they are of such minor importance in relation to the range and achievement of this book that they will not be detailed here; they have been notified to the authors so that they may correct the next edition.

The authors, their co-workers, and the publishers deserve thanks and recognition for this clearly arranged, well illustrated, and carefully selected review, which will become a standard work for all who are interested in research on drugs.

E. Biekert [NB 807 IE]

Molecularbiologie. Bausteine des Lebendigen (Molecular Biology: Units of Life). Edited by *Th. Wieland* and *G. Pfleiderer*. Umschau-Verlag, Frankfurt 1967. 2nd Edit., 296 pp., numerous illustrations, bound DM 19.80.

In this volume 20 scientists report in 17 articles "in clear style on the most important discoveries" that form the essence of modern molecular biology. An introduction by *M. F. Perutz* gives an exemplary brief and penetrating review of the decisive stages in the historical development and the "dogmas" of molecular biology, after which the reader is introduced to the world of subcellular particles. There follow accounts of the "classical" subsections of molecular biology: DNS, the genetic code, the structure and synthesis of proteins, the mode of action of enzymes, molecular evolution, and then finally discussions of photosynthesis, contractile structures, biological membranes, immunochemistry, the biochemistry of viruses, and neurobiology.

The value of the contributions lies in the fact that they are not written for the expert. All the authors have taken the greatest trouble that their material, which is in part far from simple, shall be as clear as possible, often using colored illustrations. Nevertheless this is no book for the layman, in spite of what the publisher says. The text will be intelligible only to those who already know something about the relation between chemistry and biology and, in particular, to those who are familiar with scientific vocabulary. Such readers can be advised without reservation to obtain the book for a first and reliable introduction into the principles of molecular biology. The success of this volume can best be judged by the fact that a second edition has become necessary only six months after appearance of the first; in several respects the second edition gives a more complete and rounded picture of the field.

H. Grünewald [NB 808 IE]

Synthetic Methods of Organic Chemistry, Vol. 22, Yearbook 1968. By *W. Theilheimer*. From the series: Synthetische Methoden der Organischen Chemie, Jahrbuch mit deutschem Registerschlüssel. S. Karger, Basel-New York 1968. 1st Edit., xxiv, 558 pp., DM 227.–.

The annual "Theilheimer"[1] has become such a standard work for preparative chemists that it is almost unnecessary to mention a new volume. The present volume contains a selection of 996 syntheses from 1966/1967; the well established though somewhat complicated classification system is retained. All fields of investigation are represented, and a surprisingly large number of heterocyclic and alicyclic ring syntheses are included. As before, the concise procedures given often provide an adequate working basis with no need to refer to the literature. The text is supplemented with clear formulas. A detailed keyword index (87 pp.), which also covers the two previous volumes, greatly increases the value of the book. The six pages on "Trends" are a goldmine of the latest original methods. The presentation and print are again excellent.

S. Hünig [NB 778 IE]

The Organic Compounds of Zinc and Cadmium. By *N. I. Sheverdina* and *K. A. Kocheshkov*. From the series: Methods of Elemento-Organic Chemistry. Edited by *A. N. Nesmeyanov* and *K. A. Kocheshkov*. Volume 3. North-Holland Publishing Company, Amsterdam 1967. 1st Edit., x, 252 pp., many figures, Dfl. 36.–.

In the present book 120 pages are devoted to the classical preparative chemistry of organozinc compounds and 77 to that of organocadmium compounds, both topics enjoying the same comprehensive treatment. A complete chapter is devoted to the Reformatzky reaction (*K. A. Kocheshkov* and *L. V. Abramova*, 43 pages). The task that the authors have set themselves can be summarized in the terms "Preparation of ....." and "Reactions with .....", and they have accordingly set out the voluminous subject matter in a clear manner. Each chapter has its own bibliography. The chemistry of the alkylzincs was last published as a monograph some 30 years ago, whereas that of the alkylcadmiums

[1] Cf. Angew. Chem. *79*, 283 (1967); Angew. Chem. internat. Edit. *6*, 277 (1967).

has never appeared in monograph form. A welcome fact is that experienced authors, known and valued for many years in the field of organometallic chemistry, have taken this task upon themselves.

The literature is covered as far as it has been considered in the Russian abstracts publication (Ref. Ž. Chim) up to July 1, 1963. A series of randomly chosen examples showed that publications up to the middle of 1961 have been considered; references from 1962 or 1963 are seldom encountered and concern primarily Russian papers. For instance, of the 176 references on pages 233–239, 22 are from 1959, 13 from 1960, and there are not any from 1962 or 1963. Understandably, the achievements of Russian chemists receive a broader treatment.

The analysis of the compounds covered is dealt with in short sections and considers only elemental analyses and short tables of melting points and boiling points. Analytical techniques such as spectroscopy are not included.

As a result of the preparative tone of the work, modern structural chemistry and reaction mechanisms, which have of late attracted greatly increased interest in organometallic chemistry, are not done full justice. Just an occasional reference is made to dissociation energies.

As is the case with the other volumes of this series[1], the considerable value of the present book could have been increased by inclusion of a detailed subject index. It appears to the reviewer that additional keywords would have been desirable, *e.g.* bond energies, bond lengths, dipole moments, dissociation, infrared, mechanism, NMR, Raman, reaction-spectroscopy, stereochemistry. In the case of Japanese literature and patents, translations from the Russian abstracts publication (Ref. Ž. Chim.) would have been better replaced by references from Chemisches Zentralblatt or Chemical Abstracts.

Not least because of the chapter on the Reformatzky reaction, the book is not only useful for the organometallic chemist, but represents a valuable reference work for all chemists engaged in preparative work, and certainly fills a gap in the existing literature. *W. P. Neumann* [NB 789 IE]

Atlas of Electron Microscopy. Biological Applications. Edited by *F. Scanga*. Elsevier Publishing Company, Amsterdam 1964. 1st Edit., xxvi, 331 pp. 496 illustrations, bound, *ca.* DM 118.–

Sight is man's most important sense. Experimental work indicates that the contours of an object which the eye sees distorted appear similarly distorted to the touch. It is interesting to observe the efforts made by chemists to render the objects of their research visible, in order to be able to exercize a measure of visual control over the results of the experiment. It is therefore not surprising that the development of electron microscopy has led to spectacular advances in science generally, and specially in biology, by permitting us to see a previously invisible realm of nature.

F. Scanga, of the Istituto Superiore di Sanità, in Rome, has gathered together the most interesting photographs so far taken with the electron microscope into an atlas which is, in its way, unique. The work begins with a fifteen-page summary of the technique and the possibilities of application of electron microscopy. This is followed by 482 photographs of viruses, bacteria, cell constituents, animal and plant cells, and finally of shells.

Anyone who finds the observation of nature pleasing will welcome this book, revealing as it does the forms and structures governing the elementary processes of life.

H. Grünewald [NB 776 IE]

Framework Molecular Models. Construction set with 24-page instruction leaflet. Prentice-Hall, Englewood Cliffs, N.J./USA, DM 32.80.

The need for comprehensibility has repeatedly led chemists to attempt to represent their molecules in the form of large, but correctly scaled models. The best known are the Stuart models and the stereomodels of Dreiding. Recently, in the USA, *Fieser* has developed a cheaper plastic version of the Dreiding models.

Stereomodels can also be constructed with the "Framework Molecular Models" set. This set differs from the Dreiding models, in that it provides no prefabricated "atoms," but small, rigid tetrahedra, trigonal bipyramids, and octahedra, all made of wire rods, as well as a large number of differently colored plastic tubes, which fit closely over the metal rods, and which can be cut by the user to a scale of 1 Å = 1 inch, so that they represent covalent bonds or the van der Waals radii of individual atoms. The kit also contains linear and curved connecting rods, the latter serving for the construction of π-bonds. Twelve chemical elements may be represented by the twelve colors of the plastic tubes. Plastic tubes marked with two colors are provided for a number of frequently occurring combinations of elements (O–H, N–H, C–H. C–N, and C–O). The coloring of the models permits the observer, as in the case of the Stuart models, to recognize rapidly the molecular structure.

With this set it is possible to construct atomic models of the hybridized states sp^3, sp^2, dsp^3, sp, and d^2sp^3. It would be desirable to enlarge the kit with parts that would allow representation of hepta- and octacoordinated complexes. For this it would only be necessary to produce appropriate metal frameworks onto which the plastic tubes could be fixed.

The kit has other advantages: it is easy to handle, and the corresponding models are to scale and very clear, as they also show the positions of free electron pairs. What is more, it is available at a reasonable price. One would like to see this useful set in the hands of every student of chemistry, and would recommend it especially to everyone who has to teach the subject, since in chemistry there is nothing to beat a good model. *H. Grünewald* [NB 777 IE]

[1] Cf. Angew. Chem. *80*, 764 (1968); Angew. Chem. internat. Edit. *7*, 744 (1968).

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 4 50 75, Telex 46 1855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 5
MAY 1969
PAGES 295–400

The Chemistry of Enol Ethers

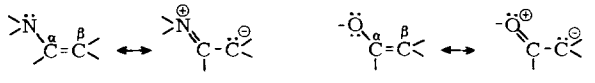
By F. Effenberger [*]

Dedicated to Professor H. Bredereck on the occasion of his 65th birthday

Enol ethers (vinyl ethers) are intermediate in their reaction behavior between olefins and enamines. This article presents a survey of reactions leading to bond formation at the β–C atom of enol ethers; polymerizations and additions of acidic H–X compounds are not reviewed.

1. Introduction

Enamines *(1)* have acquired great importance in preparative organic chemistry in the course of the past 15 years [1]. Their reactivity toward electrophiles is due to the high electron density on the β-C atom.



(1) *(1a)* *(2)* *(2a)*

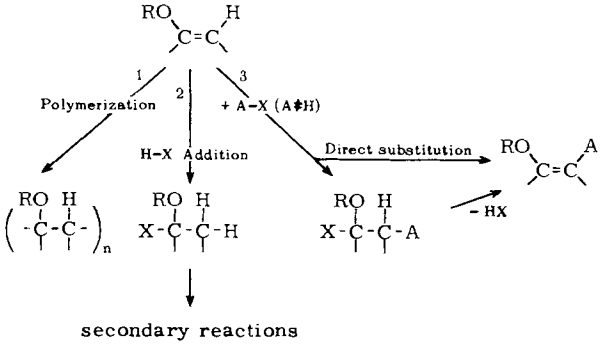
In the enol ethers *(2)* [2], which are also reactive derivatives of ketones and aldehydes, the electron density on the β-C atom is also increased, though to a smaller extent than in the enamines. Since the ammonium structure *(1a)* is energetically more favorable than the oxonium structure *(2a)*, *(1a)* makes a greater contribution to the resonance equilibrium *(1)* ↔ *(1a)* than does *(2a)* in *(2)* ↔ *(2a)*.

Thus, enol ethers are intermediate in their chemical properties between olefins and enamines. *Wislicenus*, who was the first to prepare ethyl vinyl ether, also reported on the halogenation, hydrolysis, and polymerization of this simple enol ether [3]; however, systematic study of the chemistry of enol ethers started only with the development of productive syntheses [4]. Enol ethers exhibit three fundamental types of reactions:

1) Cationic polymerization in the presence of Lewis acids.

2) Reactions with H–X compounds to form either the carbonyl compound from which the enol ether is derived or its derivatives. Examples are the hydrolysis of enol ethers to form carbonyl compounds and the addition of alcohols to enol ethers to form acetals.

3) Reactions with compounds A–X resulting in bond formation between A and the β-C atom of the enol ether; these reactions afford both addition and substitution products. The present article mainly covers reactions of this type.



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[1] *J. Szmuszkovicz*, Advances org. Chem. *4*, 1 (1963); *J. A. West*, J. chem. Educat. *40*, 194 (1963); *A. Hochrainer*, Österr. Chemiker-Ztg. *66*, 355 (1965); *H. De Pooter*, Meded. vlaamse chem. Veren. *4*, 100 (1966); *G. Laban* and *R. Mayer*, Z. Chem. *8*, 165 (1968).

[2] *L. Knorr* and *H. Hörlein*, Ber. dtsch. chem. Ges. *39*, 1409 (1906).

[3] *J. Wislicenus*, Liebigs Ann. Chem. *192*, 106 (1878).

[4] For reviews of syntheses and reactions of vinyl ethers, see *W. Reppe*, Liebigs Ann. Chem. *601*, 81 (1956); *M. F. Shostakovskii*, Chemie (Prague) *10*, 273 (1958); Chem. Abstr. *54*, 1250e (1960); *T. Mukaiyama*, Yuki Gosei Kagaku Kyokai Shi *19*, 29 (1961); Chem. Abstr. *55*, 7267f (1961); *M. Mori*, Yukagaku (J. Japan Oil Chemist's Soc.) *14*, 595 (1965); Chem. Abstr. *64*, 1945c (1966).

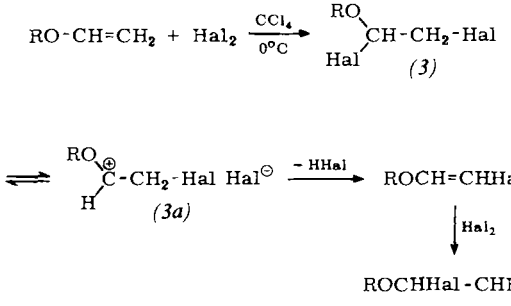
Different groups of workers have calculated the resonance interaction of a free pair of p electrons on the oxygen with the CC double bond, which largely determines the reaction behavior of the enol ethers[5]. An experimental measure of the resonance interaction is provided by the ^1H–NMR spectrum; thus, important conclusions regarding the steric configuration and possible resonance structures can be drawn from the chemical shift of the β–H atoms and the respective coupling constants[6].

2. Reactions of the β-C Atom of Enol Ethers with Hetero Atoms

2.1. Halogenation[7]

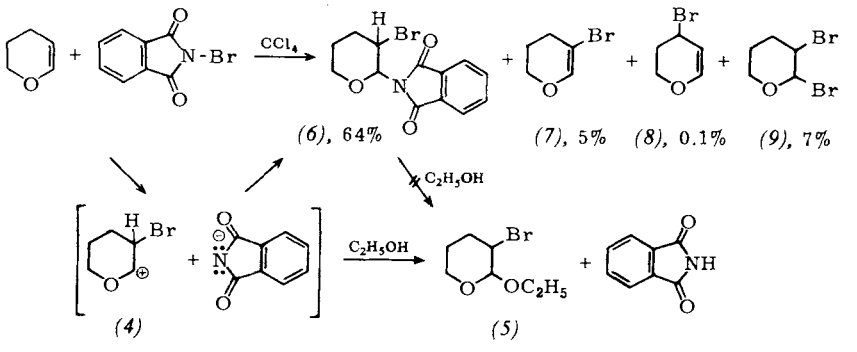
The addition of chlorine and bromine to vinyl ethers has been studied mainly by *Shostakovskii et al.*[8–10]. In the case of low molecular weight alkyl vinyl ethers the reaction is so vigorous that cooling is necessary. The reaction is generally carried out at about 0 °C in CCl_4 or $CHCl_3$. Bromination occurs without a catalyst[10], whereas peroxides are added in chlorinations to prevent polymerization[11].

1,2,2-Trihalogeno ethers are often formed as by-products together with the 1,2-dihalogeno ethers *(3)*[7,12]. E1 elimination, which is the initial step in by-product formation, is favored to such an extent by the resonance-stabilized ionic intermediate *(3a)*[9,12,13] that it proceeds even under very mild conditions.



Attempts to iodinate enol ethers with elemental iodine are unsuccessful and yield polymers[3,14]. Under the conditions of the iodoform reaction, alkyl vinyl ethers are converted into iodoform and potassium formate; 1,2-diiodo ethers and iodoacetaldehyde are assumed to occur as intermediates[15].

Enol ethers have also been treated with *N*-bromoamides instead of bromine[16,17]. For example, 2,3-dihydropyran reacts with *N*-bromophthalimide predominantly by a polar mechanism[18]. The ionic intermediate *(4)* can be intercepted by addition of alcohol to form *(5)* and phthalimide. Under these conditions, *(6)* does not react with alcohol to form *(5)*. Compound *(7)* arises from either *(4)* or *(9)*,



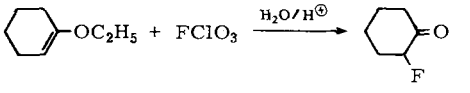
(6), 64% *(7)*, 5% *(8)*, 0.1% *(9)*, 7%

(4) *(5)*

whereas *(8)* and *(9)* are thought to be formed *via* free radicals. A polar intermediate corresponding to *(4)* is also assumed to occur in the chlorination of vinyl ethers with chlorine in alcohol[19].

The fluorination of enol ethers, which is particularly important for the introduction of fluorine into steroids, can be achieved in very good yields under mild conditions (in pyridine at 0 °C) with perchloryl fluoride[20].

Cyanogen chloride adds to ethyl vinyl ether in the presence of radical generators to give 2-ethoxy-3-



[5] *A. Julg* and *M. Bonnet*, Theoret. chim. Acta *1*, 1 (1962); *Y. L. Frolov*, Izvest. vyssich učebnych Zavedenij (Tomsk), Fiz. *8*, 177 (1965); Chem. Abstr. *63*, 10843f (1965).

[6] *R. T. Hobgood Jr.*, *G. S. Reddy*, and *J. H. Goldstein*, J. physic. Chem. *67*, 110 (1963); *K. Hatada*, *M. Takeshita*, and *H. Yuki*, Tetrahedron Letters *1968*, 4621, and further literature cited there.

[7] *L. Summers*, Chem. Reviews *55*, 301 (1955).

[8] *A. E. Favorskii* and *M. F. Shostakovskii*, Ž. obšč. Chim. *13*, 1 (1943); Chem. Abstr. *38*, 3305 (1944).

[9] *M. F. Shostakovskii*, Ž. obšč. Chim. *14*, 102 (1944); Chem. Abstr. *39*, 9059 (1945).

[10] *A. E. Favorskii* and *M. N. Shchukina*, Ž. obšč. Chim. *15*, 385 (1945); Chem. Abstr. *40*, 43476 (1946).

[11] *M. F. Shostakovskii*, *Yu. B. Kagan*, and *F. P. Sidel'Kovskaya*, Ž. obšč. Chim. *17*, 957 (1947); Chem. Abstr. *42*, 4520a (1948).

[12] *A. V. Kalabina*, *L. S. Myasnikova*, *E. F. Kolmakova*, *I. R. Shestakova*, and *M. P. Pavlova*, Chem. Abstr. *61*, 1783f (1964).

[13] *A. V. Kalabina*, *E. F. Grechkin*, *T. I. Bychkova*, *A. Kh. Filippova*, *N. A. Tyukavkina*, and *L. T. Ermakova*, Chem. Abstr. *62*, 6418g (1965).

[14] *C. E. Schildknecht*, *A. O. Zoss*, and *C. McKinley*, Ind. Engng. Chem. *39*, 180 (1947).

[15] *M. F. Shostakovskii*, *F. P. Sidel'Kovskaya*, and *M. G. Zelenskaya*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1956*, 615; Chem. Abstr. *50*, 16568e (1956).

[16] *R. Paul* and *S. Tchelitcheff*, C. R. hebd. Séances Acad. Sci. *236*, 1968 (1953).

[17] *J. C. Traynard* and *G. Pfeiffer*, C. R. hebd. Séances Acad. Sci. *258*, 3735 (1964).

[18] *J. R. Shelton* and *T. Kasuga*, J. org. Chemistry *28*, 2841 (1963).

[19] *K. Weissermel* and *M. Lederer*, Chem. Ber. *96*, 77 (1963).

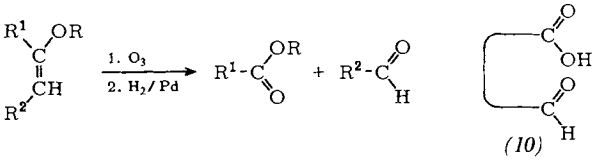
[20] *S. Nakanishi*, *K. Morita*, and *E. V. Jensen*, J. Amer. chem. Soc. *81*, 5259 (1959).

chloropropionitrile in 9 % yield; the reaction is assumed to proceed by a short-chain free-radical mechanism [21].

2.2. Oxidation

Enol ethers are relatively stable to atmospheric oxygen [22]; they are attacked only by stronger oxidizing agents such as ozone, perbenzoic acid, or salts of heavy metals in higher valency states.

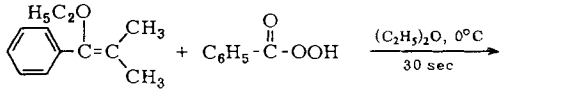
The ozonization of enol ethers, like the ozonization of olefins, leads to cleavage of the double bond and therefore is of analytical interest [23,24]. It is, however,

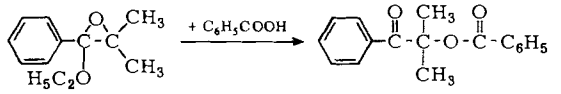


(10)

important for the preparation of the otherwise difficultly accessible ω-formyl carboxylic acids *(10)* from cyclic enol ethers [25]. In competitive ozonization of enol ethers and olefins, the polarized double bond of the enol ethers is broken more rapidly [24].

Epoxy ethers were originally formulated as stable reaction products in the reaction of enol ethers with perbenzoic acid [26,27]. This was later found to be incorrect [28,29]. Epoxy ethers *(11)* can be isolated only when structural factors are favorable and by rapid operation at low temperatures, since the benzoic acid formed otherwise reacts





(11) 90% *(12)*

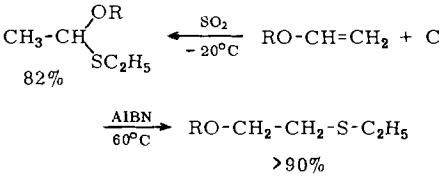
further with *(11)* to give *(12)* [28]. Thus, the epoxy ether derived from 1-ethoxy-1-cyclohexene cannot be isolated, whereas the epoxide of the corresponding acetoxy compound can be obtained in moderate yields [30].

Oxidation of enol ethers with lead tetraacetate, other lead(IV) carboxylates [35], thallium(III) acetate, or benzoyl peroxide results in addition of two acetoxy groups to the CC double bond [31–34].

The addition of benzoyl peroxide probably proceeds by a free-radical mechanism [33]; in the reaction with lead(IV) acetate, however, polar addition of $Pb(OAc)_3^{\oplus}$ + $AcO^{\ominus}$ is more likely [36] than the free-radical pathway [37].

2.3. Reactions with Sulfur Compounds

Whereas water and alcohols add to enol ethers in accordance with the Markownikoff rule to yield aldehyde derivatives, S–H compounds also give the anti-Markownikoff addition products [38–43]. The direction of addition depends entirely upon the reaction conditions [40,42]. At low temperatures and with catalytic quantities of SO_2, a polar addition mechanism leads to aldehyde derivatives. At higher



(SO$_2$) R = C_2H_5, C_4H_9

(AIBN) R = C_6H_5, p-CH_3–C_6H_7, C_4H_9, C_6H_{11}

temperatures, in the presence of radical generators such as azoisobutyronitrile (AIBN), or on UV radiation [44], anti-Markownikoff addition products are formed.

[21] *E. I. Vasil'eva, B. I. Keda,* and *R. K. Feilina,* Doklady Akad. Nauk SSSR *154,* 129 (1964); Chem. Abstr. *60,* 9112f (1964).

[22] *W. Forster,* J. Amer. chem. Soc. *31,* 596 (1909).

[23] *J. Scheiber* and *P. Herold,* Liebigs Ann. Chem. *405,* 295 (1914).

[24] *H. P. Crocker* and *R. H. Hall,* J. chem. Soc. (London) *1955,* 2052.

[25] *U. Schmidt* and *P. Grafen,* Liebigs Ann. Chem. *656,* 97 (1962).

[26] *M. Bergmann* and *A. Miekeley,* Ber. dtsch. chem. Ges. *54,* 2150 (1921).

[27] *M. Mousseron* and *R. Jacquier,* Bull. Soc. chim. France *1950,* 698.

[28] *M. Bergmann* and *A. Miekeley,* Ber. dtsch. chem. Ges. *62,* 2297 (1929).

[29] *C. L. Stevens* and *J. Tazuma,* J. Amer. chem. Soc. *76,* 715 (1954).

[30] *A. L. Draper, W. J. Heilman, W. E. Schaefer, H. J. Shine,* and *J. N. Smoolery,* J. org. Chemistry *27,* 2727 (1962).

[31] *H. O. L. Fischer, E. Bär,* and *L. Feldmann,* Ber. dtsch. chem. Ges. *63,* 1732 (1930).

[32] *B. Helferich* and *N. M. Bigelow,* Hoppe-Seylers Z. physiol. Chem. *200,* 263 (1931).

[33] *M. F. Shostakovskii, N. A. Gershtein,* and *V. A. Neterman,* Doklady Akad. Nauk SSSR *103,* 265 (1955); Chem. Abstr. *50,* 5571d (1956).

[34] *S. Uemura, R. Kito,* and *K. Ichikawa,* J. chem. Soc. Japan, pure Chem. Sect. (Nippon Kagaku Zasshi) *87,* 986 (1966); Chem. Abstr. *65,* 19962f (1966).

[35] *Y. Yukawa* and *M. Sakai,* Bull. chem. Soc. Japan *36,* 761 (1963); Chem. Abstr. *59,* 8645g (1963).

[36] *R. Criegee, P. Dimroth, K. Noll, R. Simon,* and *C. Weis,* Chem. Ber. *90,* 1070 (1957).

[37] *C. D. Hurd* and *O. E. Edwards,* J. org. Chemistry *19,* 1319 (1954).

[38] *M. F. Shostakovskii, E. N. Prilezhaeva,* and *E. S. Shapiro,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1951,* 284; Chem. Abstr. *46,* 883f (1952).

[39] *M. F. Shostakovskii, E. N. Prilezhaeva,* and *E. S. Shapiro,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1954,* 292; Chem. Abstr. *48,* 10535d (1954).

[40] *M. F. Shostakovskii, E. N. Prilezhaeva,* and *E. S. Shapiro,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1953,* 357; Chem. Abstr. *48,* 9311i (1954).

[41] *E. N. Prilezhaeva, N. P. Petukhova,* and *M. F. Shostakovskii,* Doklady Akad. Nauk SSSR *154,* 160 (1964); Chem. Abstr. *60,* 9143g (1964).

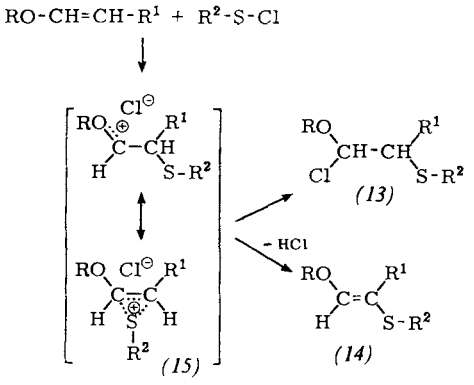
[42] *M. F. Shostakovskii, E. N. Prilezhaeva,* and *E. S. Shapiro,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1955,* 734; Chem. Abstr. *50,* 7080f (1955).

[43] *E. N. Prilezhaeva* and *M. F. Shostakovskii,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1958,* 1104; Chem. Abstr. *53,* 3119h (1959).

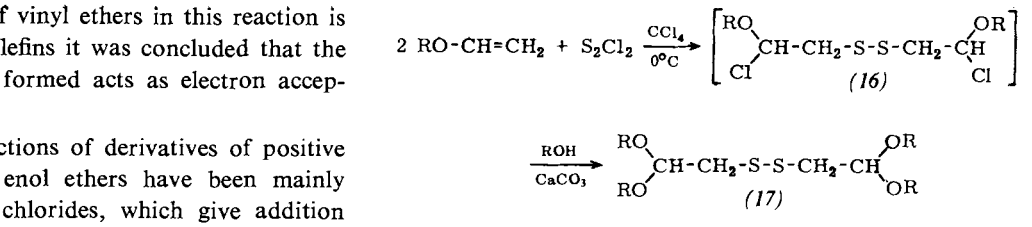
[44] *K. Yamagishi,* J. chem. Soc. Japan, pure Chem. Sect. (Nippon Kagaku Zasshi) *80,* 1361 (1959); Chem. Abstr. *55,* 4405g (1961).

Since the reactivity of vinyl ethers in this reaction is higher than that of olefins it was concluded that the thiyl radical initially formed acts as electron acceptor [45].

Investigations on reactions of derivatives of positive bivalent sulfur with enol ethers have been mainly confined to sulfenyl chlorides, which give addition



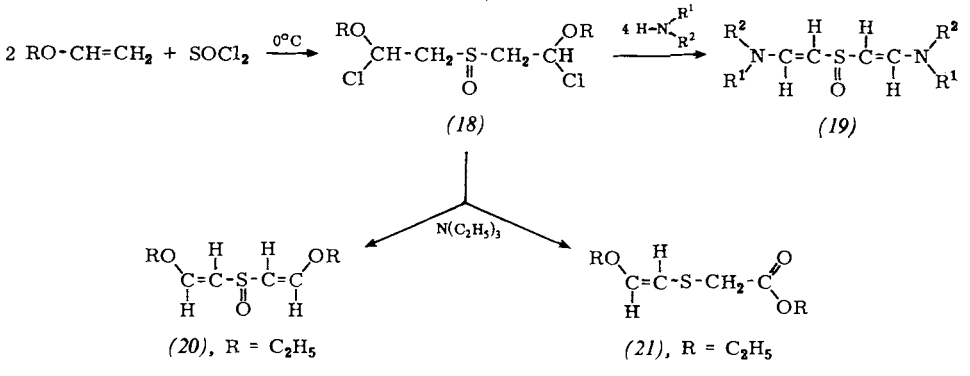
products *(13)* or substitution products *(14)*, depending on the reaction conditions and on the nature of the substituents [46–49].



isolated, but can be converted into the more stable alkoxy compounds *(17)*.

The only tetravalent sulfur compound whose reactions with enol ethers have been extensively studied is thionyl chloride [53–55], though the reaction of SF_4 with methyl trifluorovinyl ether has been mentioned [56].

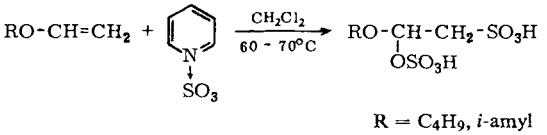
$SOCl_2$ reacts with an excess of vinyl ether under mild conditions to form bis-β-alkoxy-β-chloroethyl sulfoxides *(18)* as colorless crystalline compounds, which yield the sulfoxides *(19)* on treatment with primary and secondary amines, and the elimination product *(20)* as well as the rearrangement product *(21)* on reaction with tertiary amines [55]. Because of steric and electronic factors, the reaction proceeds more slowly with substituted vinyl ethers, leading only to 1:1-addition compounds [55].



The sulfur is always bonded to the β-C atom of the enol ether, in agreement with the reaction type proposed by *Kharasch et al.* for sulfenyl chlorides, the sulfur carrying a partial positive charge [50]. Exclusive *trans* addition [49] indicates a sulfenium ion *(15)* as intermediate [49,50].

The analogous addition compounds *(16)* of vinyl ethers with dialkoxyoxophosphoranylsulfenyl chloride [51] and with disulfur dichloride [52] cannot be

Electrophilic addition can be accomplished with the pyridine-SO_3 adduct as a sulfonating agent [57], whereas SO_2Cl_2 gives only polymers [58].



Enol ethers can be converted into thioamides by reaction with elemental sulfur in the presence of secondary amines [59].

[45] *C. Walling* and *W. Helmreich*, J. Amer. chem. Soc. *81*, 1144 (1959).

[46] *S. A. Heininger* and *G. H. Birum*, US-Pat. 2875250 (1959), Monsanto Chemical Co.; Chem. Abstr. *53*, 19978d (1959).

[47] *A. Senning* and *S. O. Lawesson*, Tetrahedron *19*, 695 (1963).

[48] *A. V. Kalabina, E. F. Kolmakova, T. L. Bychkova, Y. K. Maksyutin, E. A. Denisevich*, and *G. I. Smolina*, Ž. obšč. Chim. *35*, 979 (1965); Chem. Abstr. *63*, 9849f (1965).

[49] *M. J. Baldwin* and *R. K. Brown*, Canad. J. Chem. *46*, 1093 (1968).

[50] *W. L. Orr* and *N. Kharasch*, J. Amer. chem. Soc. *75*, 6030 (1953).

[51] *J. Michalski* and *S. Musierowicz*, Roczniki Chem. *36*, 1655 (1962); Chem. Abstr. *59*, 8634a (1963).

[52] *E. Kobayashi* and *R. Sakata*, Yakugaku Zasshi (J. Japan Oil Chemists' Soc.) *82*, 455 (1962); Chem. Abstr. *58*, 4552h (1963).

[53] *M. Seefelder* and *H. Pasedach*, German Pat. 960095 (1957), Badische Anilin & Soda-Fabrik AG; Chem. Zbl. *129*, 9908 (1958).

[54] *H. E. Simmons, O. C. Blomstrom*, and *R. O. Vest*, J. Amer. chem. Soc. *84*, 4782 (1962).

[55] *F. Effenberger* and *J. Daub*, Chem. Ber. *102*, 104 (1969).

[56] *W. R. Hasek*, US-Pat. 2928870 (1960), du Pont; Chem. Abstr. *54*, 18361h (1960).

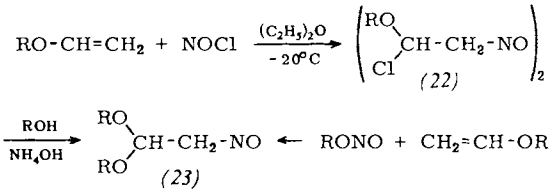
[57] *A. P. Terent'ev* and *N. P. Volynskii*, Ž. obšč. Chim. *19*, 784 (1949); Chem. Abstr. *44*, 1095f (1950).

[58] *J. Daub*, Dissertation, Universität Stuttgart, 1966.

[59] *C. L. Levesque*, US-Pat. 2489094 (1949), Rohm & Haas Co.; Chem. Abstr. *44*, 6427h (1950).

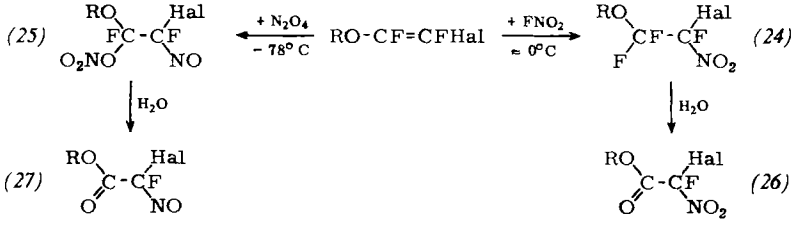
2.4. Reactions with Nitrogen Compounds

Nitrosyl halides add smoothly to enol ethers below −20 °C [60–62]. The resulting β-nitroso α-halogeno ethers *(22)* are generally dimeric [61], and, with the exception of the perfluorinated derivatives [63], they are not very stable. They react with alcohols and bases to form the stable acetals *(23)*, which can also be obtained directly from enol ethers and alkyl nitrites [63].

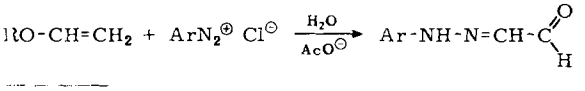


The reaction of nitryl halides and dinitrogen tetroxide with enol ethers is much less satisfactory. For example, the reaction of butyl vinyl ether with nitryl chloride at −20 °C in chloroform yields 20 % of 1,2-dichloroethyl butyl ether and only traces of 1-chloro-2-nitroethyl butyl ether [64]. Reaction with N_2O_4 leads only to decomposition and polymerization of the vinyl ethers [65].

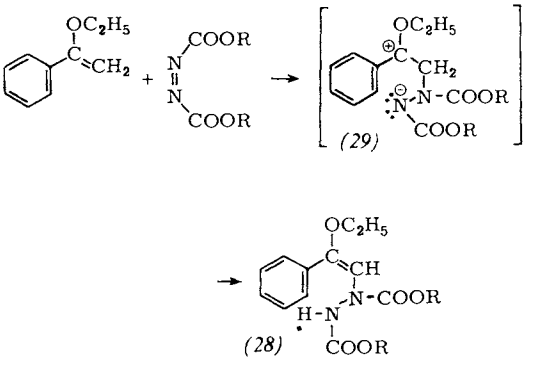
Only alkyl perhalogenovinyl ethers react with nitryl halides or N_2O_4 to give definite addition compounds *(24)* and *(25)* respectively, which can be converted into the esters *(26)* and *(27)* by hydrolysis [66,67].



Diazonium salts undergo an electrophilic reaction with enol ethers to form glyoxal phenylhydrazones at 0 °C in sodium acetate buffer solution [68]. Attempts to isolate the unhydrolyzed substitution products in non-aqueous media were unsuccessful [69].



The nitrogen in azodicarboxylic esters is also electrophilic, and can react with enol ethers; reaction with α-ethoxystyrene, for example, yields the Diels-Alder cycloadduct together with a comparable amount of the substitution product *(28)* [70], which *Huisgen* assumes to be formed *via* a dipolar intermediate *(29)* [71].



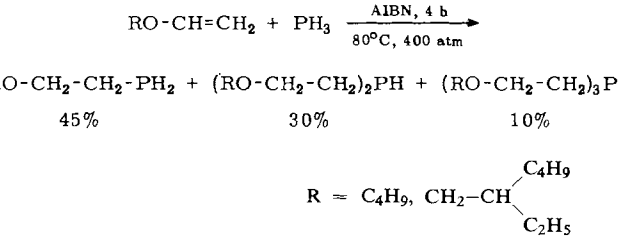
2.5. Phosphorylation

The enol ethers can react with P–H compounds or with phosphorus halides to form compounds containing C–P bonds. Dialkyl phosphites add smoothly to vinyl ethers in the presence of free radical generators to give exclusively anti-Markownikoff products



(30)

(30) [72,73]. Reaction with phosphine under similar conditions leads *via* a free-radical chain mechanism to a mixture of mono-, di-, and trialkylphosphines [74].



[60] *S. Tchelitcheff*, US-Pat. 2674625 (1954), Rhône-Poulenc; Chem. Abstr. *49*, 6301h (1955).

[61] *K. A. Ogloblin* and *V. P. Semenov*, Ž. org. Chim. *1*, 401 (1965); Chem. Abstr. *63*, 1691h (1965).

[62] *B. L. Dyatkin*, *R. A. Bekker*, *Y. S. Konstantinov*, and *I. L. Knunyants*, Doklady Akad. Nauk SSSR *165*, 1305 (1965); Chem. Abstr. *64*, 9581b (1966).

[63] *S. Tchelitcheff*, US-Pat. 2674625 (1954), Rhône-Poulenc; Chem. Abstr. *49*, 6301h (1955).

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[65] *S. V. Vasil'ev*, Chem. Abstr. *55*, 3415i (1961).

[66] *B. L. Dyatkin*, *R. A. Bekker*, and *I. L. Knunyants*, Doklady Akad. Nauk SSSR *168*, 1319 (1966); Chem. Abstr. *65*, 12102c (1966).

[67] *B. L. Dyatkin*, *R. A. Bekker*, and *I. L. Knunyants*, Doklady Akad. Nauk SSSR *166*, 106 (1966); Chem. Abstr. *64*, 11080c (1966).

[68] *A. P. Terent'ev* and *W. A. Zagorvskii*, Ž. obšč. Chim. *26*, 200 (1956); Chem. Abstr. *50*, 13777i (1956).

[69] *F. Effenberger*, unpublished results.

[70] *K. Alder* and *H. Niklas*, Liebigs Ann. Chem. *585*, 97 (1954).

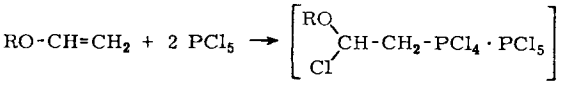
[71] *R. Huisgen* and *H. Pohl*, Chem. Ber. *93*, 527 (1960).

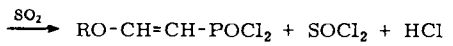
[72] *A. N. Pudovik*, *I. V. Konovalova*, and *A. A. Guryleva*, Ž. obšč. Chim. *33*, 2924 (1963); Chem. Abstr. *60*, 5541g (1964).

[73] *T. Nishiwaki*, Tetrahedron *22*, 711 (1966).

[74] *M. M. Rauhut*, *H. A. Currier*, *A. M. Semsel*, and *V. P. Wystrach*, J. org. Chemistry *26*, 5138 (1961).

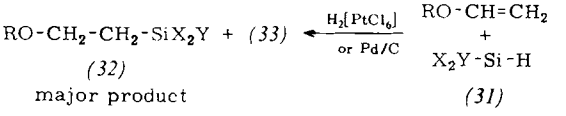
Halides used include phosphorus pentachloride [75,76] and ethyl- and phenyltetrachlorophosphoranes [77-79], all of which give β-substitution products of the vinyl ethers. Acceleration of the reaction on addition of $FeCl_3$ supports the assumption of an ionic mechanism [77].

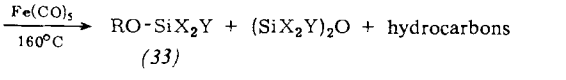




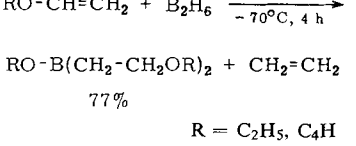
2.6. Reactions with Hydrides of Silicon, Boron, and Aluminum

The reaction of silanes *(31)* with vinyl ethers results either in addition to form *(32)* or in cleavage of the ether linkage to yield *(33)*, depending on the catalyst and the reaction conditions [80-83].



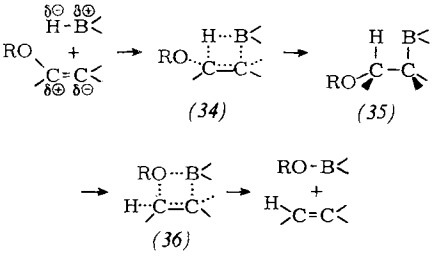


Addition and cleavage occur concurrently in the reaction of diborane with alkyl vinyl ethers [84].

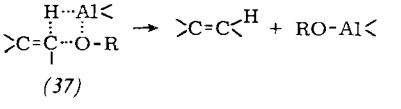


Dialkylboranes and dialkylaluminum hydrides lead only to cleavage of the ether linkage, with formation of the expected olefins [85,86].

The uncatalyzed reactions of these hydrides with enol ethers proceed by like mechanisms. The polarized metal-H bond adds across the polarized CC double bond, the reaction proceeding *via* the transition state *(34)* [87]. The addition compound *(35)* can then undergo ether cleavage *via (36)* [88]. Addition and elimination proceed stereospecifically as *cis*



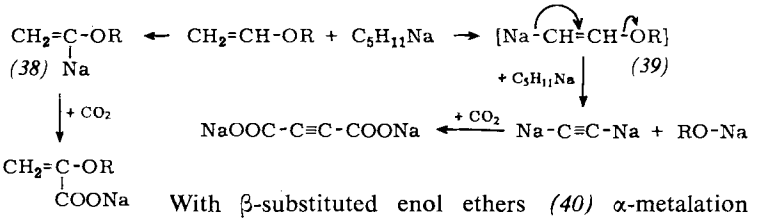
reactions [87,88]. In the reaction with dialkylaluminum hydrides direct cleavage *via* the transition state *(37)* is less likely [86].



2.7. Reactions with Organometallic Compounds

This section will deal only with reactions whose course is influenced by the CC double bond. Pure ether reactions are not discussed.

Paul and *Tchelitcheff* found that pentylsodium metalates enol ethers in the α- or β-position of the double bond [89]. Whereas the α-metalated compound *(38)* is stable under the reaction conditions, the β-metalated enol ether *(39)* immediately rearranges into an alkyne and an alcohol.



With β-substituted enol ethers *(40)* α-metalation predominates, while α-substituted compounds are metalated only in the β position [89].

[75] *K. N. Anisimov* and *A. N. Nesmeyanov*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1954*, 610; Chem. Abstr. *49*, 11540i (1955).

[76] *B. A. Arbuzov, V. S. Vinogradova, N. A. Polezhaeva*, and *A. K. Shamsutdinova*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1963*, 675; Chem. Abstr. *59*, 11551d (1963).

[77] *V. S. Tsivunin, G. Kamai*, and *D. B. Sultanova*, Ž. obšč. Chim. *33*, 2149 (1963); Chem. Abstr. *59*, 12839a (1963).

[78] *K. N. Anisimov* and *N. E. Kolobova*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1962*, 444; Chem. Abstr. *57*, 12529c (1962).

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[80] *R. Calas, N. Duffaut*, and *J. Valade*, Bull. Soc. chim. France *1955*, 790; Chem. Abstr. *50*, 5536f (1956).

[81] *L. Goodman, R. M. Silverstein*, and *A. Benitez*, J. Amer. chem. Soc. *79*, 3073 (1957).

[82] *M. F. Shostakovskii, B. A. Sokolov, G. V. Dmitrieva*, and *G. M. Alekseeva*, Ž. obšč. Chim. *33*, 3778 (1963); Chem. Abstr. *60*, 9306g (1964); Ž. obšč. Chim. *34*, 2839 (1964); Chem. Abstr. *61*, 14703d (1964).

[83] *R. K. Freidlina, N. A. Kuz'mina*, and *E. T. Chukovskaya*, Izvest. Akad. Nauk SSSR, Ser. chim. *1966*, 176; Chem. Abstr. *64*, 12712e (1966).

[84] *B. M. Mikhailov* and *A. N. Blokhina*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1962*, 1373; Chem. Abstr. *58*, 5707e (1963).

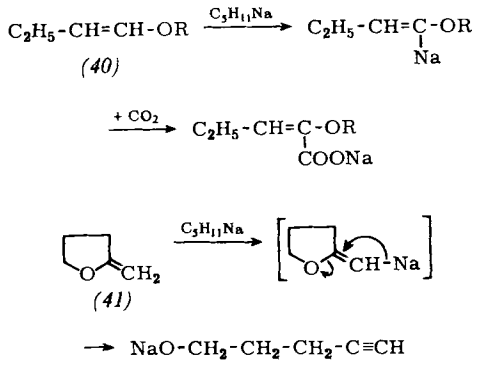
[85] *B. M. Mikhailov* and *E. N. Safonova*, Izvest. Akad. Nauk SSSR, Ser. chim. *1965*, 1487; Chem. Abstr. *63*, 16374b (1965).

[86] *P. Pino* and *G. P. Lorenzi*, J. org. Chemistry *31*, 329 (1966).

[87] *H. C. Brown*: Hydroboration. W. A. Benjamin, New York 1962, p. 133ff.

[88] *D. J. Pasto* and *Sr. R. Snyder*, J. org. Chemistry *31*, 2777 (1966).

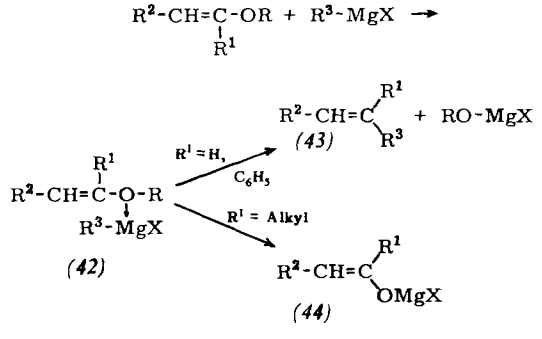
[89] *R. Paul* and *S. Tchelitcheff*, C. R. hebd. Séances Acad. Sci. *235*, 1226 (1952).



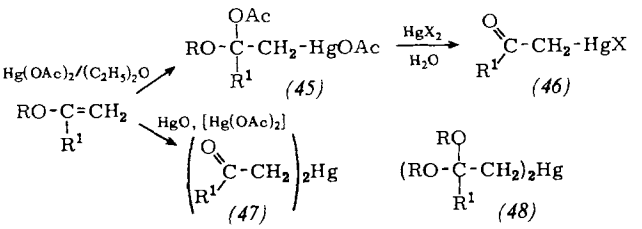
Acetylene was also obtained in the reaction of phenyl vinyl ether with triphenylmethylsodium [90], indicating β-metalation in this case.

Organolithium compounds, which are less reactive than the sodium derivatives, do not react with enol ethers below −30 °C [91]. At higher temperatures, no definite reaction products are obtained apart from a little acetylene [92].

Grignard compounds, in which the polarity of the C-metal bond is even lower than that of the Li–C bond, evidently do not metalate enol ethers, but form normal adducts *(42)*. The negative alkyl residue of the Grignard compound can then react with the α-C atom of the vinyl group to form an olefin *(43)*, or a ketone *(44)* may be formed by cleavage of the ether linkage [93–95]. The reaction course depends on the nature of R^1.



Organomercury compounds often exhibit different behavior, owing to substantially homopolar character of the C-metal bond [96]. Mercury salts add to enol ethers smoothly and in excellent yields [97–100]. The acylals *(45)* formed with mercury(II) acetate can be



easily converted into *(46)* by treatment with other Hg salts and water [98]. With yellow mercuric oxide and catalytic quantities of mercury(II) acetate, *(47)* is formed [99]. Reaction in the presence of alcohol leads directly to the acetals *(48)* [100]. Since the addition takes place exclusively in one direction, electrophilic addition of the mercury salt to the enol ether must be assumed.

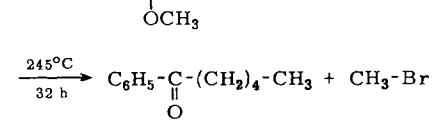
3. Reactions of Enol Ethers leading to the Formation of C–C Bonds

The nucleophilic enol ethers should undergo polar C–C linkage with electrophilic carbon compounds. The difficulty with this reaction arises from the fact that few reactants are sufficiently electrophilic to react with enol ethers in the absence of Friedel-Crafts catalysts, which, however, usually cause polymerization of the enol ether.

3.1. Alkylation of Enol Ethers

Whereas enamines are sufficiently nucleophilic to undergo *C*-alkylation without the need for catalysts [101], this reaction is generally not feasible with enol ethers.

The only data available regarding alkylation with alkyl halides refer to the reactions of α-methoxystyrene with benzyl bromide, *n*-butyl bromide, and chloroacetic ester [102]. It is, however, by no means certain that enol ether is stable at the high temperatures used.



Solvolysis of 1,4-dihydro-3,5-dimethoxybenzyl *p*-toluenesulfonate *(49)*, which leads *via (50)* to 1,6-dimethoxycycloheptatriene *(51)* [103], may be regarded as an intramolecular alkylation of an enol ether. The S_N2 alkylation of the enol ether is made possible by the favorable steric conditions.

[90] *G. Wittig* and *D. Wittenberg*, Liebigs Ann. Chem. *606*, 1 (1957).

[91] *C. D. Broaddus*, J. org. Chemistry *30*, 4131 (1965).

[92] *K. E. Piotrovskii* and *M. P. Stotskaya*, Doklady Akad. Nauk SSSR *135*, 868 (1960); Chem. Abstr. *55*, 13300h (1961).

[93] *C. M. Hill*, *R. A. Walker*, and *M. E. Hill*, J. Amer. chem. Soc. *73*, 1663 (1951).

[94] *C. M. Hill*, *R. M. Prigmore*, and *G. J. Moore*, J. Amer. chem. Soc. *77*, 352 (1955).

[95] *C. M. Hill*, *R. Woodberry*, *D. E. Simmons*, *M. E. Hill*, and *L. Haynes*, J. Amer. chem. Soc. *80*, 4602 (1958).

[96] *D. J. Cram*: Fundamentals of Carbanion Chemistry. Academic Press, New York 1965, p. 116ff.

[97] *A. N. Nesmeyanov*, *I. F. Lutsenko*, and *N. I. Vereshchagina*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1947*, 63; Chem. Abstr. *42*, 4148i (1948).

[98] *I. F. Lutsenko*, *R. M. Khomutov*, and *L. V. Eliseeva*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1956*, 181; Chem. Abstr. *50*, 13730e (1956).

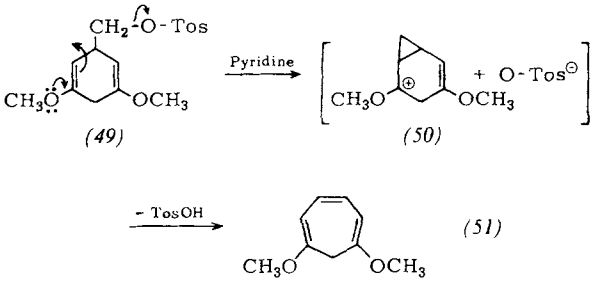
[99] *I. F. Lutsenko* and *R. M. Khomutov*, Doklady Akad. Nauk SSSR *102*, 97 (1955); Chem. Abstr. *50*, 4773b (1956).

[100] *A. N. Nesmeyanov*, *I. F. Lutsenko*, and *R. M. Khomutov*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1957*, 942; Chem. Abstr. *52*, 4476b (1958).

[101] *G. Stork*, *A. Brizzolara*, *H. Landesman*, *J. Szmuszkovicz*, and *R. Terrell*, J. Amer. chem. Soc. *85*, 207 (1963).

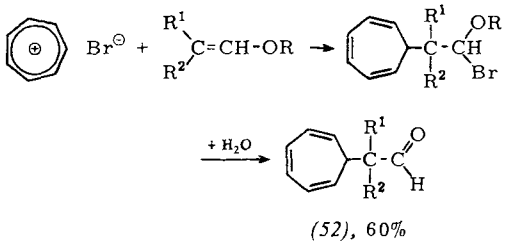
[102] *C. W. Mortenson* and *M. A. Spielman*, J. Amer. chem. Soc. *62*, 1609 (1940).

[103] *O. L. Chapman* and *P. Fitton*, J. Amer. chem. Soc. *85*, 41 (1963).



(49) (50) (51)

The reaction with tropylium salts, which yields cycloheptatrienylacetaldehydes *(52)* [104], may also be regarded as an alkylation of an enol ether.



(52), 60%

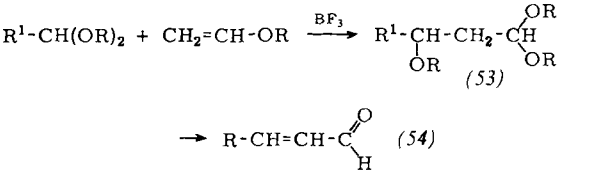
$R^1 = R^2 = CH_3$, H; R = C_2H_5, $CH(CH_3)_2$, C_4H_9

The importance of correct choice of reaction conditions is emphasized by the ease of polymerization of vinyl ethers under the action of tropylium salts [105].

3.2. Reaction of Acetals with Enol Ethers

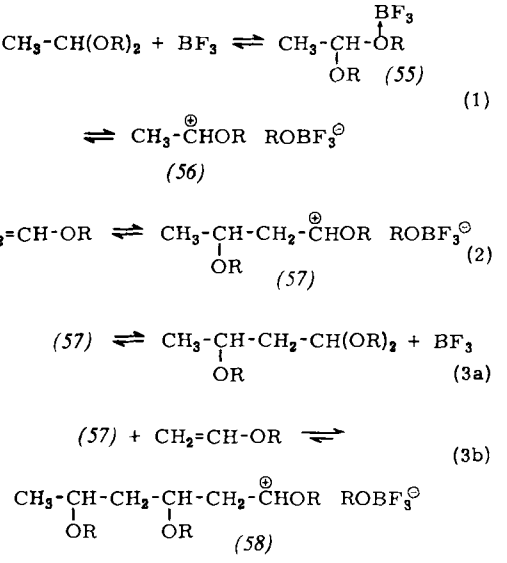
In contrast with alkylation, the polar C–C linkage of enol ethers with aldehydes and ketones or their derivatives is of considerable importance [106]. The reaction of acetals with enol ethers is particularly important, providing a valuable supplement to the aldol condensation, to which it is greatly superior in many cases by virtue of the specificity of the reaction.

It was first observed in 1939 that acetals add to enol ethers in the presence of BF_3 [107]. The addition compounds *(53)* can lose alcohol to yield α,β-unsaturated aldehydes *(54)* [108]. Since the new acetal *(53)* can again add to the enol ether, a definite chain lengthening by two C atoms per step is possible.



(53) *(54)*

Hoaglin and *Hirsh* have proposed a carbonium ion mechanism [108] comparable to the mechanism of the acidic aldol condensation, with R in place of H.



(1)

(2)

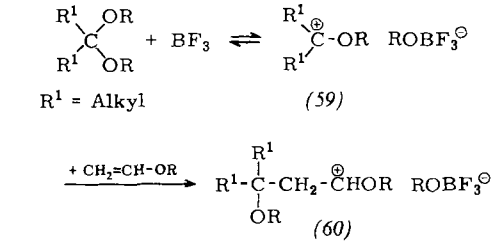
(3a)

(3b)

(56) *(57)* *(58)*

The acetal reacts with the catalyst to form an adduct *(55)*, which ionizes because of the stabilization of both cation and anion; whether dissociation is complete or proceeds only as far as the formation of ion pairs will not be discussed. Nucleophilic reaction of the vinyl ether with the carbonium fluoroborate *(56)* yields *(57)*, which adds either the anion in accordance with eq. (3a) or a further mol. equiv. of vinyl ether to give *(58)* as in eq. (3b). *(58)* can then again react with the anion or with another mol. equiv. of vinyl ether. Reaction (3a) is favored by a high acetal/vinyl ether ratio [108] and by higher reactivity of *(56)* as compared with *(57)*.

Comparison of the reactions of ketals with those of aromatic aldehyde acetals demonstrates the influence of the reactivity of the carbonium ion. Ketals give practically no 1:1 addition product, even when less than 1 mol. equiv. of the vinyl ether is present, since *(60)*, being more reactive than *(59)*, immediately



R^1 = Alkyl *(59)* *(60)*

reacts further with the vinyl ether. The acetals of aromatic aldehydes, on the other hand, give mainly the 1:1 adduct even at an acetal/vinyl ether ratio of only 1:1, since *(61)* is much more reactive than *(62)*, and so reacts preferentially with the vinyl ether [109].

The reactivity of acetals toward vinyl ethers increases in the order: saturated acetals < aromatic acetals <

[104] *M. E. Vol'pin, I. S. Akhrem,* and *D. N. Kursanov,* Ž. obšč. Chim. *30*, 159 (1960); Chem. Abstr. *54*, 22535h (1960); Chem. Abstr. *60*, 13180g (1964).

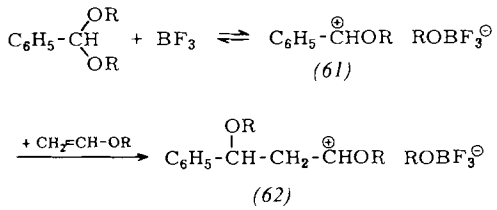
[105] *C. E. Bawn, C. Fitzsimmons,* and *A. Ledwith,* Proc. chem. Soc. (London) *1964*, 391.

[106] For reviews, see *L. S. Povarov,* Russ. chem. Rev. (English translation of Usp. Chim.) *1965*, 639; Houben-Weyl-Müller: Methoden der organischen Chemie. Thieme-Verlag, Stuttgart 1954, 4th Edit., Vol. VII/1, p. 115ff.

[107] *M. Müller-Cunradi* and *K. Pieroh,* US-Pat. 2165962 (1939), IG Farben; Chem. Abstr. *33*, 8210^2 (1939).

[108] *R. I. Hoaglin* and *D. H. Hirsh,* J. Amer. chem. Soc. *71*, 3468 (1949).

[109] *M. F. Shostakovskii* and *E. P. Gracheva,* Ž. obšč. Chim. *26*, 1679 (1956); Chem. Abstr. *51*, 1895h (1957).



(61)

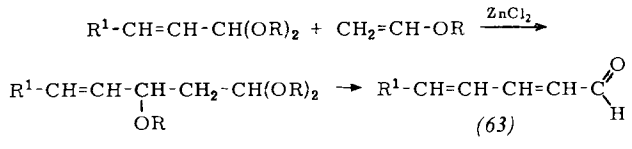
(62)

α,β-unsaturated acetals. Even the inert saturated acetals react with normal vinyl ethers to give the 1:1 compound in 60 to 70 % yield if the acetal is present in excess [108].

Since the catalysts used can also cause polymerization of vinyl ethers, the addition of acetals is also influenced by the tendency of the enol ether toward polymerization, which increases in the order 1-unsubstituted enol ethers < 1-substituted enol ethers < 1-alkoxydienes [110, 111]. Thus saturated acetals add to 1-unsubstituted enol ethers; with 1-substituted enol ethers and 1-alkoxydienes, on the other hand, polymerization predominates. The more reactive aromatic acetals undergo addition even with readily polymerizable enol ethers.

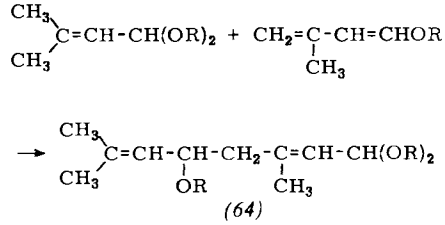
The advantage of this reaction over the aldol condensation is that the enol ether, as a potential carbonyl compound, acts only as a nucleophile, and the acetal only as an electrophile [112, 113]. For example, four products are to be expected, and are in fact found, in the alkaline aldol reaction of propionaldehyde with acetaldehyde, whereas the reactions of propionaldehyde acetal with ethyl vinyl ether and of acetaldehyde acetal with ethyl propenyl ether each give only one product.

The reaction of α,β-unsaturated aldehyde acetals with vinyl ethers is often used for the synthesis of polyenes *(63)* [114]. Alkoxydienes have also been used as the



(63)

enol ether component, *e.g.* for the synthesis of ethoxycitral acetal *(64)* [112, 115].



(64)

R = C_2H_5

[110] *M. F. Shostakovskii, E. P. Gracheva,* and *N. K. Kul'bovskaya,* Ž. obšč. Chim. *28,* 2344 (1958); Chem. Abstr. *53,* 3124i (1959).

[111] *W. Flaig,* Liebigs Ann. Chem. *568,* 1 (1950).

[112] *B. M. Mikhailov* and *L. S. Povarov,* Ž. obšč. Chim. *29,* 2079 (1959); Chem. Abstr. *54,* 10851e (1960).

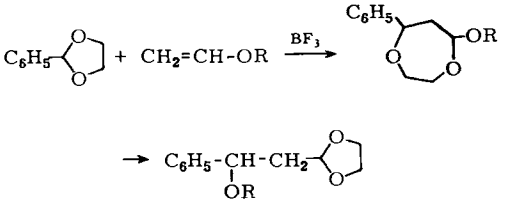
[113] *H. Normant* and *G. Martin,* Bull. Soc. chim. France *1963,* 1646.

[114] *I. N. Nazarov, I. I. Nazarova,* and *I. V. Torgov,* Doklady Akad. Nauk SSSR *122,* 82 (1958); Chem. Abstr. *53,* 1123f (1959).

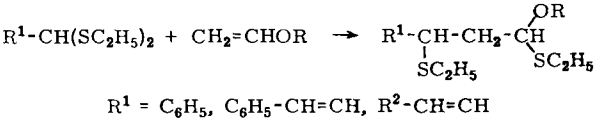
[115] *I. N. Nazarov* and *Z. A. Krasnaya,* Doklady Akad. Nauk SSSR *118,* 716 (1958); Chem. Abstr. *52,* 11737e (1958).

The reaction of enol ethers with acetals is also important in carotenoid syntheses. Thus, one industrial synthesis of β-carotene involves condensation of a vinyl ether and a propenyl ether with acetals [116]. Another process for the synthesis of symmetrical carotenoids (C_{40}) starts with C_{14} acetals and a symmetrical C_{12} dienol ether [117].

Cyclic acetals also add to vinyl ethers, an additional possibility in this case being transacetalization if this yields more stable products [118, 119].

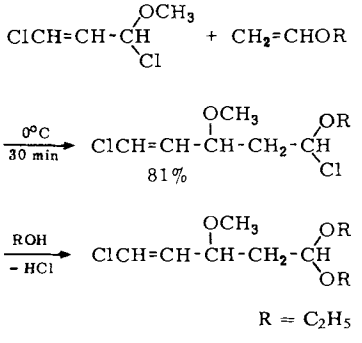


In the case of the thioacetals, only the most reactive members add to enol ethers [120], since the alkylthio group does not stabilize the carbonium ion so well as an alkoxy group.



R^1 = C_6H_5, C_6H_5-CH=CH, R^2-CH=CH

On the other hand, ionization should be facilitated in α-halogeno ethers, and these compounds do, in fact, react particularly readily with vinyl ethers [121].



R = C_2H_5

A reaction comparable with that of enol ethers with acetals is the dimerization of vinyl ethers with BF_3 in the presence of mercury salts, which proceeds *via* an Hg-addition compound [122, 123].

[116] *O. Isler, H. Lindlar, M. Montavon, R. Rüegg,* and *P. Zeller,* Helv. chim. Acta *39,* 249 (1956).

[117] *O. Isler, M. Montavon, R. Rüegg,* and *P. Zeller,* Liebigs Ann. Chem. *603,* 129 (1957).

[118] *B. M. Mikhailov* and *L. S. Povarov,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1960,* 1903; Chem. Abstr. *55,* 13409f (1961).

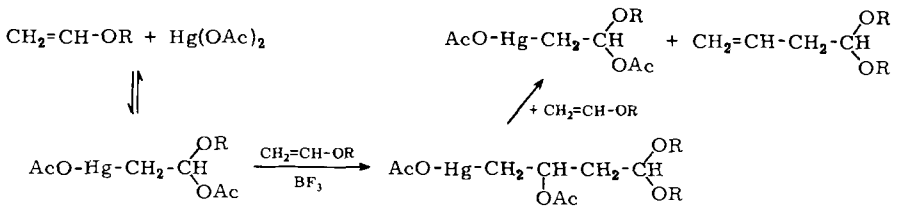
[119] *H. Pommer,* German Pat. 1031301 (1958), Badische Anilin- & Soda-Fabrik AG.

[120] *B. M. Mikhailov* and *G. S. Ter-Sarkisyan,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1960,* 1888; Chem. Abstr. *55,* 17562a (1961).

[121] *R. Y. Popova, T. V. Protopopova, V. G. Vinokurov,* and *A. P. Skoldinov,* Ž. obšč. Chim. *34,* 114 (1964); Chem. Abstr. *60,* 10535g (1964).

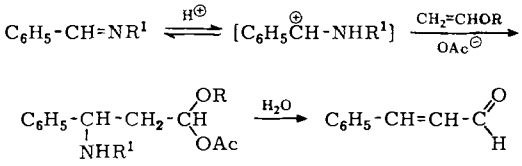
[122] *R. I. Hoaglin, D. G. Kubler,* and *A. E. Montagna,* J. Amer. chem. Soc. *80,* 5460 (1958).

[123] *S. M. Makin* and *B. K. Kruptsov,* Ž. obšč. Chim. *30,* 3276 (1960); Chem. Abstr. *55,* 21043a (1961).



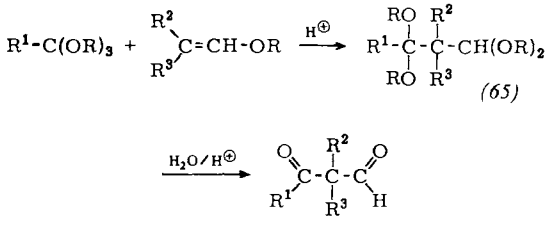
Polymerization of the enol ether is prevented by addition of Hg salts. The resulting acetal can react further with an excess of vinyl ether in the presence of BF_3, but this occurs only to a small extent [122].

The reaction of Schiff bases with enol ethers in acetic acid may be included in the same group as the acetal reaction [124].

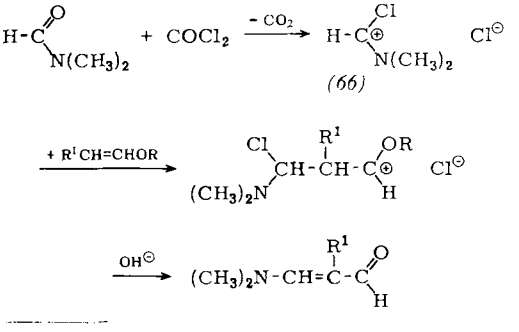


3.3. Formylation and Acylation of Enol Ethers

An important variant of the acetal reaction is the reaction of enol ethers with ortho esters [106].



The most extensively studied reaction in this group is the formylation of enol ethers with orthoformates [106, 125, 126] to give derivatives of malonic dialdehyde *(65)*, which are valuable starting materials for the synthesis of heterocycles [127]. The higher ortho esters ($R^1 \neq H$) are much less reactive, and apart from formylation, the only other acylations of enol ethers so far have been with orthoacetates, with limited success [128].



[124] *L. S. Povarov* and *B. M. Mikhailov*, Izvest. Akad. Nauk SSSR, Ser. chim. *1964*, 1910; Chem. Abstr. *62*, 2730g (1965).

[125] Houben-Weyl-Müller: Methoden der organischen Chemie. Thieme Verlag, Stuttgart 1954, 4th Edit., Vol. VI/3, p. 248.

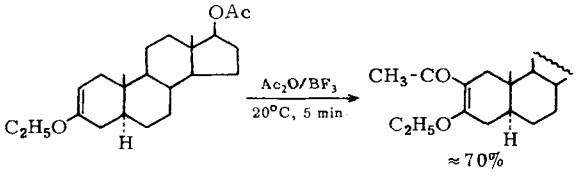
[126] *K. C. Brannock*, J. org. Chemistry *25*, 258 (1960).

[127] *H. Bredereck, R. Gompper*, and *G. Morlock*, Chem. Ber. *90*, 942 (1957).

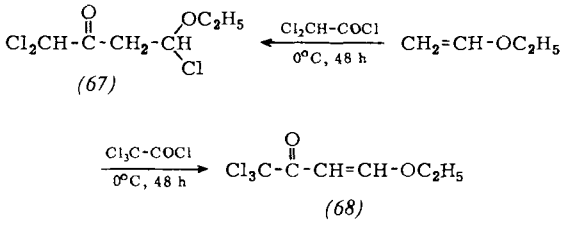
[128] *L. A. Yanovskaya, V. T. Kucherov*, and *B. A. Rudenko*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1962*, 2182; Chem. Abstr. *58*, 12410g (1963).

Enol ethers can also be formylated by reaction with Vilsmeier-Haack agents [129]. The formylating agent *(66)* formed from dimethylformamide and phosgene is the most suitable for reaction with enol ethers [130,131], since it shows little tendency to initiate polymerization.

Acylation of enol ethers in the presence of Friedel-Crafts catalysts is possible only if the enol ether has little tendency to polymerize. This condition is met *e.g.* by enol ethers of the steroids, which can therefore be acylated in the presence of BF_3 [132].



The electrophilic potential of acylating agents can also be increased by substituents. While acetyl chloride itself does not react with vinyl ethers, monochloroacetyl chloride causes polymerization, dichloroacetyl chloride yields the addition compound *(67)*, and trichloroacetyl chloride gives the substitution product *(68)*. *(67)* and *(68)* are formed in very good yields [133].



Oxalyl chloride also has a high electrophilic potential. It adds to enol ethers at room temperature, with primary formation of the α-halogeno ether *(69)* which reacts readily with nucleophiles, such as triethylamine, to give *(70)* [134].

Exclusive *cis*-addition of oxalyl chloride has been found for dihydropyran [135].

[129] Houben-Weyl-Müller: Methoden der organischen Chemie. Thieme Verlag, Stuttgart 1954, 4th Edit., Vol. VII/1, p. 29.

[130] *Z. Arnold* and *F. Šorm*, Collect. czechoslov. chem. Commun. *23*, 452 (1958); *Z. Arnold* and *J. Žemlička*, *ibid. 24*, 786 (1959); *Z. Arnold*, *ibid. 25*, 1308 (1960).

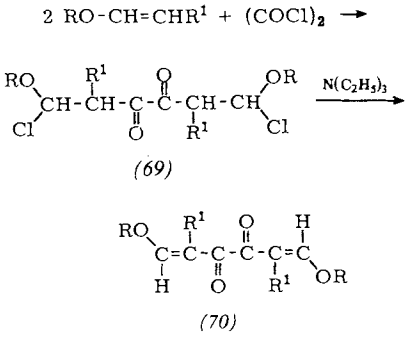
[131] *G. Martin* and *M. Martin*, Bull. Soc. chim. France *1963*, 637; *H. Normant* and *G. Martin*, *ibid. 1963*, 1646.

[132] *D. Sieff* and *R. D. Youssefyeh*, J. Amer. chem. Soc. *85*, 3901 (1963).

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[134] *F. Effenberger*, Chem. Ber. *98*, 2260 (1965).

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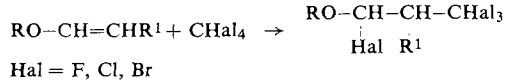
(69)

(70)

Phosgene, which is also a strongly electrophilic acid chloride, reacts with enol ethers at about 0 °C to form acyl chlorides of α,β-unsaturated carboxylic acids [136, 137], while at about 50 °C polymerization occurs [138]. The β-alkoxyacryloyl chlorides readily obtainable by this reaction are useful starting compounds for the synthesis of heterocycles [139].

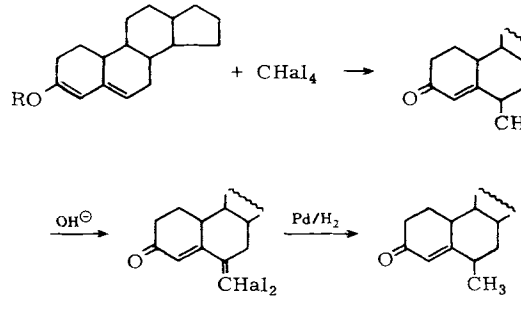
3.4. Reaction of Tetrahalogenomethanes with Enol Ethers

A new C–C bond is also formed in the addition reactions of enol ethers with tetrahalogenomethanes, which proceed by a radical mechanism (in the presence of benzoyl peroxide or on irradiation) [140–143].



Hal = F, Cl, Br

Fluorine, chlorine, and bromine compounds are used. When mixed tetrahalogenomethanes are employed, bromine, which is most readily removed as a free radical, becomes attached



to the α-carbon atom of the enol ether [144]. The reaction with tetrahalogenomethanes can also be applied to steroids, and permits *e.g.* the introduction of a methyl group [145].

4. Cycloadditions

Enol ethers are particularly suitable for use in the study of cycloadditions for the following reasons:

1) They are electron-rich olefins, intermediate between olefins and enamines in their polarization, and can therefore react both by a concerted mechanism and *via* dipolar intermediates. A polar reaction is favored in the case of enamines [146] and a synchronous reaction in the case of olefins.

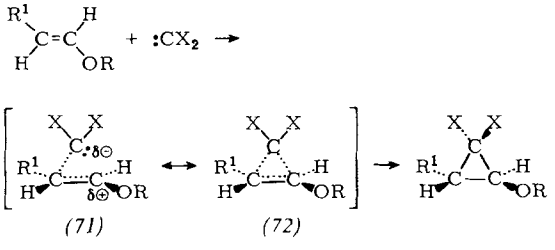
2) The ratio of addition to substitution with enol ethers is also intermediate between that with enamines, which tend to undergo substitution, and that with olefins, most of which undergo addition. The reactions with enol ethers often lead to primary addition products, whose conversion into the substitution products is amenable to study [147].

3) Stereoisomeric enol ethers are easy to prepare, and generally do not isomerize during the reaction, so that the steric course of the cycloadditions can be readily observed.

Most of the cycloadditions with enol ethers described so far result in the formation of two new σ bonds, leading to three-, four-, five-, or six-membered rings. Following a suggestion by *Huisgen*, these are known as 2+1, 2+2, 2+3, and 2+4 cycloadditions [148], the enol ether being the 2-component, though it may also be the 4-component in the 2+4 combination.

4.1. 2+1 Cycloadditions

This type of cycloaddition is represented by the reaction of carbenes or nitrenes with enol ethers.



(71) (72)

[136] *P. A. Hawkins* and *N. Bennet*, Brit. Pat. 570974 (1945), ICI; Chem. Abstr. *40*, 7238⁵ (1946).

[137] *R. E. Paul* and *S. Tchelitcheff*, US-Pat. 2768174 (1956), Société des Usines chimiques Rhône-Poulenc; Chem. Abstr. *51*, 5818f (1957).

[138] *F. Grosser*, US-Pat. 2464747 (1949), General Aniline & Film Corp.; Chem. Abstr. *43*, 4051c (1949).

[139] *F. Effenberger* and *W. Hartmann*, Angew. Chem. *76*, 188 (1964); Angew. Chem. internat. Edit. *3*, 230 (1964).

[140] *M. Levas* and *E. Levas*, C. R. hebd. Séances Acad. Sci. *230*, 1669 (1950); Bull. Soc. chim. France *1959*, 1800.

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[142] *K. S. Bagdasar'yan* and *R. I. Milyutinskaya*, Ž. fiz. Chim. *28*, 498 (1954); Chem. Abstr. *48*, 13439e (1954); *A. F. Revzin* and *K. S. Bagdasar'yan*, *ibid.* *38*, 215 (1964); Chem. Abstr. *60*, 13113g (1964).

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[144] *P. Tarrant* and *E. C. Stump jr.*, J. org. Chemistry *29*, 1198 (1964).

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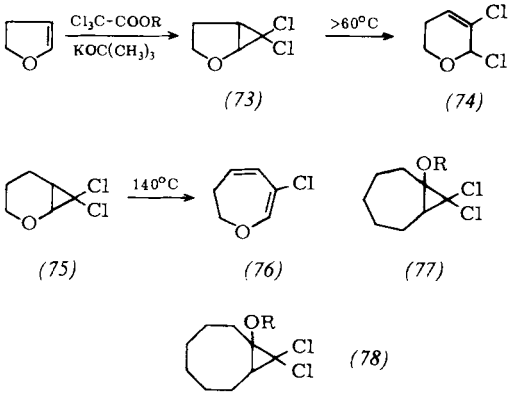
[147] *F. Effenberger*, Habilitationsschrift, Universität Stuttgart, 1964.

[148] *R. Huisgen*, Angew. Chem. *80*, 329 (1968); Angew. Chem. internat. Edit. *7*, 321 (1968).

Dihalogenocarbenes react more readily as electrophiles with enol ethers than with olefins [149, 150]. The reactions lead almost exclusively to cycloaddition, insertion occurring only in isolated cases.

The stereospecific *cis*-addition observed with olefins [151] was confirmed also for the addition of halogenocarbenes to enol ethers [152]. The reaction may therefore be concluded to be an essentially synchronous cycloaddition of the singlet carbene to the double bond [149].

The stability of the resulting cyclopropane derivatives depends on the enol ether used, and in the case of cyclic ethers it increases with increasing ring size [153, 154]. Thus *(73)* can be distilled under greatly reduced pressure, but rearranges quantitatively into *(74)* above 60 °C [153]. The ring expansion in *(75)* occurs only at 140 °C, and, on heating in quinoline, one mol. equiv.



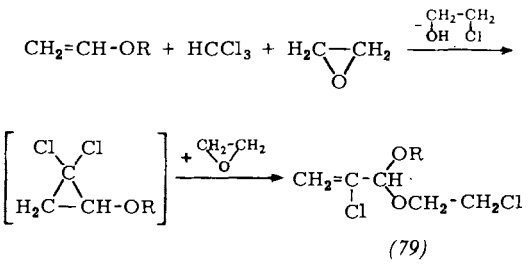
(73) *(74)* *(75)* *(76)* *(77)* *(78)*

of HCl is simultaneously eliminated with formation of *(76)*. *(77)* and *(78)* do not give isolable quantities of ring expansion products when heated [155].

The difference in the tendency toward rearrangement is due not only to ring strain, but also to the ionization of the C-halogen bond, which is distinctly influenced by the neighboring group participation of the ether oxygen [154].

Entropy measurements [156] show, in agreement with the Woodward-Hoffmann rules for a thermal reaction [157], synchronous opening of the three-membered ring.

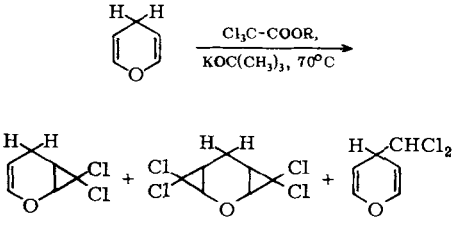
When enol ethers are allowed to react with haloforms and two mol. equiv. of ethylene oxide, the intermediate



(79)

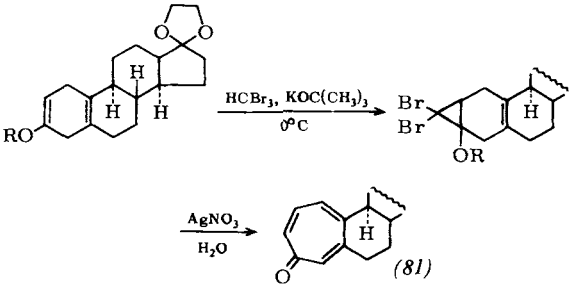
cyclopropane derivative in most cases immediately undergoes secondary reaction to form *(79)* [158].

Carbenes also add to divinyl ethers [159] and to the moderately stable 4*H*-pyrans [160]; in the latter case, mono- and dicycloaddition are accompanied to a small extent by insertion to form *(80)* [160].



(80)

The addition of carbenes to enol ethers followed by ring expansion is frequently used in syntheses [158, 161, 162]. Tropolone-analogous steroids *(81)* can be prepared particularly easily in this way [163, 164].



(81)

4.2. 2+2 Cycloadditions

As electron-rich alkenes, enol ethers very readily enter into 2+2 cycloadditions with electrophilic π systems. *Staudinger* and *Suter* reported on the addition of diphenylketene to ethyl vinyl ether as early as 1920 [165].

[149] *P. S. Skell* and *A. Y. Garner*, J. Amer. chem. Soc. *78*, 5430 (1956).

[150] *W. v. E. Doering* and *W. A. Henderson*, J. Amer. chem. Soc. *80*, 5274 (1958).

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[154] *E. E. Schweizer* and *W. E. Parham*, J. Amer. chem. Soc. *82*, 4085 (1960).

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[161] *W. E. Parham*, *R. W. Soeder*, and *R. M. Dodson*, J. Amer. chem. Soc. *84*, 1755 (1962).

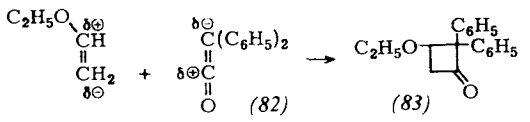
[162] *A. J. Birch* and *J. M. Graves*, Proc. chem. Soc. (London) *1962*, 282.

[163] *A. J. Birch*, *J. M. H. Graves*, and *J. B. Siddal*, J. chem. Soc. (London) *1963*, 4234.

[164] *A. Blade Font*, Bull. Soc. chim. France *1964*, 419, 906; *1965*, 3516.

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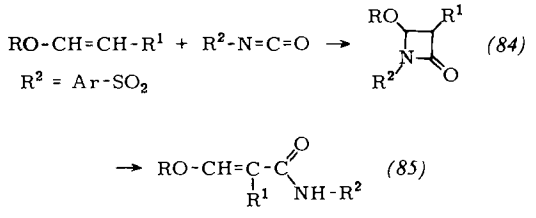
The orientation in these cycloadditions is unequivocally fixed by the polarization of the starting compounds in the ground state[166].



(82) (83)

Apart from ketenes[167,168], halogeno and cyano olefins[169–171] have also been treated with enol ethers. Cyclobutane derivatives, which are stable under the reaction conditions, are formed in each case.

Heterocumulenes, *e.g.* isocyanates, react with enol ethers to yield four-membered heterocycles *(84)*, which are less stable than cyclobutanes, and therefore enter into secondary reactions such as the formation of substitution compounds *(85)*[172,173].



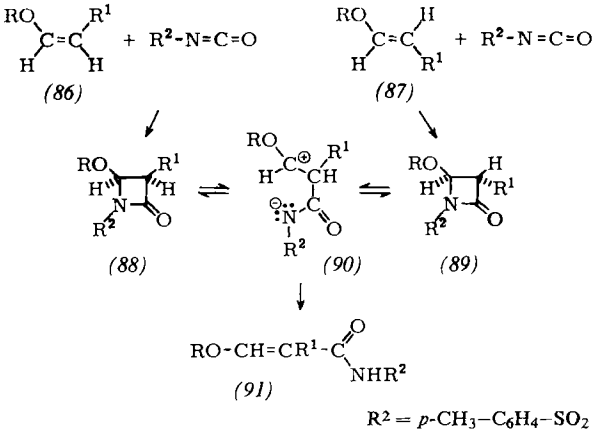
(84)

(85)

N-Sulfinylsulfonamides and sulfenes react in a like manner[174–176].

These 2+2 cycloadditions are of interest not only for synthetic purposes, but more so from the point of view of their mechanism, and particularly in connection with the question whether the process is a two-step reaction *via* a polar intermediate or a one-step multicenter addition. Both the stereospecific and the non-stereospecific cyclobutane ring closures of *cis*- and *trans*-1,2-dicyano-1,2-bis(trifluoromethyl)ethylene with *cis* and *trans* enol ethers are interpreted as proceeding *via* a polar intermediate[171]. The experimental data on the addition of ketenes to enol ethers, however, can be better interpreted by a one-step multicenter process[167].

cis and *trans* Enol ethers *(86)* and *(87)* react stereospecifically with sulfonyl isocyanates to give the β-lactams *(88)* and *(89)*, respectively, which isomerize *via* ring cleavage into an equilibrium mixture, or are converted irreversibly into the substitution product *(91)*[177,178].



(86) (87) (88) (90) (89) (91)

$R^2 = p\text{-}CH_3\text{–}C_6H_4\text{–}SO_2$

For $R = R^1 = CH_3$, the kinetics of hydrolysis reactions prove *(86)* to be more stable by 0.53 kcal/mole than *(87)*[179]. The position of the equilibrium *(88)*/*(89)*, on the other hand, indicates that *(89)* is 0.27 kcal/mole more stable than *(88)*[178].

According to the correlation proposed by *Hammond* between reactivity and the transition state[180], therefore, the relative stabilities of the starting compounds and end products in the above cycloadditions show that the transition state for the addition of the *cis* enol ether is closer to the four-membered ring than the transition state for the addition of the *trans* ether (see Fig. 1).

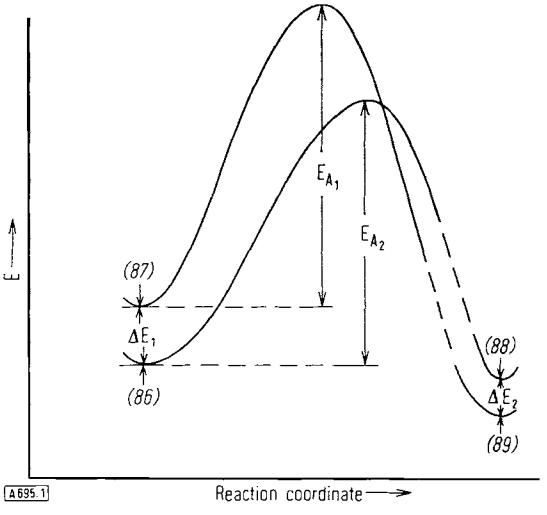


Fig. 1. Energy profiles for the cycloaddition of *cis*-*(86)* and *trans*-1-methoxy-1-propene *(87)* to tosyl isocyanate to give the azetidinones *(88)* and *(89)*, respectively.
$E_{A_1} = 10.2$ kcal/mole, $E_{A_2} = 9.4$ kcal/mole.

The reaction rate of *cis* enol ethers increases more rapidly than that of *trans* ethers with increasing dielectric constant of the solvent[178]. If the bonds in the transition state are assumed to differ in length[181], the observed solvent dependency of the reaction rate does not allow greater charge separation in the transition state for the addition of the *trans* ether than for the addition of the *cis* ether. We therefore conclude that the

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[173] *T. Mukaiyama, R. Yoda*, and *I. Kuwajima*, Tetrahedron Letters *1966*, 6247.

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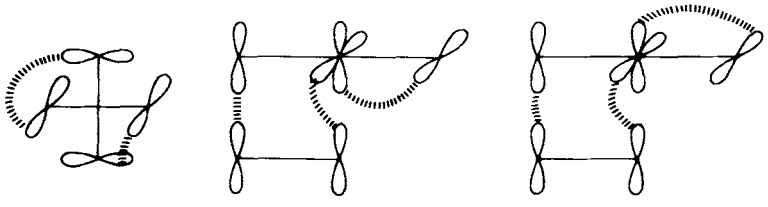
[179] *P. Salomaa* and *P. Nissi*, Acta chem. scand. *21*, 1386 (1967).

[180] *G. S. Hammond*, J. Amer. chem. Soc. *77*, 334 (1955).

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intermediate *(90)* does not occur in the cycloaddition itself. *(90)* must be postulated, however, for the isomerization *(88)* → *(89)* as well as for formation of *(91)*.

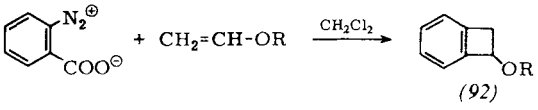
The Woodward-Hoffmann rules in their original form forbid thermal 2+2 multicenter cycloadditions[182], but in their further developed form they allow synchronous mechanisms for the cycloadditions mentioned. One possibility would be the assumption of a crossed arrangement of the double bonds, for which a synchronous $\pi_s^2 + \pi_a^2$ cycloaddition is thermally allowed[157].



$\pi_s^2 + \pi_a^2$ $\quad$ $\pi_s^2 + \pi_s^2 + \pi_s^2$ $\quad$ $\pi_s^2 + \pi_a^2 + \pi_a^2$

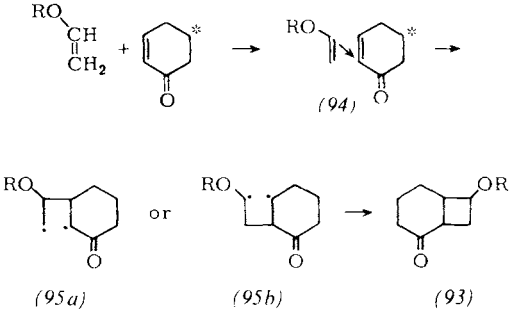
If the C=O double bond is taken into consideration, the reactions of ketenes and isocyanates with enol ethers may also be regarded as 2+2+2 cycloadditions. As $\pi_s^2 + \pi_a^2 + \pi_a^2$ and $\pi_s^2 + \pi_s^2 + \pi_s^2$ processes, respectively, these reactions are thermally allowed[183].

Dehydrobenzene also undergoes a 2+2 cycloaddition with enol ethers to give *(92)*[184]. There is no evidence for a polar intermediate.



(92)

Photochemical 2+2 cycloadditions have also been investigated. The formation of bicyclo[4.2.0]octanones *(93)* in good yields from enol ethers and 2-cyclohexen-1-ones is formulated as a reaction of the enol ether in the ground state with the excited ketone *via* an oriented π complex *(94)* and a diradical intermediate *(95)*[185].

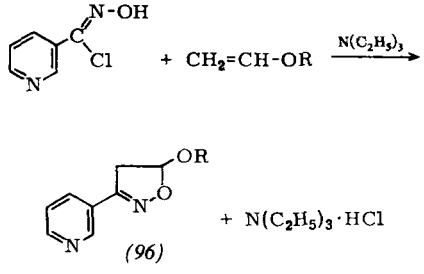


(94) $\quad$ *(95a)* $\quad$ *(95b)* $\quad$ *(93)*

In the photo-cycloaddition of diphenylacetylene to 2,3-dihydropyran, the first excited triplet state of the acetylene is assumed to react with the enol ether in the ground state[186].

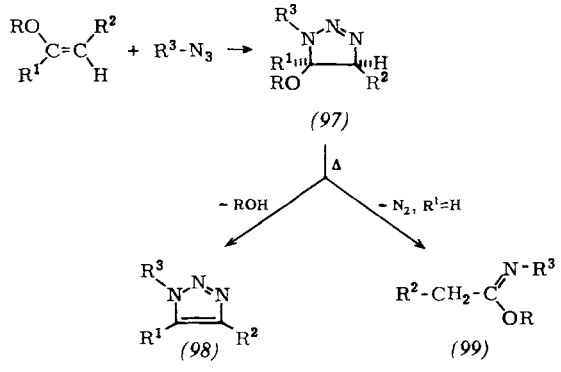
It should be generally possible to employ enol ethers as dipolarophiles in 1,3-dipolar cycloadditions, which were developed by *Huisgen* and his school[187]. Enol ethers do indeed react smoothly with nitrile oxides produced *in situ* to form substituted isoxazolines *(96)*[188]. Diazomethane forms 3-alkoxypyrazolines[189], and phenylsydnone gives alkoxypyrazoles[190].

The reactions with organic azides are particularly illuminating as regards the reaction mechanism[191–193].



(96)

These compounds combine with open-chain and cyclic enol ethers in a stereoselective *cis* addition to form 1,2,3-triazol-1-ines *(97)*. Depending on the structure of the enol ether, either alcohol is eliminated with



(97) $\quad$ *(98)* $\quad$ *(99)*

[182] *R. Hoffmann* and *R. B. Woodward*, J. Amer. chem. Soc. *87*, 2046 (1965).

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[193] *A. S. Bailey* and *J. E. White*, J. chem. Soc. (London) *B 1966*, 819.

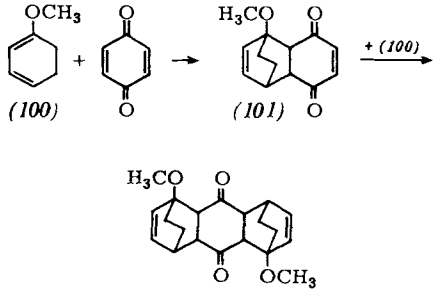
formation of triazoles *(98)* or N_2 is given off to yield esters of imidic acids *(99)* [191]. The mechanism proposed is a one-step multicenter reaction with bonds of different lengths in the transition state [187, 191, 193].

The formulation of partial charges in the transition state is substantiated by the fact that the direction of addition is determined purely electronically [191], in contrast with the steric control otherwise found in 1,3-dipolar cycloadditions. Further evidence of a polarized transition state is provided by comparison of the rates of reaction with picryl azide and phenyl azide; whereas the ratio of the reaction rates with olefins is 590–1434:1, that with enol ethers is 46000:1 [193]. Despite this evidence of polar structures, a true σ complex can be ruled out.

4.4. 2 + 4 Cycloadditions

Recent reviews have dealt in detail with the influence of substituents, including alkoxy groups, on the course of Diels-Alder reactions [194, 195]. Consequently, this influence need not be discussed in detail here. Alkoxy groups in the diene favor the addition with normal electronic requirements [195, 196], even though steric effects often play a more important part than electronic effects [196].

The increased reactivity of alkoxydienes is exemplified by the fact that paraformaldehyde reacts with 1-alkoxybutadienes, but not with butadiene [197]. If the electronic influence is reinforced by favorable steric effects, as in *(100)*, the reaction proceeds particularly readily with formation of *(101)* or possibly *(102)* [198].

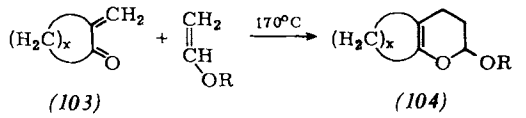


(102)

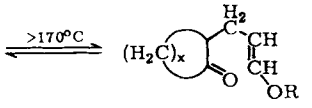
Less clear than the influence of alkoxy groups in the diene is the reaction of enol ethers as dienophiles in Diels-Alder additions with "inverse" electronic requirements [194, 199]. Cyclones, hexachlorocyclopentadiene, and 1,2,4,5-tetrazines have mainly been employed as electron-deficient dienes, all of which react smoothly with enol ethers [200–203].

Little sensitivity of the rates of reaction toward substituent effects, as in other diene additions, comparable energy and entropy of activation, as well as large steric influence all make a multicenter mechanism a rather probable one for diene addition with "inverse" electronic requirements.

The cycloadditions of α,β-unsaturated carbonyl compounds *(103)* with electron-rich olefins to form dihydropyrans *(104)* [204] may also be regarded as Diels-Alder additions with "inverse" electronic requirements, though there are



(103) *(104)*



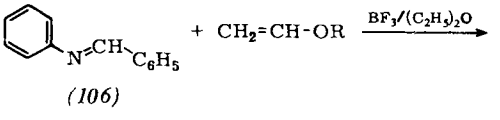
(105)

some mechanistic differences. On addition of acid, for example, the reaction rate is increased if the diene component is protonated but decreased if the olefin is protonated; the reaction is therefore assumed to involve an electrophilic attack on the olefin with a polar intermediate [205].

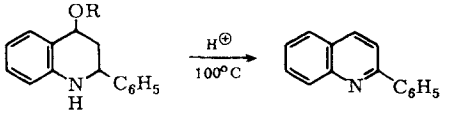
Moreover, the conversion of *(104)*, $x = 3$, $R = C_2H_5$, into *(105)* above 170 °C [206] does not correspond to the behavior of Diels-Alder adducts but suggests ring opening with a possibly polar intermediate, which is transformed into the substitution product *(105)* by tautomerism.

The cycloaddition of α,β-unsaturated carbonyl compounds with enol ethers is used, *inter alia*, in steroid chemistry [207].

Schiff bases *(106)* also act as "diene components" in cycloadditions with enol ethers [208]. Since the reactions



(106)



(107) *(108)*

[194] *J. Sauer*, Angew. Chem. *78*, 233 (1966); Angew. Chem. internat. Edit. *5*, 211 (1966); Angew. Chem. *79*, 76 (1967); Angew. Chem. internat. Edit. *6*, 16 (1967).

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[197] *D. G. Kubler*, J. org. Chemistry *27*, 1435 (1962).

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[199] *J. Sauer* and *H. Wiest*, Angew. Chem. *74*, 353 (1962); Angew. Chem. internat. Edit. *1*, 269 (1962).

[200] *V. S. Abramov* and *A. P. Pakhomova*, Ž. obšč. Chim. *24*, 1198 (1954); Chem. Abstr. *49*, 12419d (1955).

[201] *M. F. Shostakovskii*, *A. V. Bogdanova*, and *T. M. Ushakova*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1961*, 709; Chem. Abstr. *55*, 24598f (1961).

[202] *A. V. Kalabina*, *D. E. Stepanov*, *V. A. Kron*, and *A. B. Chernov*, Izvest. sibirskogo, Otd. Akad. Nauk SSSR, Ser. chim. Nauk *1964*, 106; Chem. Abstr. *62*, 7668a (1965).

[203] *J. Sauer*, *A. Mielert*, *D. Lang*, and *D. Peter*, Chem. Ber. *98*, 1435 (1965).

[204] *R. I. Longley Jr.* and *W. S. Emerson*, J. Amer. chem. Soc. *72*, 3079 (1950); *C. W. Smith*, *D. G. Norman*, and *S. A. Ballard*, *ibid. 73*, 5267 (1951).

[205] *M. Mizuta*, *A. Zuzuki*, and *Y. Ishii*, J. chem. Soc. Japan, ind. Chem. Sect. (Kogyo Kagaku Zasshi) *69*, 77, 79 (1966); Chem. Abstr. *65*, 5320ab (1966).

[206] *M. Muelstaedt* and *G. Mueller*, Tetrahedron Letters *1968*, 1811.

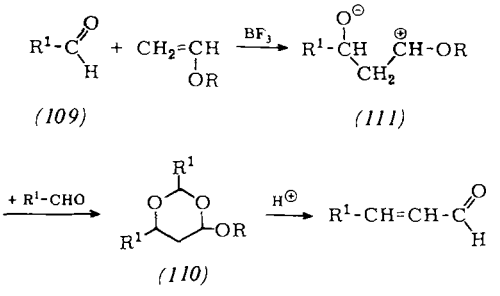
[207] *J. E. Pike*, *M. A. Rebensdorf*, *G. Slomp*, and *F. A. McKellar*, J. org. Chemistry *28*, 2499 (1963).

[208] *V. I. Grigos*, *L. S. Povarov*, and *B. M. Mikhailov*, Izvest. Akad. Nauk SSSR, Ser. chim. *1965*, 2163; Chem. Abstr. *64*, 9680c (1966).

are stereospecific, a cyclic six-center mechanism is postulated [208]. However, the catalyst used indicates at least partial charge separation.

A two-step or multi-step mechanism is assumed for the 2+4 cycloaddition of thioaroyl isocyanates to enol ethers and enamines [209].

The reaction of aldehydes with enol ethers, in which 1,3-dioxanes *(110)* are formed as isolable intermediates [210,211], offers a possible synthetic route to α,β-unsaturated carbonyl compounds (cf. Section 3.2).



(109) *(111)*

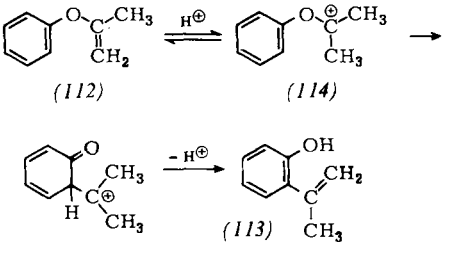
(110)

If the (hypothetical) intermediate *(111)* [210,211] is assumed to occur, the enol ether is no longer a true cycloaddition partner in this case.

5. Rearrangements of Enol Ethers [212]

5.1. Acid-Catalyzed Rearrangement

When *(112)* is heated for 5 hours with 10 % glacial acetic acid/sulfuric acid, the principal product is 2-isopropenylphenol *(113)* [213]. The mechanism is unknown [212]. Since *(112)* is converted almost entirely



(112) *(114)*

(113)

into *(113)*, and not into the *p* derivative, an intramolecular mechanism involving electrophilic substitution of the protonated compound *(114)* is probable. An approximately synchronous course with a four-membered transition state for the *o* rearrangement and a six-membered transition state for the *p* rearrangement is more likely than complete cleavage, in view of the instability of the cleavage products resulting from heterolysis.

[209] *J. Goerdeler* and *H. Schenk*, Chem. Ber. *98*, 3831 (1965).

[210] *R. I. Hoaglin, D. G. Kubler*, and *R. E. Leech*, J. Amer. chem. Soc. *80*, 3069 (1958).

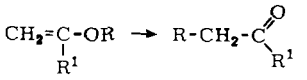
[211] *H. Saikachi* and *H. Ogawa*, J. Amer. chem. Soc. *80*, 3642 (1958).

[212] Houben-Weyl-Müller: Methoden der organischen Chemie. Thieme Verlag, Stuttgart 1965, 4th Edit., Vol. VI/3, p. 177ff.

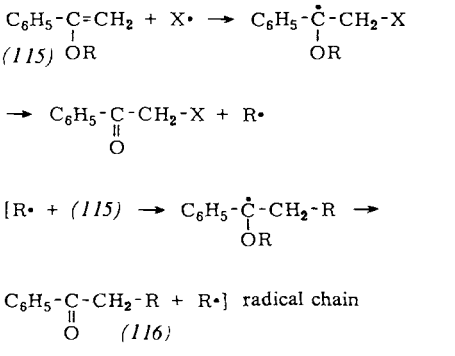
[213] *J. B. Niederl* and *E. A. Storch*, J. Amer. chem. Soc. *55*, 284 (1933).

5.2. Thermal Rearrangement of Alkyl Vinyl Ethers

Normal alkyl vinyl ethers rearrange into aldehydes or ketones in the presence of dehydration catalysts such as aluminum oxide, zirconium oxide, and B-phosphate at 200–300 °C [214–216].



The α-alkoxystyrenes *(115)* isomerize more readily into alkyl phenyl ketones *(116)* [217–219]. On the strength of stereochemical observations in the rearrangement of ethers with optically active alkyl residues, the use of labeled compounds, and the study of the influence of free-radical generators (X–X), *Wiberg et al.* have shown this rearrangement to involve an intermolecular free-radical chain reaction [219].



(115) *(116)*

Chain termination reactions

$$2\ X\cdot \rightarrow X\text{-}X;\quad X\cdot + R\cdot \rightarrow X\text{-}R;\quad 2\ R\cdot \rightarrow R\text{-}R$$

The rearrangement of α-benzyloxystyrene *(115)*, R = CH_2–C_6H_5, proceeds *e.g.* in 88 % yield at only 70 °C in the presence of azoisobutyronitrile, whereas, in the absence of free radical generators, a comparable yield is obtained only on heating to 207 °C [219].

5.3. Thermal Rearrangement of Allyl Vinyl Ethers

The synthesis of allyl vinyl ethers and their tendency to rearrange were first described in 1938 [220]. The rearrangement proceeds much more readily than in the case of normal alkyl vinyl ethers, and is further favored by α-substituents on the vinyl group [220]. The rearrangement temperatures of the allyl vinyl ethers

[214] *D. C. Hull* and *H. J. Hagemeyer*, US-Pat. 2642460 (1953), Eastman Kodak Co.; Chem. Abstr. *48*, 3994g (1954).

[215] *M. J. Molera* and *J. A. López Quirós*, An. Real Soc. espan. Fisica Quim. *54* B, 127 (1958); Chem. Abstr. *54*, 10471a (1960).

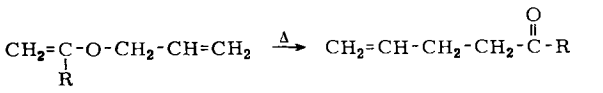
[216] *N. I. Schuikin, I. F. Belski*, and *R. A. Karachonow*, Z.Chem. *3*, 222 (1963).

[217] *L. Claisen*, Ber. dtsch. chem. Ges. *29*, 2931 (1896).

[218] *W. M. Lauer* and *M. A. Spielman*, J. Amer. chem. Soc. *55*, 4923 (1933).

[219] *K. B. Wiberg* and *B. I. Rowland*, J. Amer. chem. Soc. *77*, 1159 (1955); *K. B. Wiberg, T. M. Shryne*, and *R. R. Kintner*, *ibid.* *79*, 3160 (1957); *K. B. Wiberg, R. R. Kintner*, and *E. L. Motell*, *ibid.* *85*, 450 (1963).

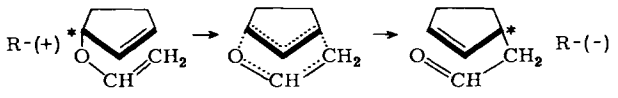
[220] *C. D. Hurd* and *M. A. Pollack*, J. Amer. chem. Soc. *60*, 1905 (1938); J. org. Chemistry *3*, 550 (1939).



with R = H, CH_3, and C_6H_5 are 255, 210, and 175 °C respectively.

The activation parameters of the strictly monomolecular rearrangement point to a cyclic transition state [221,222]. The assumption of a cyclic electron shift is further supported by experiments with compounds labeled with ^{14}C [223] and by the possibility of stereospecific angular alkylation [224].

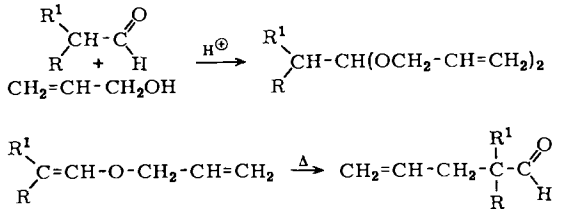
A particularly elegant proof of the cyclic transition state is the rearrangement of the optically active vinyl ether *(117)* into the optically active aldehyde *(118)* at 180 °C, which shows conclusively that the new C–C bond is *cis* to the broken C–O bond [225]. The rearrangement mechanism of allyl vinyl ethers is therefore



(117) *(118)*

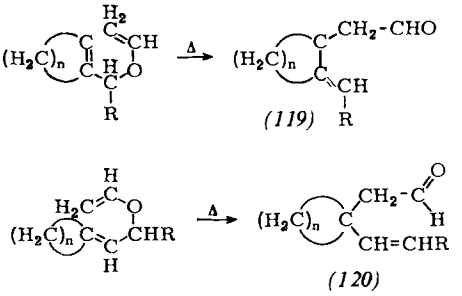
similar to that of allyl phenyl ethers, though the tautomerization leading to the more stable phenol in the Claisen rearrangement does not occur in this case.

The rearrangement of allyl vinyl ethers is also of preparative value. In addition to the angular alkylation [224], it provides an easy route to substituted 4-pentenals; the allyl vinyl ethers formed by elimination of alcohol from the diallyl acetal cannot as a rule be isolated, but immediately react further [226].



4,7,10-Undecatrienal (triallylacetaldehyde) can be synthesized by repetition of this reaction step, R = R^1 = H [227].

If H atoms in the allyl group are substituted, it is possible [228] to synthesize compounds such as *(119)* and *(120)*.

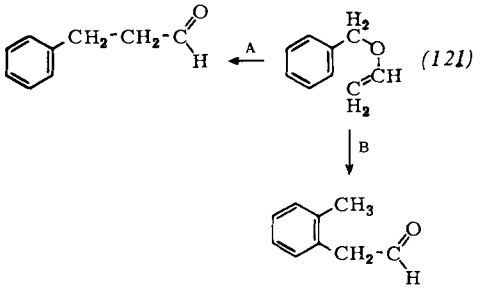


(119)

(120)

Propargyl vinyl ethers can be rearranged in the same way as allyl vinyl ethers [229,230]. However, one-electron shifts and combination of radical fragments are assumed to be involved in this case [229].

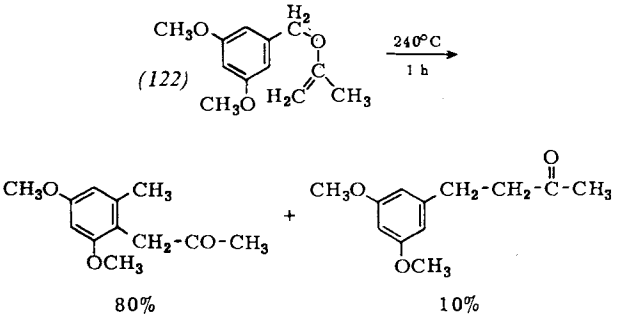
For benzyl vinyl ethers such as *(121)*, thermal rearrangement can be formulated in two ways, *i.e.* by a free-radical mechanism for an alkyl vinyl ether (pathA) or synchronously for an allyl vinyl ether (path B).



(121)

Benzyl vinyl ether itself does not rearrange below 300 °C; with di-*tert*-butyl peroxide, free-radical reaction by path A occurs at 170 °C [231].

3,5-Dimethoxybenzyl isopropenyl ether *(122)*, on the other hand, reacts mainly by path B, emphasizing the favorable effect of electron-donating groups on the rearrangement of allyl vinyl ethers [232].



80% 10%

The 3-methoxybenzyl compound gives both rearrangement products in comparable yields [232].

6. Closing Remarks

The chemistry of enol ethers is characterized by its similarity to the chemistry of enamines. The advantage of the enhanced nucleophilic character of the enamines

[221] *F. W. Schuler* and *G. W. Murphy*, J. Amer. chem. Soc. *72*, 3155 (1950).

[222] *L. Stein* and *G. W. Murphy*, J. Amer. chem. Soc. *74*, 1041 (1952).

[223] *Y. Pocker*, Proc. chem. Soc. (London) *1961*, 141.

[224] *A. W. Burgstahler* and *I. C. Nordin*, J. Amer. chem. Soc. *81*, 3151 (1959); *A. W. Burgstahler*, *ibid. 82*, 4681 (1960); *A. W. Burgstahler* and *I. C. Nordin*, *ibid. 83*, 198 (1961).

[225] *R.K.Hill* and *A.G.Edwards*, Tetrahedron Letters *1964*, 3239.

[226] *K. C. Brannock*, J. Amer. chem. Soc. *81*, 3379 (1959).

[227] *R. F. Webb*, *A. J. Duke*, and *J. A. Parsons*, J. chem. Soc. (London) *1961*, 4092.

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[229] *D. K. Black* and *S. R. Landor*, J. chem. Soc. (London) *1965*, 6784.

[230] *P. Cresson*, C. R. hebd. Séances Acad. Sci. *261*, 1707 (1965).

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[232] *W. J. Le Noble* and *P. J. Crean*, J. Amer. chem. Soc. *86*, 1649 (1964).

is frequently offset by the disadvantage that they form stable nitrogen addition products, thus forestalling a *C* reaction. It is often difficult, on the other hand, to find agents of sufficiently high electrophilic potential to react with enol ethers without initiating polymerization. Thus, the two classes of compounds complement each other well in their reactions as derivatives of ketones and aldehydes. *C*-Substitution reactions with phosgene, oxalyl chloride, and sulfonyl isocyanates, for example, which proceed very smoothly with enol ethers, are impracticable with enamines because of the formation of comparatively stable *N*-reaction products. Halogenation, and, in general, reactions tending to proceed *via* free-radical rather than polar mechanisms are also easier to carry out with enol ethers than with enamines. Since, in addition to the electrophilic and free-radical reactions discussed here, enol ethers may also react with nucleophiles, there is a wide field for their preparative use.

We are grateful to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for the support of our work on enol ethers.

Received: January 20, 1969 [A 695 IE]
German version: Angew. Chem. *81*, 374 (1969)
Translated by Express Translation Service, London

Cycloadditions with Polar Intermediates

By R. Gompper[*]

Dedicated to Professor H. Bredereck on the occasion of his 65th birthday

A discussion of the criteria that have been used to distinguish experimentally between one-step and two-step cycloadditions shows that in most cases useful information can be obtained only by isolation or interception of intermediates; the isolation of intermediates is also of preparative importance.

1. Introduction: Mechanistic Criteria

The preparative and theoretical importance of cycloadditions as a reaction principle is obvious from the many original papers and reviews on the subject [1]. Cycloadditions can proceed in one step or in two (even more than two are possible when more than two components are involved). The one-step reaction (cf. Fig. 1) has only a single transition state; in the two-step reaction, a dipolar intermediate is formed first (free-radical processes will not be considered here), and this is then cyclized or, if prototropy is possible, it reacts further to form a substitution product. Other possibilities are the conversion of "synchronously" formed cycloadducts into dipoles and the simultaneous occurrence of one-step and two-step cycloadditions.

When is a two-step cycloaddition to be expected?

1. Two-step cycloadditions are to be expected when concerted processes are forbidden according to the Woodward-Hoffmann rules [2–4].

2. Polar two-step cycloadditions may be possible if the charges occurring in dipolar intermediates can be adequately stabilized by substituents.

Under these conditions it is necessary to check experimentally whether a cycloaddition proceeds in one step or in two. The following criteria have been used:

1. Isolation or detection (spectroscopic, kinetic, by interception reactions) of intermediates.

2. Stereochemistry. Stereospecificity is the logical result of a synchronous cycloaddition. In two-step cycloadditions, the stereochemical course depends on the relative rates of the ring closure and of the internal rotation in the dipole. Several examples (*tert*-butyl vinyl sulfide or ethyl vinyl ether + 1,2-dicyano-1,2-bis(trifluoromethyl)ethylene [5], tetramethoxyethylene + 1,2-dicyanoethylenes [6], 4-methyl-1,2-butadiene + dimethyl maleate or fumarate [7,8], dehydrobenzene +

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[1] For definition see *R. Huisgen*, Angew. Chem. *80*, 329 (1968); Angew. Chem. internat. Edit. *7*, 321 (1968).

[2] *R. B. Woodward* and *R. Hoffmann*, J. Amer. chem. Soc. *87*, 395, 2046, 2511, 4388, 4389 (1965).

[3] *R. Hoffmann* and *R. B. Woodward*, Accounts chem. Res. *1*, 17 (1968).

[4] *S. I. Miller*, Advances in Physical Organic Chemistry *6*, 185 (1968); *G. B. Gill*, Quart. Reviews (chem. Soc., London) *22*, 338 (1968).

[5] *S. Proskov*, *H. E. Simmons*, and *T. L. Cairns*, J. Amer. chem. Soc. *88*, 5254 (1966).

[6] *R. W. Hoffmann*, Angew. Chem. *80*, 823 (1968); Angew. Chem. internat. Edit. *7*, 754 (1968).

[7] *E. Kiefer* and *M. Y. Okamura*, J. Amer. chem. Soc. *90*, 4187 (1968).

[8] *W. R. Dolbier jr.* and *S. Dai*, J. Amer. chem. Soc. *90*, 5028 (1968).

ethyl propenyl ether[9] or 1,2-dichloroethylene[10]; decomposition of episulfones[11,12], and decarboxylation of β-lactones[13]) show that two-step cycloadditions or the two-step decomposition of cycloadducts can be stereospecific or strongly stereoselective. This stereospecificity is possible only if the intermediate dipole has the structure *(2)*, which is "fixed" mainly by charge transfer, rather than the structure *(1)*, which is favored only by electrostatic attraction of the charge centers (illustrated for 1,4-dipoles). The fact that some stable 1,4-dipoles are colored suggests that they have



(1) *(2)*

D = electron donor, A = electron acceptor

the structure *(2)*. Another argument in favor of *(2)* is the fact that the reaction of *trans*-1,2-dicyano-1,2-bis-(trifluoromethyl)ethylene with *cis-n*-propyl propenyl ether (and also the *cis-cis* combination) gives less rearranged cycloadduct in polar than in apolar solvents[5].

3. Substituent effects and orientation phenomena. Substituents that help to stabilize the charges in polar or dipolar intermediates should also do so in the transition state, and should thus either make two-step cycloadditions possible or increase their rate in relation to systems with "neutral" substituents. It should therefore be possible to recognize two-step cycloadditions in this way. On the other hand, one-step cycloadditions have polar transition states (cf. Fig. 1), and may therefore also be influenced by variation of substituents.

Cycloadditions in which the orientation of the partners in the adduct is contrary to the polarity of the substituents are certainly not two-step polar reactions.

4. Effect of the solvent on the reaction rate. It is often argued that polar two-step cycloadditions should be strongly accelerated by polar solvents, and that a reaction rate that is influenced only slightly or not at all by the solvent is evidence of a concerted cycloaddition. This view is based on the solvent theory developed by *Hughes* and *Ingold*[14] for S_N reactions (because of the many specific interactions between the solvent and the substrate, however, it deals with only one aspect of the solvent problem[15,16]); the deciding factor in cycloadditions should thus be the difference in the dipole moments of the starting materials and of the transition state (for the theoretical treatment of the reaction of dipole molecules with dipole molecules, cf. [17,18]).

In connection with the above-mentioned specific interactions between the solvent and the reactants or the transition state, the following factors must also be considered in the discussion of the effect of the solvent on cycloadditions: rearrangement of the solvent structure (cf.[19]); "built-in solvation"[20,21] corresponding to *(1)* and *(2)*; different "hardness"[22,23] of the charge centers in the species that occur along the reaction coordinate, and hence different interactions with the chosen solvents.

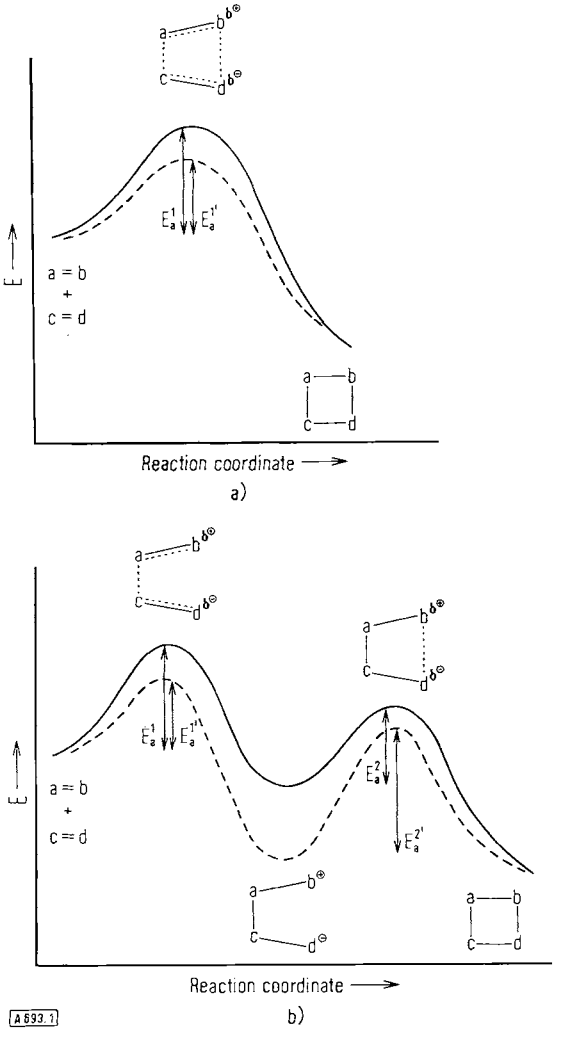


Fig. 1. Effect of solvent on the activation energy E_a of (a) one-step cycloadditions with polar transition state and (b) of two-step cycloadditions.

—— nonpolar solvent, ---- polar solvent.

[9] *H. H. Wassermann, A. J. Solodar,* and *L. S. Keller,* Tetrahedron Letters *1968*, 5597; cf. *I. Tabushi, R. Oda,* and *K. Okazaki, ibid. 1968*, 3743.

[10] *M. Jones jr.* and *R. H. Levin,* Tetrahedron Letters *1968*, 5593.

[11] *F. G. Bordwell, J. M. Williams jr., E. B. Boyt jr.,* and *B. B. Jarvis,* J. Amer. chem. Soc. *90*, 429 (1968).

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[15] *Ch. Reichardt* and *K. Dimroth,* Fortschr. chem. Forsch. *11*, 1 (1968).

[16] *A. J. Parker,* Advances in Physical Organic Chemistry *5*, 173 (1967).

[17] *S. Gladstone, K. J. Laidler,* and *H. Eyring*: The Theory of Rate Processes. McGraw-Hill, New York 1941, p. 422.

[18] *E. S. Amis*: Solvent Effects on Reaction Rates and Mechanisms. Academic Press, New York 1966, p. 59–69.

[19] *C. Ritchie, G. A. Skinner,* and *V. G. Badding,* J. Amer. chem. Soc. *89*, 2063 (1967).

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[21] *G. Illuminati,* Advances in Heterocyclic Chemistry *3*, 308 (1964).

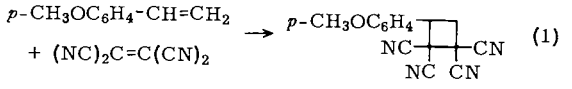
[22] *R. G. Pearson* and *J. Songstad,* J. Amer. chem. Soc. *89*, 1827 (1967).

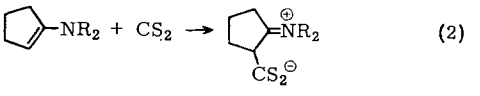
[23] *G. Klopman,* J. Amer. chem. Soc. *90*, 223 (1968).

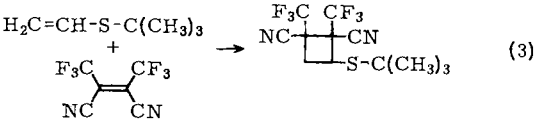
Even when only the Hughes-Ingold theory is used, however, it is necessary to start with the idea that two-step cycloadditions are consecutive reactions, so that the solvent effect depends on the relation of the activation energies E_a^1 and E_a^2 of the two steps (cf. Fig. 1; for sake of simplicity, the solvation of starting materials and products is not considered). If the dipole formation is irreversible and $E_a^1 \gg E_a^2$, the first step is rate-determining in all solvents, and a change from polar to apolar solvents should be associated with an increase in the reaction rate. If $E_a^1 \ll E_a^2$, on the other hand, the reaction rate must be expected to decrease. Finally, if $E_a^1 \approx E_a^2$, the case illustrated in Figure 1b is also possible, *i.e.* $E_a^1 > E_a^2$ in nonpolar solvents while $E_a^{1'} < E_a^{2'}$ in polar solvents. Since $E_a^1 < E_a^{2'}$, a change from an apolar to a polar solvent should, as a simplification, lead to a (small) decrease in the reaction rate. Relatively small positive or negative solvent effects should generally result in this case. The reaction rate is also expected to increase in polar solvents when the dipole formation is reversible. A one-step and a two-step cycloaddition can therefore be distinguished only if the solvent effect is very large.

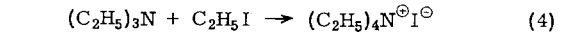
Moreover, the transition state of the first step of a two-step cycloaddition and that of a one-step cycloaddition (Fig. 1a) in which the formation of the two new bonds is not quite synchronous should have similar structures and polarities. Thus if the first step of a two-step cycloaddition is rate-determining, the solvent must have a similar effect on the reaction rate in these two types of cycloadditions.

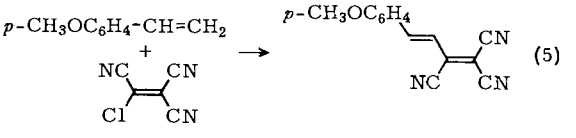
The validity of these remarks is borne out by Table 1. It can be seen that while reactions (1) to (3) exhibit relatively large solvent effects, (5), though mechanistically closely related to (1), shows a marked decrease in the solvent effect, which is not much higher than for the ketene-enol ether reaction (7). The addition (6), which proceeds *via* a dipole intermediate, the S_N2 reaction (4), and the two-step Diels-Alder reaction (8) also belong to this group. The cycloadditions (10) and (14) of a ketene to vinyl ketones, which tend to be regarded as two-step reactions (ketenes normally give four-membered rings on reaction with 1,3-dienes; see Section 2.2.1), exhibit practically the same solvent effect as the synchronous cycloadditions (12) and (13). The effect of the solvent on the rate of the S_N2 reaction (11), the transition state of which should lie close to the

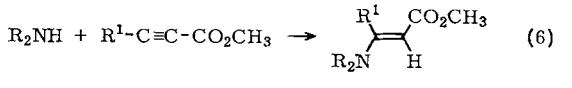

(1)


(2)


(3)


(4)


(5)


(6)

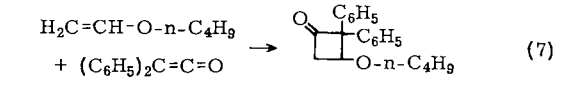

(7)

Table 1. Effect of the solvent on the rates of cycloadditions and reference reactions (the reactions are given on this page and p. 315).

Reaction	Ref.	$\Delta H^{\neq}$ (kcal mole^{-1})	$\Delta S^{\neq}$ (cal deg^{-1} mole^{-1})	$k_{\text{acetonitrile}}/k_{\text{cyclohexane}}$
(1)	[24]		−53	6.3×10^4
(2)	[25]	6	−49	$\approx 10^3$ [a]
(3)	[5]			2160 [b]
(4)	[26]			1100 [c]
(5)	[27]			200
(6)	[28]			35–830
(7)	[29]	9.3	−40	160
(8)	[30]			120
(9)	[31]			26 [d] [32]
(10)	[33]	6	−41	26
(11)	[34]			23 [e]
(12)	[35]	12	−36	≤10 [f]
(13)	[36]	7.5	−38	≤10 [f]
(14)	[33]	10	−47	4.5
(15)	[37]			≈2 [g]
(16)	[7]			<2 [h]

[a] $k_{\text{acetone}}/k_{CFCl_3}$. [b] k_{CH_3}/k_{CCl_4}.
[c] $k_{C_6H_5CN}/k_{\text{cyclohexane}}$. [d] $k_{n\text{-hexane}}/k_{CH_3CN}$.
[e] $k_{C_6H_5CN}/k_{\text{ether}}$. [f] Average values for 1,3-dipolar cycloadditions [38, 39] and Diels-Alder reactions [39, 40].
[g] $k_{C_6H_5NO_2}/k_{CCl_4}$. [h] $k_{DMSO}/k_{\text{cyclohexane}}$.

[24] *J. K. Williams, D. W. Wiley*, and *B. C. McKusick*, J. Amer. chem. Soc. *84*, 2210 (1962); *D. W. Wiley*, personal communication to *R. Huisgen*.

[25] *R. Gompper, B. Wetzel*, and *W. Elser*, Tetrahedron Letters *1968*, 5519.

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[27] *J. K. Williams, D. W. Wiley*, and *B. C. McKusick*, J. Amer. chem. Soc. *84*, 2216 (1962).

[28] *B. Giese*, Dissertation, Universität München 1969.

[29] *R. Huisgen, L. A. Feiler*, and *P. Otto*, Tetrahedron Letters *1968*, 4485.

[30] *R. Gompper* and *G. Hultzsch*, unpublished.

[31] *W. Steglich, G. Höfle, W. König*, and *F. Weygand*, Chem. Ber. *101*, 308 (1968).

[32] *R. Gompper* and *J. Stetter*, unpublished.

[33] *R. Gompper* and *K.-P. Paul*, unpublished; *K.-P. Paul*, Dissertation, Universität München 1969.

[34] *J. C. Cox*, J. chem. Soc. (London) *119*, 142 (1921).

[35] *R. Huisgen, G. Szeimies*, and *L. Möbius*, Chem. Ber. *100*, 2494 (1967).

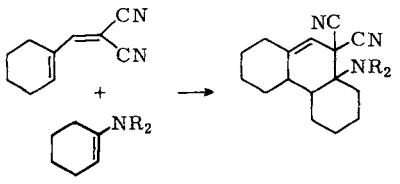
[36] *J. Sauer, H. Wiest*, and *A. Mielert*, Chem. Ber. *97*, 3183 (1964).

[37] *W. Steglich* and *G. Höfle*, personal communication.

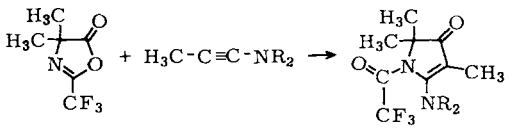
[38] *R. Huisgen*, Angew. Chem. *75*, 604, 742 (1963); Angew. Chem. internat. Edit. *2*, 564, 633 (1963).

[39] *R. Huisgen, R. Grashey*, and *J. Sauer* in *S. Patai*: The Chemistry of Alkenes. Interscience, London 1964, p. 739.

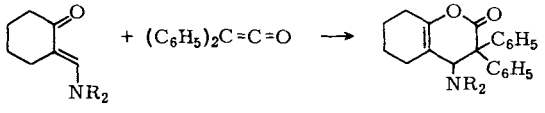
[40] *J. Sauer*, Angew. Chem. *79*, 76 (1967); Angew. Chem. internat. Edit. *6*, 16 (1967).



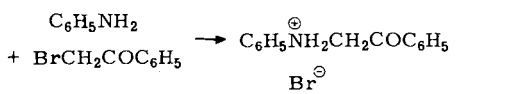
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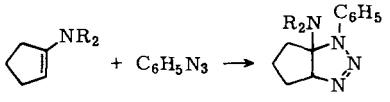
(9)



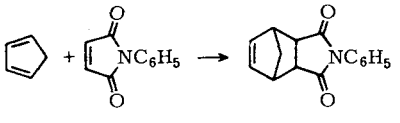
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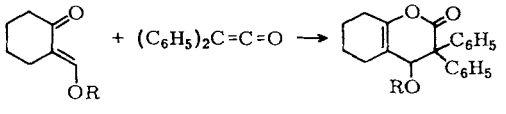
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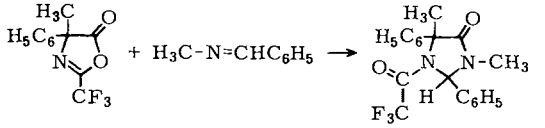
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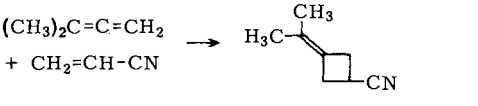
(13)



(14)



(15)



(16)

Reaction (2), $R = CH_3$

Reaction (6), $R_2 = C_6H_{11}$, 2H, $-(CH_2)_2-$, $-(CH_2)_5-$
$R^1 = H$, CO_2CH_3

Reaction (8), $R_2 = -(CH_2)_4-$

Reaction (9), $R = C_2H_5$

Reaction (10), $R_2 = -CH_2-CH_2-O-CH_2-CH_2-$

Reaction (12), $R_2 = -(CH_2)_4-$

Reaction (14), $R = C_2H_5$

product[41], is also very small. As expected, the solvent is of no importance in the free-radical cycloaddition (16). On the other hand, the cycloadditions (9) and (15), which undoubtedly proceed *via* dipolar intermediates, show remarkably little effect.

The solvent can influence not only the rates of cycloadditions but also the composition of the products. The solvation of the dipoles changes their reactivity; ring closure to form the cycloadduct may be accompanied in certain circumstances by prototropy (formation of substitution products) and/or addition of dipolarophiles. There are probably different types of solvated dipoles in cycloadditions, corresponding to ion pairs in S_N reactions. In nonpolar solvents, dipoles corresponding to intimate ion pairs could make it difficult to distinguish between a two-step cycloaddition and a one-step cycloaddition with a polar transition state.

5. Kinetic isotope effects (cf. [8,40]).

6. Activation parameters. On the basis of experimental values for the Diels-Alder reaction[39,40] (as a model concerted cycloaddition), relatively low activation enthalpies and strongly negative activation entropies must generally be expected for one-step cycloadditions, in agreement with theoretical considerations. It can be seen from Table 1 that these are in fact necessary conditions for one-step cycloadditions, but not sufficient, since the values for two-step cycloadditions lie in the same range.

In conclusion, therefore, the criteria 2–6 can be used only in special cases. This basically leaves criterion 1. The most important examples of two-step cycloadditions will be presented below from this point of view (a different interpretation from that given may also be possible for some reactions). It must be emphasized that one-step and two-step cycloadditions, like S_N1 and S_N2 reactions, should be regarded as limiting cases.

2. Preparative Examples

2.1. Cycloadditions a=b + c=d

According to the Woodward-Hoffmann rules[2–4], the "synchronous" formation of cyclobutanes from olefins is thermally forbidden. Thus such reactions are mainly free-radical processes[39,42,43] (even here there is evidence of polar effects[44]). Exceptions are the reactions of electron-rich olefins (*e.g.* enol ethers, enamines) with electron-deficient olefins (tetracyanoethylene[45], tetracyanovinyl chloride[45], 1,1-dicyano-1,1-bis(trifluoromethyl)ethylene[46], 1,2-dicyano-1,2-bis(trifluoromethyl)ethylene[5], acrylic acid derivatives, methyl vinyl sulfone, and nitroolefins[47,48]). Existing evidence of the occurrence of dipolar intermediates in these reactions includes: the absence of stereospecificity[5]; the anomalous course of the reaction of tetracyanoethylene with 2-ethoxy-3,4-dihydro-2*H*-pyran[24]; the fact that cyclobutanones are formed from enamines and nitroolefins in nonpolar solvents, whereas β-nitroethyl enamines are formed in polar solvents and even 1:2 cycloadducts can be detected[48];

[41] See ref. [17], p. 418, 419.

[42] *D. J. Roberts* and *C. M. Sharts*, Org. Reactions *12*, 1 (1962).

[43] *J. S. Swenton* and *P. D. Bartlett*, J. Amer. chem. Soc. *90*, 2056 (1968).

[44] *P. D. Bartlett*, *G. E. H. Walbillich*, and *L. Montgomery*, J. org. Chemistry *32*, 1290 (1967).

[45] *T. L. Cairns* and *B. C. McKusick*, Angew. Chem. *73*, 520 (1961); *D. N. Dhar*, Chem. Reviews *67*, 611 (1967).

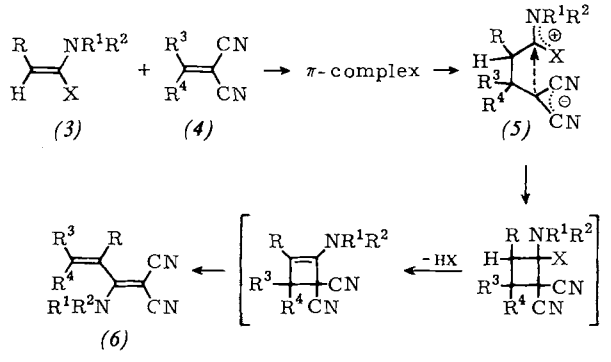
[46] *W. J. Middleton*, J. org. Chemistry *30*, 1402 (1965).

[47] *K. C. Brannock*, *A. Bell*, *R. D. Burpitt*, and *C. A. Kelly*, J. org. Chemistry *26*, 625 (1961); *29*, 801 (1964).

[48] *M. E. Kuehne* and *L. Foley*, J. org. Chemistry *30*, 4280 (1965).

the formation of 2:1 cycloadducts from styrene and tetracyanoethylene (on heating in xylene)[24] and from enamines and methylenemalonic ester[47]; the synthesis of benzofurans[49–51] and of a tetrahydrocarbazole[52] from enamines and *p*-benzoquinone or 1,4-cyclohexadienediylidenebis-(benzenesulfonylamine); the formation of *o*-acetylphenyl acetate from dehydrobenzene and α-ethoxyvinyl acetate[53].

The isolation, and hence the direct detection, of 1,4-dipoles *(5)* was achieved for the first time in the reaction of compounds of the ketene acetal series *(3)*, in particular ketene *S,N*-acetals *(3a)*[54], with methylenemalononitriles *(4)* in acetonitrile at −40 °C[55].

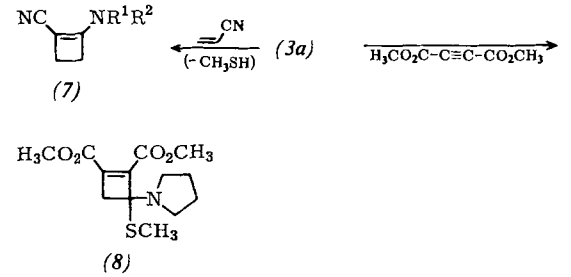


(3) *(4)* *(5)* *(6)*

(a), X = SCH_3; *(b)*, X = $N(CH_3)_2$
R = H, CH_3, C_2H_5, *n*-C_3H_7, C_6H_5; $R^1 + R^2 = (CH_2)_{2-4}$
R^3 = C_6H_5, $C_6H_4NO_2$-*p*, CF_3, CN; R^4 = H, CF_3, CN

Red to blue π complexes are formed first. The yellow to orange-red color of the crystalline 1,4-dipoles *(5)* is probably due to intramolecular charge transfer. The butadienes *(6)* are formed from *(5)* as the final products.

Reaction of *(3a)*, R = H, with acrylonitrile yields the cyclobutenes *(7)*[55,56] (cf. the reactions of other ketene acetal derivatives with esters of acrylic acid[57]), and reaction of *(3a)*, R = H, $R^1 + R^2 = (CH_2)_4$, with acetylenedicarboxylic ester leads to cyclobutene *(8)*[54]

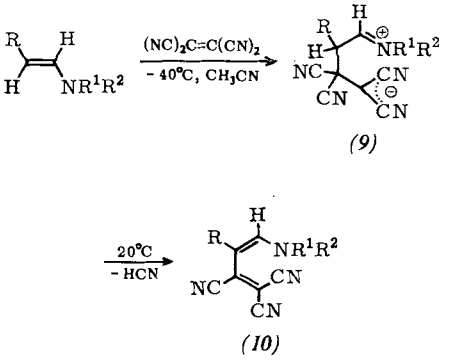


(7)

(8)

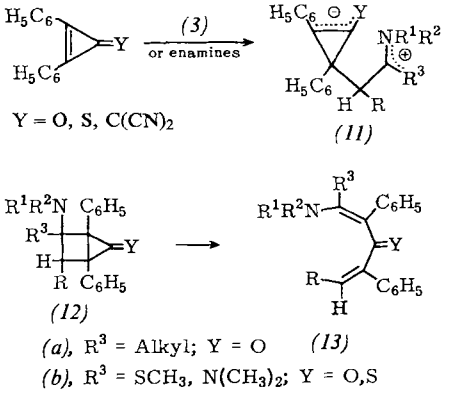
(cf. also[58]; other ketene acetals give only butadienes[59]). No 1,4-dipoles have yet been detected here. On the other hand, it has been verified experimentally that the formation of benzocyclobutenes from dehydrobenzene and enamines[52] or enol ethers[9] proceeds in two steps.

Except in the case of *N*-acyl-enamines[24], no definite products had formerly been obtained by the reaction of enamines with tetracyanoethylene. The 1,4-dipoles *(9)* have now also been obtained in the same manner as *(5)*[60]. When the temperature is raised they are converted into the butadienes *(10)*.



(9) *(10)*

The interesting reaction of enamines with diphenylcyclopropenone to give *(13)*[61] is thought to proceed *via* a primary (one- or two-step) cycloaddition to give *(12a)*. Since the dipoles *(11b)* were obtained in the reaction of ketene *S,N*-acetals with diphenylcyclopropenone and diphenylcyclopropenethione[62], the



Y = O, S, $C(CN)_2$ *(11)*

(12)

(a), R^3 = Alkyl; Y = O *(13)*
(b), R^3 = SCH_3, $N(CH_3)_2$; Y = O,S

dipoles *(11)* are probably generally intermediates in the (intermediate) formation of *(12)*. An important point for the discussion of the solvent effect is the fact that the formation and further reaction of *(11b)* are only slightly (factor <10) accelerated or retarded by a change from nonpolar to polar solvents[62]. The reaction

[49] *K. C. Brannock, R. D. Burpitt, H. E. Davis, H. S. Pridgen,* and *J. G. Thweatt*, J. org. Chemistry *29*, 2579 (1964).

[50] *G. Domschke*, Chem. Ber. *99*, 930 (1966).

[51] *W. E. Noland* and *F. J. Baude*, J. org. Chemistry *31*, 3321 (1966).

[52] *M. E. Kuehne*, J. Amer. chem. Soc. *84*, 837 (1962).

[53] *H. H. Wasserman* and *J. Solodar*, J. Amer. chem. Soc. *87*, 4002 (1965).

[54] *R. Gompper* and *W. Elser*, Tetrahedron Letters *1964*, 1971; Liebigs Ann. Chem. *725* (1969), in press.

[55] *R. Gompper, W. Elser,* and *H.-J. Müller*, Angew. Chem. *79*, 473 (1967); Angew. Chem. internat. Edit. *6*, 453 (1967).

[56] *T. Mukaiyama, S. Aizawa,* and *T. Yamaguchi*, Bull. chem. Soc. Japan *40*, 2641 (1967).

[57] *K. C. Brannock, R. D. Burpitt,* and *J. G. Thweatt*, J. org. Chemistry *29*, 940 (1964).

[58] *E. Winterfeldt*, Angew. Chem. *79*, 389 (1967); Angew. Chem. internat. Edit. *6*, 423 (1967).

[59] *K. C. Brannock, R. D. Burpitt,* and *J. G. Thweatt*, J. org. Chemistry *28*, 1697 (1963).

[60] *R. Gompper* and *H.-J. Müller*, unpublished.

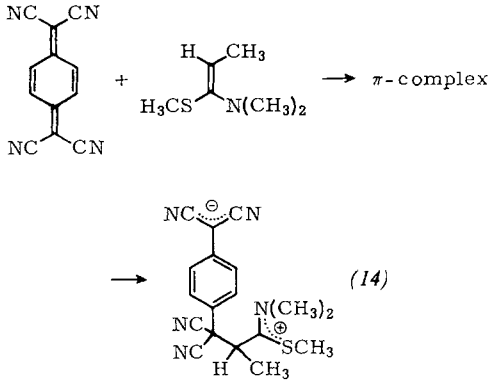
[61] *J. Ciabattoni* and *G. A. Berchtold*, J. org. Chemistry *31*, 1336 (1966); diphenyl(dicyanomethylene)cyclopropene reacts similarly, *J. Ciabattoni* and *E. C. Nathan*, J. Amer. chem. Soc. *89*, 3081 (1967).

[62] *J. Sauer*, personal communication; *H. Krapf*, Diplomarbeit, Universität München 1967.

of ynamines with diphenylcyclopropenone [63] probably proceeds similarly.

Ynamines [64,65] and ynediamines [66,67] react with acetylenedicarboxylic ester to give benzene derivatives. It is not yet known whether only 1,4-dipoles or also cyclobutadienes occur as intermediates. A two-step reaction is also conceivable for the formation of cyclobutanes from 9-*tert*-butoxybicyclo[6.2.0]decapentaenes [68] and tetracyanoethylene (cf. related reactions with dimethylenecyclobutenes [69] and 1,2-dibenzylidene-3,4-phenylcyclobutane [70]).

It should also be mentioned that 7,7,8,8-tetracyano-*p*-benzoquinodimethane adds ketene *S,N*-acetals at C-7 (unlike other *p*-benzoquinones [49–52], which take up enamines at C-2) and gives the dipole *(14)* [60].



(14)

Acetonitrile surprisingly favors the formation of the green π-complex, and tetrahydrofuran that of the yellow dipole *(14)*.

There are many examples of cycloadditions in which hetero-1,4-dipoles occur as intermediates, and which give either four-membered heterocycles in accordance with the scheme 2 + 2 → 4 or six-membered heterocycles by 2 + 2 + 2 → 6 in the course of a 1,4-dipolar cycloaddition [71]. In addition to the examples presented in reviews [58,71–73], mention should also be made of the following. The cycloaddition of chloral to morpholinoisobutene to form a 1,3-dioxane [49] may be regarded as a model for the Prins reaction (for the mechanism, see [74]); ynamines react with carbonyl compounds and imines [75]; diazanorcaradienes undergo cycloaddition with two molecules of acetylenedicarboxylic ester, and probably form 1,4-dipoles with tetracyanoethylene [76]; iminoborons react with phenylacetylene to give benzo-1,2-azaborines *via* a 1,4-dipole [77]; cyclic enamines react with cyanoallene to form methylenecyclobutanes and cyclopentenes [78]; ketene acetal and benzenediazonium chloride give a pyridazine [79]; 1:2 and 2:1 cycloadducts are obtained from dimethylcyanamide and hexafluoroacetone [80]; two 2:1 cycloadducts formed *via* 1,4-dipoles can be isolated by the action of acetylenedicarboxylic ester on tetramethylthiourea [81]; hexafluoroacetone and hexaphenylcarbodiphosphorane combine to form a 1,2-oxaphosphetane [82].

2.2. Cycloadditions a=b + d=e=f

A large volume of data exists on cycloadditions of heterocumulenes d=e=f (*e.g.* ketenes, isocyanates, isothiocyanates, carbodiimides, carbon disulfide [73,83,84], carbon dioxide, sulfur dioxide, sulfenes [83,85], sulfinylamines [82,86]) to double and triple bonds. A selection of such reactions will be discussed below.

2.2.1. Reactions with Ketenes

Are the 2 + 2 cycloadditions of ketenes to C=C bonds one- or two-step reactions? It is significant for the answer to this question that "apolar" 1,3-dienes do not react by the Diels-Alder scheme, but always give almost exclusively cyclobutanones [87–89]. Retro-Diels-Alder reactions in which ketenes are split off are thermally possible only under extreme conditions [90]. This indicates a multi-center process for the ketene-olefin reaction, which is also thermally allowed according to the Woodward-Hoffmann theory in its new form [91,92].

It is concluded from the stereospecificity of the cycloaddition of ketenes to enol ethers [89,93–95] and from

[63] *M. Franck-Neumann*, Tetrahedron Letters *1966*, 341.

[64] *J. Ficini* and *C. Barbara*, Bull. Soc. chim. France *1964*, 871; *1965*, 2787.

[65] *H. G. Viehe*, *R. Fuks*, and *M. Reichstein*, Angew. Chem. *76*, 571 (1964); Angew. Chem. internat. Edit. *3*, 581 (1964).

[66] *L. Ghosez*, personal communication.

[67] *R. Gompper* and *G. Seybold*, unpublished.

[68] *G. Schröder* and *H. Röttele*, Angew. Chem. *80*, 665 (1968); Angew. Chem. internat. Edit. *7*, 635 (1968).

[69] Cf. *M. P. Cava* and *M. J. Mitchell*: Cyclobutadiene and Related Compounds. Academic Press, New York 1967, p. 161, 167.

[70] *E. V. Dehmlov*, Chem. Ber. *100*, 3260 (1967).

[71] *R. Huisgen*, Z. Chem. *8*, 290 (1968).

[72] *R. M. Acheson*, Advances in Heterocyclic Chemistry *1*, 125 (1963).

[73] *L. L. Muller* and *J. Hamer*: 1,2-Cycloaddition Reactions. Interscience, New York 1967.

[74] *L. J. Dolby*, *C. L. Wilkins*, and *R. M. Rodia*, J. org. Chemistry *33*, 4155 (1968).

[75] *H. G. Viehe*, Angew. Chem. *79*, 744 (1967), especially p. 753; Angew. Chem. internat. Edit. *6*, 767 (1967), especially p. 775.

[76] *G. Maier* and *U. Hepp*, Chem. Ber. *101*, 1371 (1968).

[77] *P. I. Paetzold*, *G. Stohr*, *H. Maisch*, and *H. Lenz*, Chem. Ber. *101*, 2881 (1968).

[78] *W. Ried* and *W. Kaeppler*, Liebigs Ann. Chem. *687*, 183 (1965).

[79] *S. M. McElvain* and *A. Jelinek*, J. Amer. chem. Soc. *65*, 2236 (1943).

[80] *M. E. Hermes* and *R. A. Braun*, J. org. Chemistry *31*, 2568 (1966).

[81] *E. Winterfeld*, Chem. Ber. *100*, 3679 (1967).

[82] *G. H. Birum* and *C. N. Matthews*, J. org. Chemistry *32*, 3554 (1967).

[83] *H. Ulrich*: Cycloaddition Reactions of Heterocumulenes. Academic Press, New York 1967.

[84] *R. N. Lacey* in *S. Patai* [39], p. 1161.

[85] *G. Opitz*, Angew. Chem. *79*, 161 (1967); Angew. Chem. internat. Edit. *6*, 107 (1967).

[86] *G. Kresze* and *W. Wucherpfennig*, Angew. Chem. *79*, 109 (1967); Angew. Chem. internat. Edit. *6*, 149 (1967).

[87] *R. Huisgen* and *P. Otto*, Tetrahedron Letters *1968*, 4491.

[88] *L. Ghosez*, *R. Montaigne*, *H. Vanlierde*, and *F. Dumay*, Angew. Chem. *80*, 630 (1968); Angew. Chem. internat. Edit. *7*, 643 (1968).

[89] *G. Binsch*, *L. A. Feiler*, and *R. Huisgen*, Tetrahedron Letters *1968*, 4497.

[90] *R. K. Murray jr.* and *H. Hart*, Tetrahedron Letters *1968*, 4995.

[91] *R. B. Woodword*, Lecture at IUPAC Symposium on Valence Isomerization, Karlsruhe September 10, 1968.

[92] *R. B. Woodward* and *R. Hoffmann*, Angew. Chem., in press.

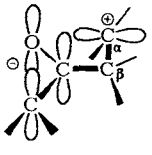
[93] *R. Huisgen*, *L. Feiler*, and *G. Binsch*, Angew. Chem. *76*, 892 (1964); Angew. Chem. internat. Edit. *3*, 753 (1964).

[94] *J. C. Martin*, *V. W. Goodlett*, and *R. D. Burpitt*, J. org. Chemistry *30*, 4309 (1965).

[95] *R. Montaigne* and *L. Ghosez*, Angew. Chem. *80*, 194 (1968); Angew. Chem. internat. Edit. *7*, 221 (1968).

the relatively small solvent effect [29] (see Table 1) that this is a multi-center process with a polar transition state. In the reactions of enamines [73,83,96–98] and ketene acetals [73,83], on the other hand, there is considerable evidence of a two-step reaction. Ynamines evidently also undergo two-step cycloaddition with ketenes [99–101]; the same is true of ethoxyacetylene [102,103]. If ynamines and alkoxyacetylenes exhibit similar mechanistic behavior here, the same could also be expected of the enamines and enol ethers, in which the reactivity varies in the same manner as in the acetylene derivatives. Thus a two-step mechanism should not be rejected *a priori* for the cycloadditions of ketenes and enol ethers. One might even ask whether cycloadditions of ketenes to olefins could also be two-step processes. Still, bis(trifluoromethyl)ketene takes up vinyl benzoate [104] and olefins [105] on the C=C and C=O bonds, and 1,1-diphenylethylene reacts with diphenylketene to give a 1:2 cycloadduct [106].

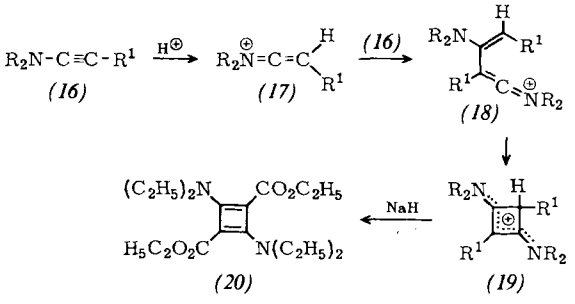
A similar picture is found for the course of the cycloaddition of ketenes to C=C bonds when the problem is approached with the aid of a simple HMO model [107]. According to this treatment, the transition state of the two-step process has a lower energy, at least in the case of the electron-rich olefins, than that of the synchronous process; there appears to be no great difference between the two transition states in the case of "normal" olefins. However, there still remains the question how a two-step mechanism can be reconciled with stereospecificity. The model *(2)* for dipoles cannot be used because of the special bonding in the ketene or in a dipole derived from ketene and olefin. It must be replaced by the dipole *(15)*, a dipolar homoallyl system with hindered rotation about $C_\alpha - C_\beta$ (the formation of cyclobutanones from ketenes and 1,3-dienes can also be explained on the basis of *(15)* by



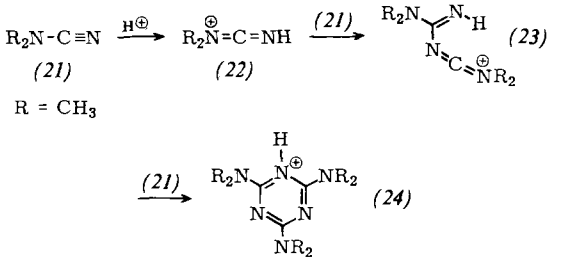
(15)

orbital symmetry considerations [107]). It will be shown in the following sections that electron-rich olefins often react with heterocumulenes to give 1,4-dipoles.

A particularly interesting reaction is the "dimerization" of ynamines *(16)* to form cyclobutenecyanines *(19)* [75,108,109]. This may be formulated as an attack of the ketene iminium ion *(17)* on *(16)*. The intermediate *(18)* then cyclizes to give *(19)*, from which the crystalline cyclobutadiene *(20)* can be prepared if



suitable substituents are present [108]. Dimethylcyanamide *(21)*, the aza analog of *(16)*, reacts similarly to form the protonated hexamethylmelamine *(24)* [110] (for the trimerization of nitriles cf. [111]). However, the cation *(23)* formed from *(22)* and *(21)* does not



give a four-membered ring, but undergoes cycloaddition with *(21)* in accordance with the scheme for polar 1,4-cycloadditions [112].

The two-step course of the formation of β-lactams from azomethines or amidines and ketene [73,83,84,113–116] is indicated by the fact that 1:2 adducts are often obtained. It has been shown [117] that the lactam and the 1:2 cycloadduct are formed from a common dipolar intermediate. In liquid SO_2, the solvent can add to the 1,4-dipole [118]. It is possible that the reaction of diphenylketene with 4-phenylimino-2-cyclo-

[96] *J. C. Martin, P. G. Gott,* and *H. U. Hostettler,* J. org. Chemistry *32,* 1654 (1967).

[97] *R. H. Hasek* and *J. C. Martin,* J. org. Chemistry *28,* 1468 (1963).

[98] *P. Otto, L. A. Feiler,* and *R. Huisgen,* Angew. Chem. *80,* 759 (1968); Angew. Chem. internat. Edit. *7,* 737 (1968).

[99] *M. E. Kuehne* and *P. J. Sheerhan,* Abstr. 156th Meeting Amer. chem. Soc., Atlantic City, N.J., September 9, 1968; J. org. Chemistry *33,* 4406 (1968).

[100] *M. Delaunois* and *L. Ghosez,* Angew. Chem. *81,* 33 (1969); Angew. Chem. internat. Edit. *8,* 72 (1969).

[101] *W. E. Truce, R. H. Bavry,* and *P. S. Bailey jr.,* Tetrahedron Letters *1968,* 5651.

[102] *J. Druey, E. F. Jenny, K. Schenker,* and *R. B. Woodward,* Helv. chim. Acta *45,* 600 (1962).

[103] *R. H. Hasek, P. G. Gott,* and *J. C. Martin,* J. org. Chemistry *29,* 2510 (1964).

[104] *D. C. England* and *G. C. Krespan,* J. Amer. chem. Soc. *87,* 4019 (1965).

[105] Cf. ref. [5] in ref. [100].

[106] *H. Staudinger* and *E. Suter,* Ber. dtsch. chem. Ges. *53,* 1092 (1920).

[107] *H.-U. Wagner* and *R. Gompper,* unpublished.

[108] *R. Gompper* and *G. Seybold,* Angew. Chem. *80,* 804 (1968); Angew. Chem. internat. Edit. *7,* 824 (1968).

[109] *M. Neuenschwander* and *A. Niederhauser,* Chimia *22,* 491 (1968).

[110] *R. Gompper* and *G. Seybold,* unpublished.

[111] *C. Grundmann, G. Weisse,* and *S. Seide,* Liebigs Ann. Chem. *577,* 77 (1952).

[112] *R. R. Schmidt,* Tetrahedron Letters *1968,* 3443.

[113] *S. A. Procter* and *G. A. Taylor,* Chem. Commun. *1965,* 569.

[114] *C. Metzger* and *R. Wegler,* Chem. Ber. *101,* 1120 (1968).

[115] *H. B. Kagan* and *J. L. Luche,* Tetrahedron Letters *1968,* 3093.

[116] *A. K. Bose* and *I. Kugajevsky,* Tetrahedron *23,* 957 (1967).

[117] *R. Huisgen, B. A. Davis,* and *M. Morikawa,* Angew. Chem. *80,* 802 (1968); Angew. Chem. internat. Edit. *7,* 826 (1968).

[118] *A. Gomes* and *M. M. Juolié,* Chem. Commun. *1967,* 935.

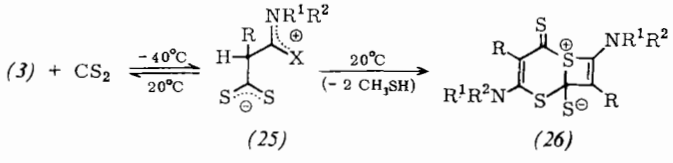
hexadien-1-one[119] proceeds *via* two dipolar intermediates, *i.e.* one in the formation of a β-lactam and the other in the rearrangement of the latter into 5-hydroxy-1,3,3-triphenyloxindole.

The combination of carbodiimides with ketenes to form azetinones[120,121] also involves 1,4-dipole intermediates. Hydrolysis experiments show[121] that these dipoles are relatively long-lived.

Little is known about the mechanism of the cycloaddition of ketenes to C=O bonds[73,122]. The detection of 1:2 and 2:1 cycloadducts[122] and the fact that liberation of CO_2 occurs even at 0 °C in the system dichloroketene/isatin or 2,3-coumarandione[122] are indications of the occurrence of dipolar intermediates.

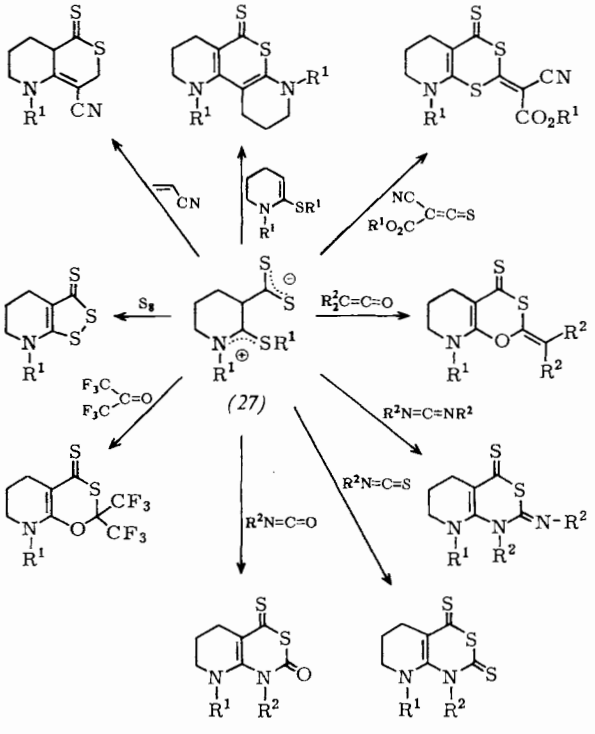
2.2.2. Reactions with Carbon Disulfide, Carbon Oxide Sulfide, and Carbon Dioxide

Introduction of carbon disulfide into solutions of ketene acetals *(3)* in acetonitrile at −40 °C leads to the crystalline red 1,4-dipoles *(25)*[123]. The structure of



(25) *(26)*

the latter has been confirmed by IR and NMR spectra and by their reactions. When heated, they decompose partly into the starting materials and partly with

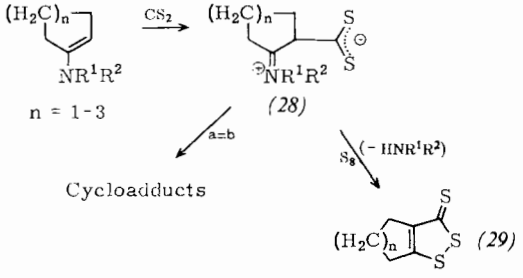


Scheme 1. $R^1 = CH_3$, $R^2 = C_6H_5$.

formation of "dimers", which probably have the structure *(26)*[124].

The compounds *(25)* are the first 1,4-dipoles that can be used to examine the scope of a 1,4-dipolar cycloaddition. Scheme 1 shows the variety of possible reactions for *(27)* (the cycloaddition is always followed by loss of CH_3SH from the primary adduct), which is practically as wide as that of other types of cycloaddition. Heterocumulenes are particularly suitable for use as 1,4-dipolarophiles.

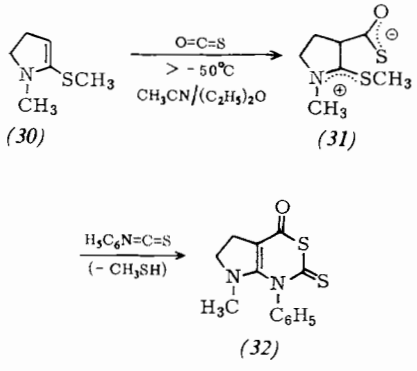
Instead of *(3)*, enamines can also react with carbon disulfide to form 1,4-dipoles *(28)*[25] (for solvent effect and activation parameters, see Table 1).



(28) *(29)*

The cycloadditions of *(28)* correspond to those of *(25)* and *(27)*; the formation of *(29)* proves the course of the synthesis of trithiones from enamines, carbon disulfide, and sulfur.

Reaction of the ketene *S,N*-acetal *(30)* with carbon oxide sulfide yields the 1,4-dipole *(31)*, which is stable up to about −35 °C[125], and which can react with phenyl isothiocyanate to give *(32)*.



(30) *(31)* *(32)*

Passage of carbon dioxide into solutions of *(3a)* in acetonitrile/ether at −70 °C leads to the 1,4-dipoles *(33)* (sometimes crystalline and sometimes only in solution)[125]. These dipoles are extremely sensitive to heat, and vigorous evolution of CO_2 begins at −60 °C. Addition of acetylenedicarboxylic ester to solutions of *(33)* leads to the α-pyrones *(34)*. Diphenylketene and phenyl isocyanate on the other hand react, not with *(33)*, but with the *(3a)* that is present in equilibrium to form *(35)* and *(36)*. Different products are obtained at higher temperatures (and in other solvents).

The 1,4-dipoles *(33)* are model substances for the "intimate ion pairs"[126] that occur on decarboxylation of β-lactones,

[119] *C. W. Bird*, J. chem. Soc. (London) *1965*, 3016.

[120] *R. Hull*, J. chem. Soc. (London) *C 1967*, 1154.

[121] *W. T. Brady* and *E. D. Dorsey*, Chem. Commun. *1968*, 1638.

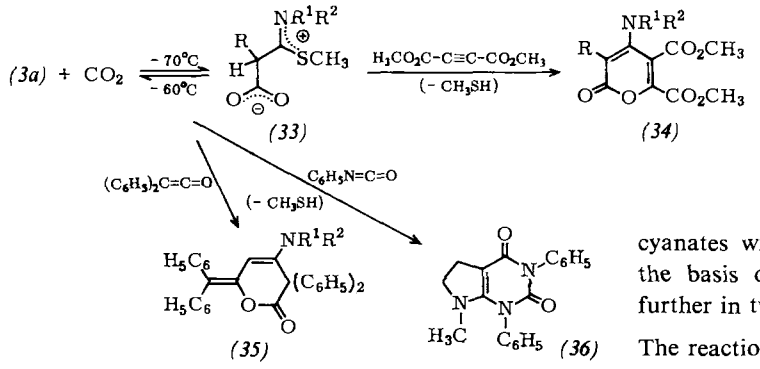
[122] *D. Borrmann* and *R. Wegler*, Chem. Ber. *102*, 64 (1969).

[123] *R. Gompper* and *W. Elser*, Angew. Chem. *79*, 382 (1967); Angew. Chem. internat. Edit. *6*, 366 (1967).

[124] *R. Gompper* and *W. Elser*, unpublished; cf. *W. Elser*, Dissertation, Technische Hochschule Stuttgart 1965.

[125] *R. Gompper* and *B. Wetzel*, unpublished.

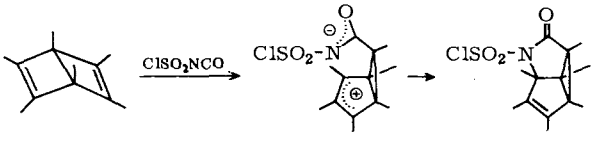
[126] *P. D. Bartlett* and *H. T. Liang*, J. Amer. chem. Soc. *80*, 3585 (1958).



and possibly also in their formation from β-hydroxy and β-halogeno carboxylic acids[13]. The (presumably) dipolar intermediate in the rearrangement of 2-oxabicyclo[2.2.0]-hex-5-en-3-one to 2-oxatricyclo[2.1.1.$0^{5,6}$]hexan-3-one[127] should also be mentioned here.

2.3.3. Reactions with Isocyanates, Isothiocyanates, and Carbodiimides

The mechanisms of the cycloadditions of chlorosulfonyl isocyanate[128–130] and of arylsulfonyl isocyanates[131] have been particularly extensively studied. If the addition of chlorosulfonyl isocyanate to allenes is a polar two-step process, it must be concluded that the cycloaddition to olefins proceeds in a similar manner, though it is stereospecific[129]. This is impressively supported by the formation of the lactam *(38)* from hexamethyl(Dewar benzene) and chlorosulfonyl isocyanate with *(37)* as a dipolar intermediate[132].



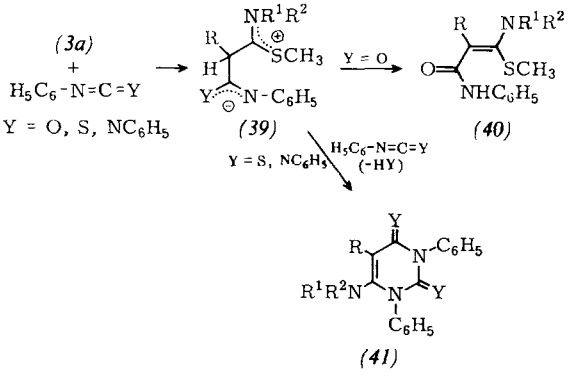
p-Toluenesulfonyl isocyanate undergoes stereospecific cycloaddition to ethyl 1-butenyl ether[131,131a]. These kinetic data are consistent both with a concerted and with a two-step process[131a]. The concept of a dipolar intermediate, which could be formulated similarly to *(2)* or analogously to *(15)* is supported by the observation that ethyl isobutenyl ether gives a 1:2 cycloadduct with chlorosulfonyl isocyanate[133].

The formation of mixtures of 4-amino-2-quinolones and 2-amino-4-quinolones[99] on reaction of aryl isocyanates with ynamines[99,134] can be explained on the basis of a dipolar primary adduct that reacts further in two directions.

The reaction of azines and azomethines with sulfonyl isocyanates unquestionably proceeds *via* 1,4-dipolar intermediates[135]; not only do azines give triazolotriazoles and azomethines give 1:2 and 2:1 cycloadducts (perhydro-*s*-triazines), but caprolactim methyl ether actually gives a stable zwitterion. The same picture is found in the cycloadditions of isocyanates and isothiocyanates to amidines and guanidines (2:1 cycloadducts)[136,137] and to carbodiimides[138]. In the absence of catalysts, fluoro ketones and alkyl isocyanates give mainly 1,3-oxazetidinones[139].

Dimethylamino isocyanate surprisingly dimerizes *via* an ylid intermediate to give a triazole derivative[140].

The reactions of *(3a)* with phenyl isocyanate, phenyl isothiocyanate, and diphenylcarbodiimide[124] at room temperature are summarized in Scheme 2. Whereas the isocyanate gives the substitution product *(40)* [compare, however, the formation of the pyrimidine



Scheme 2.

(36) under different conditions], the reactions with the isothiocyanate and the carbodiimide lead *via* the 1,4-dipoles *(39)* to the pyrimidines *(41)*. Reactions with benzenesulfonyl isocyanate and isothiocyanate lead to the stable 1,4-dipoles *(42)*[125], which undergo cycloaddition with *(3a)* or diphenylketene.

[127] *E. C. Corzy* and *W. H. Pirkle*, Tetrahedron Letters *1967*, 5255.

[128] *R. Graf*, Angew. Chem. *80*, 179 (1968); Angew. Chem. internat. Edit. *7*, 172 (1968).

[129] *E. J. Moriconi* and *J. F. Kelly*, J. org. Chemistry *33*, 3036 (1968); Tetrahedron Letters *1968*, 1435.

[130] *E. Moriconi* and *W. C. Meyer*, Tetrahedron Letters *1968*, 3823.

[131] *F. Effenberger* and *G. Kiefer*, Angew. Chem. *79*, 936 (1967); Angew. Chem. internat. Edit. *6*, 951 (1967).

[131a] *F. Effenberger*, personal communication.

[132] *L. A. Paquette*, Tetrahedron Letters *1968*, 2133.

[133] *K. Matterstock*, see ref. [30] in ref. [128].

[134] *J. Ficini* and *A. Krief*, Tetrahedron Letters *1968*, 947.

[135] *W. Bartmann*, Chem. Ber. *100*, 2938 (1967).

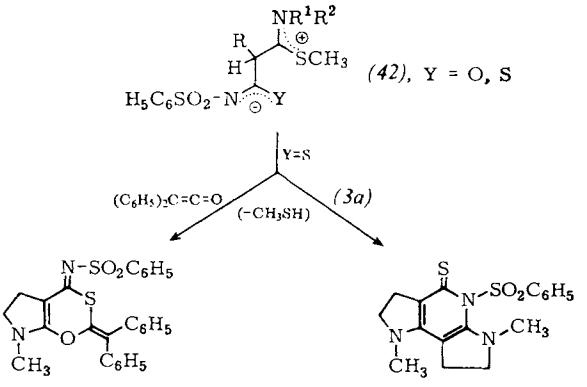
[136] *H. Ulrich*, *B. Tucker*, and *A. A. Sayigh*, Angew. Chem. *80*, 281 (1968); Angew. Chem. internat. Edit. *7*, 291 (1968).

[137] *R. Richter*, Chem. Ber. *101*, 3002 (1968); Tetrahedron Letters *1968*, 5037.

[138] *H. Ulrich*, *B. Tucker*, and *A. A. R. Sayigh*, J. Amer. chem. Soc. *90*, 528 (1968).

[139] *R. J. Shozda*, J. org. Chemistry *32*, 2961 (1967).

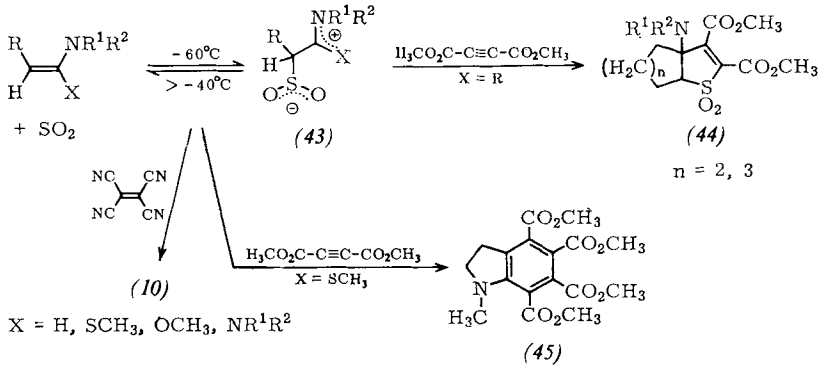
[140] *W. S. Wadsworth* and *W. D. Emmons*, J. org. Chemistry *32*, 1279 (1967).



(42), Y = O, S

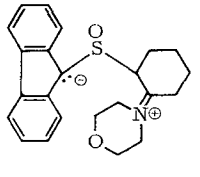
2.2.4. Reactions with Sulfur Dioxide, Sulfenes, Sulfines, and Sulfinylamines

Ketene *S(O),N*-acetals, ketene aminals, and enamines combine with liquid sulfur dioxide at −60 °C to give the dipoles *(43)*, which are stable in solution up to about −40 °C [125]. Their reaction with acetylenedicarboxylic ester leads in the case of the "enamine



dipole" to dihydrothiophene *S,S*-dioxides *(44)*. In the case of the "*(3a)* dipoles", only the *(3a)* present in equilibrium reacts, and *(45)* is formed *via* a new 1,4-dipole [compare the formation of the cyclobutene *(8)* under different conditions]; a similar situation is found for the reaction of tetracyanoethylene with *(43)*. Zwitterions of the type *(43)* have been suggested as intermediates in the conversion of episulfones into olefins [11,12].

Sulfenes attack only electron-rich olefins [85]; the resulting mixture of four-membered ring sulfones and vinyl sulfones can be explained on the basis of dipolar intermediates. Polar solvents favor the formation of the open-chain products [141,142]. Sulfene does not undergo stereoselective cycloaddition with *cis*-propen-



(46)

[141] *R. H. Hasek, R. H. Meen,* and *J. C. Martin,* J. org. Chemistry *30,* 1495 (1965).

[142] *W. E. Truce, D. J. Abraham,* and *P. Son,* J. org. Chemistry *32,* 990 (1967).

ylmorpholine; stereospecificity is, however, found in the cycloaddition of mesylsulfene to *cis*- and *trans*-butenyl butyl ethers [143].

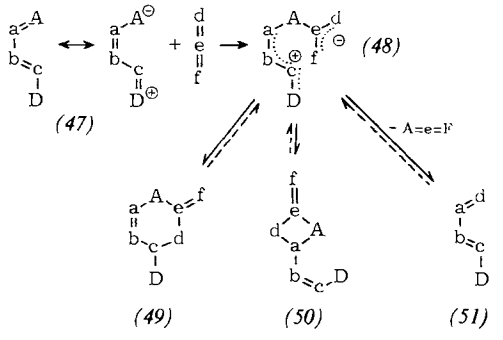
An interesting zwitterionic 1:1 adduct *(46)* is formed from 9-sulfinylfluorene and morpholinocyclohexene [144].

Enol ethers combine stereospecifically with *N*-sulfinylsulfonamides to form thiazetidine 1-oxides [131]; pyridine 1-oxide gives a 1,5-dipole [145].

2.3. Cycloadditions of Heterocumulenes to Polar 1,3-Dienes and Hetero-1,3-dienes

In the discussion of the cycloadditions of ketenes to olefins, it was mentioned that 1,3-dienes give only cyclobutanones [146] (even methyl 1-buten-3-yn-1-yl ether adds diphenylketene only at the triple bond [97]). The isolation or detection of 1,4-dipoles in reactions of electron-rich ("polar") olefins with heterocumulenes suggests that reactions of "polar" 1,3-dienes or hetero-

1,3-dienes *(47)* with heterocumulenes d=e=f might also lead to the formation of dipolar intermediates *(48)*, which then change into either four-membered rings *(50)* or six-membered rings *(49)*. The elimination of a different heterocumulene from *(48)* to give new



A = electron acceptor; D = electron donor

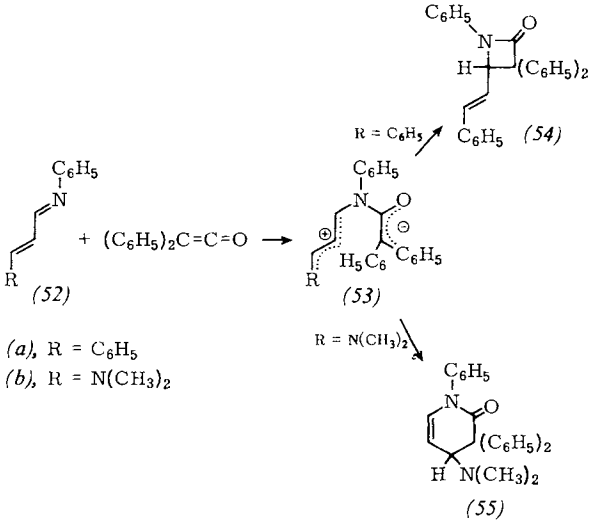
[143] *G. Opitz,* Angew. Chem. *80,* 633 (1968); Angew. Chem. internat. Edit. *7,* 646 (1968).

[144] *W. A. Sheppard* and *J. Diekmann,* J. Amer. chem. Soc. *86,* 1891 (1964).

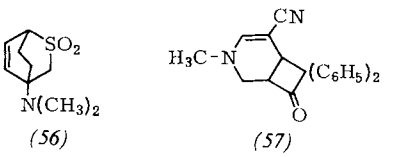
[145] *R. Albrecht* and *G. Kresze,* Chem. Ber. *98,* 1205 (1965).

[146] 2-Methoxy-1,3-butadiene appears to be an exception: *J. C. Martin, P. G. Gott, V. W. Goodlett,* and *R. H. Hasek,* J. org. Chemistry *30,* 4175 (1965).

hetero-1,3-dienes *(51)* would also be conceivable. The relative importance of the ring closure of *(48)* to form *(49)* should increase with increasing stability of *(48)*, since the most favorable conformation for the formation of *(49)* can then be reached by internal rotation [*(47)* will often be transoid]. This view is strongly supported by the reactions of the azomethines *(52a)* and *(52b)* with diphenylketene[33]: *(52a)* gives the azetidinone *(54)*, and *(52b)* gives the dihydropyridone *(55)*, since the positive charge of the dipole *(53)* is much more strongly delocalized in the case of *(52b)* than in that of *(52a)*.

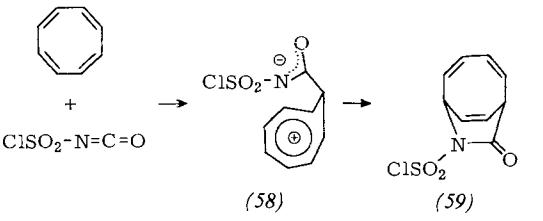


(a), R = C_6H_5
(b), R = $N(CH_3)_2$



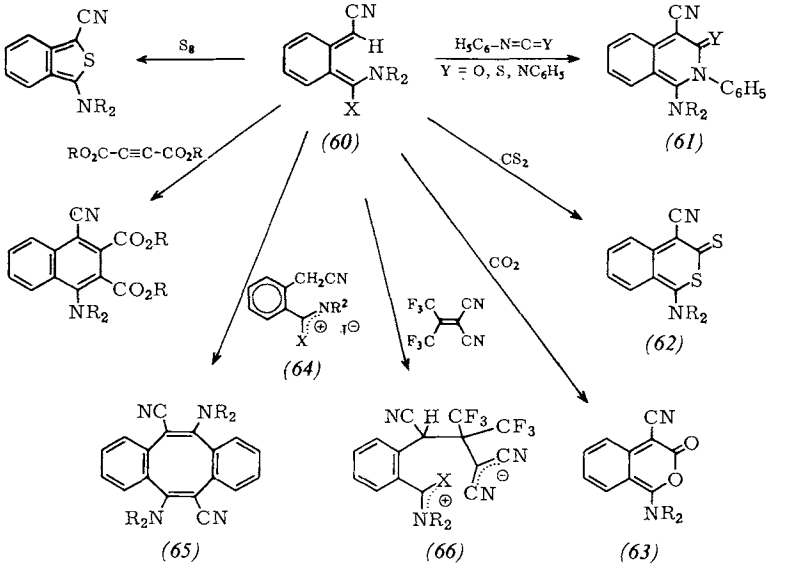
(56) *(57)*

sulfide has also been reported[149]. Whereas ketene undergoes 1,4-cycloaddition with 1-piperidinobutadiene[150], the reaction of 2,3-dihydrodimethylaniline with diphenylketene yields only acylation products[33]. 5-Cyano-1-methyl-1,2-dihydropyridine again undergoes cycloaddition with diphenylketene to give *(57)*[33]. An important 1,4-cycloaddition is the addition of chlorosulfonyl isocyanate to cyclooctatetraene[151,152]. The dipolar intermediate *(58)*, in which



(58) *(59)*

the positive charge in the homotropylium system is delocalized, achieves stability by formation of *(59)*. (It is not certain whether the 1,4-cycloadditions of dehydrobenzene[153] and 4-phenyl-1,2,4-triazoline-3,5-dione[154] to cyclooctatetraene proceed *via* dipolar intermediates.) The reaction of simple 1,3-dienes with chlorosulfonyl isocyanate leads first to β-lactams,



(60) *(61)* *(62)* *(63)* *(64)* *(65)* *(66)*

X = SCH_3, NR_2^1; R = CH_3

2.3.1. Reactions of Polar 1,3-Dienes

As the simplest butadiene derivatives of the type *(47)*, 1-dialkylaminobutadienes undergo 4 + 2 cycloaddition as a minor reaction, together with a double 2 + 2 cycloaddition, on reaction with sulfene[147,148]. 2,3-Dihydrodimethylaniline, on the other hand, gives only the adduct *(56)* on reaction with sulfene[85]. The synthesis of α-pyrones from dienamines and carbon di-

[147] *G. Opitz* and *F. Schweinsberg*, Angew. Chem. *77*, 811 (1965); Angew. Chem. internat. Edit. *4*, 786 (1965).

[148] *L. A. Paquette* and *M. Rosen*, Tetrahedron Letters *1966*, 311.

[149] *R. Mayer* and *K. Gewald*, Angew. Chem. *79*, 298 (1967); Angew. Chem. internat. Edit. *6*, 294 (1968).

[150] *G. Opitz* and *F. Schweinsberg*, vgl. [85].

[151] *P. Wegener*, Tetrahedron Letters *1967*, 4985.

[152] *L. A. Paquette* and *T. J. Barton*, J. Amer. chem. Soc. *89*, 5480 (1967).

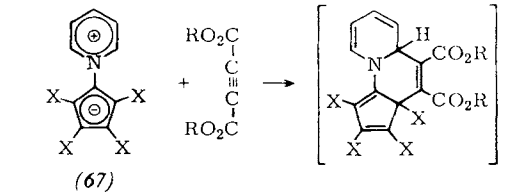
[153] *E. Vedejs*, Tetrahedron Letters *1968*, 2633.

[154] *A. B. Evnin*, *R. D. Miller*, and *G. R. Evanega*, Tetrahedron Letters *1968*, 5863.

which change into dihydropyridones when heated to 40 °C [130].

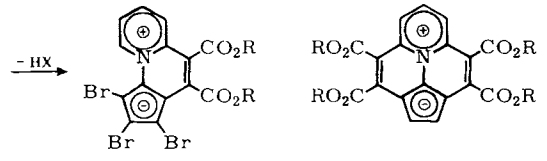
The deep blue *o*-quinodimethanes *(60)* form a class of very strongly polar or polarizable 1,3-dienes [155]. Unlike "normal" *o*-quinodimethanes, they do not undergo valence isomerization to form benzocyclobutenes. They readily enter into cycloadditions with heterocumulenes (as well as with sulfur and acetylenedicarboxylic ester); after elimination of HX from the primary adducts (which cannot be isolated), it is possible to isolate the heterocyclic "*o*-quinodimethanes" *(61)–(63)*. The dibenzocyclooctene *(65)* is probably formed, not by direct dimerization of *(60)*, but by the action of *(64)* on *(60)*. The assumption that 1,6-dipoles occur as intermediates in all these reactions is supported by the isolation of *(66)* [156].

The pyridinocyclopentadienylides *(67)* are both 1,*x*-dipoles and 1,3-dienes. The reaction with acetylenedicarboxylic ester (which is related to the ketenes) to give *(68)* and *(69)*, as well as other products [157]. Though the mechanism of these reactions is not yet known (the formation of substitution products points to dipolar intermediates), there is little doubt that two steps are involved in the conversion [157] of the pyridinobenzimidazolylides *(70)* [157,158] into the adducts *(71)*.

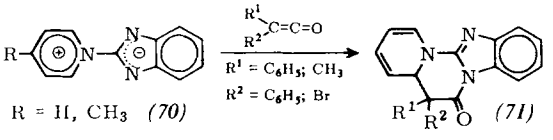


(67)

X = H, Br



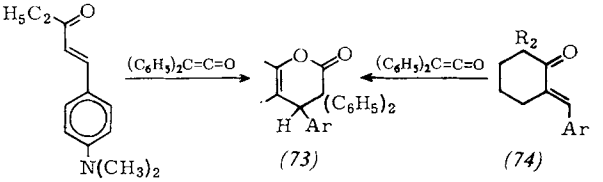
(68) *(69)*



R = H, CH_3 *(70)* *(71)*

2.3.2. Reactions of Vinyl Ketones and Related Compounds

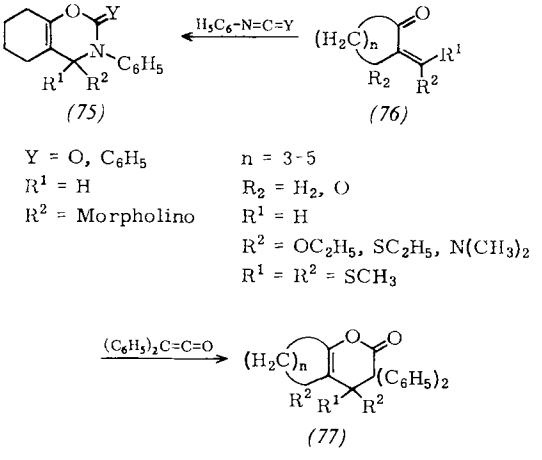
In reactions of α-β-unsaturated ketones with ketenes, δ-lactones have mostly been obtained only as by-products [159–163] (for the reaction in the presence of Lewis acids, see [164]). Good yields of 1,4-cycloadducts *(73)* are, however, obtained when *(72)* or *(74)* is heated with diphenylketene [33]. The stabilization of the positive charge in the intermediate corresponding to *(48)* by the electron-donating substituents present in *(72)* and *(74)* evidently favors the formation of the six-membered ring.



(72) *(73)* *(74)*

(a), Ar = *p*-$C_6H_4N(CH_3)_2$, $R_2 = H_2$
(b), Ar = C_6H_5, $R_2 = C_6H_5CH$

Better examples of *(47)* than the simple vinyl ketones are β-acyl enol ethers, thioenol ethers, enamines, ketene acetals, ketene *O,N*-acetals, ketene aminals, and ketene mercaptals. Some of their reactions [83] with ketenes [165–169] (cyclobutanones are assumed to occur as intermediates in some cases [167,168]) and sulfenes [142,170] to give α-pyrones and δ-sultones, respectively, and the cycloadditions of diphenylketene, phenyl isocyanate, and diphenylcarbodiimide



(75) *(76)*

Y = O, C_6H_5
R^1 = H
R^2 = Morpholino

n = 3-5
$R_2 = H_2$, O
R^1 = H
$R^2 = OC_2H_5$, SC_2H_5, $N(CH_3)_2$
$R^1 = R^2 = SCH_3$

(77)

to *(76)*, which lead to *(75)* and *(77)* [33], illustrate the strong tendency toward the formation of the six-membered ring (cf. Table 1 for the solvent effect).

[155] *R. Gompper, E. Kutter*, and *H. Kast*, Angew. Chem. *79*, 147 (1967); Angew. Chem. internat. Edit. *6*, 171 (1967).

[156] *R. Gompper* and *U. Mengdehl*, unpublished.

[157] *R. Gompper* and *V. Figala*, unpublished.

[158] *G. V. Boyd*, Tetrahedron Letters *1966*, 3369.

[159] *H. Staudinger* and *R. Endle*, Liebigs Ann. Chem. *401*, 263 (1913).

[160] *F. O. Rice, J. Greenberg, C. E. Waters*, and *R. E. Vollrath*, J. Amer. chem. Soc. *56*, 1760 (1934).

[161] *N. Campbell, P. S. Davison*, and *H. G. Heller*, J. chem. Soc. (London) *1963*, 993.

[162] *H. G. Heller, D. Auld*, and *K. Salisbury*, J. chem. Soc. (London) *1967*, 1552.

[163] *H. Hopff* and *W. Rapp*, US-Pat. 2265165 (1941); Chem. Abstr. *36*, 1614 (1942).

[164] *H. E. Zaugg*, Org. Reactions *8*, 305 (1954).

[165] *G. A. Berchtold, G. R. Harvey*, and *G. E. Wilson*, J. org. Chemistry *26*, 4776 (1961); *30*, 2642 (1965).

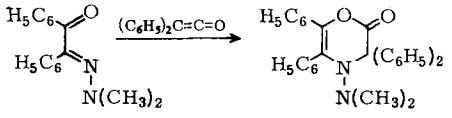
[166] *G. Opitz* and *F. Zimmermann*, Chem. Ber. *97*, 1266 (1964).

[167] *J. C. Martin, P. G. Gott*, and *H. U. Hostettler*, J. org. Chemistry *32*, 1654 (1967).

[168] *A. Gandini, P. Schenone*, and *G. Bignardi*, Mh. Chem. *98*, 1518 (1967).

[169] *R. Scarpati, D. Sica*, and *C. Sanatcroce*, Tetrahedron *20*, 2735 (1964).

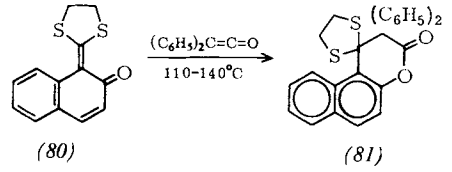
[170] *G. Opitz* and *E. Tempel*, Angew. Chem. *76*, 921 (1964); Angew. Chem. internat. Edit. *3*, 754 (1964); Liebigs Ann. Chem. *699*, 68 (1966).



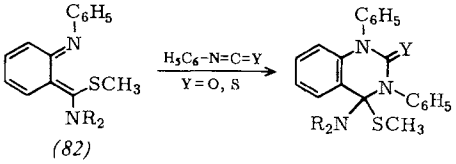
(78) (79)

Another example is the synthesis of *(79)* from the benzil hydrazone *(78)* and diphenylketene [33].

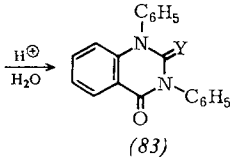
The reactions of the *o*-quinodimethanes *(60)* are related to the cycloadditions of diphenylketene to the *o*-quinonemethide *(80)* to form *(81)* [171] and of phenyl isocyanate and phenyl isothiocyanate to the *o*-quinonemethidimine *(82)* to form the quinazoline *(83)* [173].



(80) (81)



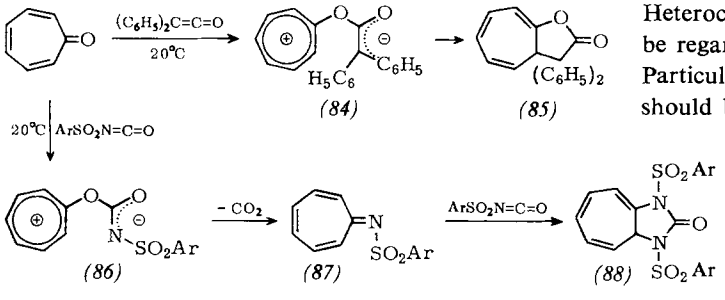
(82)



(83)

Special mention should be made of the synthesis of 1,3-oxazines from fluorinated *N*-acetylimines and ketenes [174].

Compounds of the type *(47)*, for which the positive charge in dipolar intermediates *(48)* is distributed only



(84) (85) (86) (87) (88)

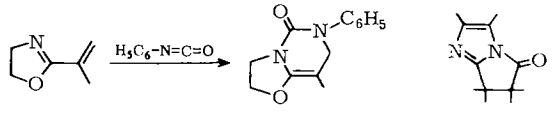
over C atoms (partly in aromatic ring systems), include tropone, cyclopropenone, and phenalenone [172]; these compounds should be predisposed to two-step cycloadditions with heterocumulenes. Tropone actually undergoes cycloaddition with diphenylketene even at room temperature [172, 175], and the product *(85)* can be isolated in practically quantitative yield (for proof of structure, see [172]). Evidence in favor of the intermediate occurrence of *(84)* includes the fact that the imidazole derivative *(88)* is formed as well as the tropone imine *(87)* in the corresponding reaction with *p*-toluenesulfonyl isocyanate [172, 176], indicating the formation of *(86)* as an intermediate.



(89) (90)

Tropone gives *(89)* on reaction with dichloroketene [177], and *(90)* on reaction with mesylsulfene [178]. In the reactions of diphenylcyclopropenone [172, 179] and phenalenone [172] with ketenes and sulfonyl isocyanates, the cyclopropenone imines, methylphenalenes, and phenalenone imines remaining on elimination of CO_2 from the zwitterionic primary adducts can no longer undergo cycloaddition with heterocumulenes.

Further examples of reactions of vinyl ketone imines [cf. *(52)* and *(87)*] are the additions of phenyl isocyanate to *(91)* to form *(92)* [180] (a two-step course is



(91) (92) (93)

indicated by the fact that no reactions occur with dienophiles) and those of ketenes, phenyl isocyanate, benzylideneaniline, and *anti*-benzaldoxime to 1,4-diazafulvenes [181] *e.g.* to form *(93)*.

2.3.3. Reactions of "*o*-Quinoid" Ketenes and Acylheterocumulenes

Heterocumulenes having the general formula *(94)* may be regarded as polar diene systems of the type *(47)*. Particularly strong polarization or polarizability should be found in the "*o*-quinoid" derivatives *(95)*.

[171] *A. Studeneer*, Dissertation, Universität Stuttgart 1968.

[172] *R. Gompper, A. Studeneer*, and *W. Elser*, Tetrahedron Letters *1968*, 1019.

[173] *R. Gompper* and *H.-D. Lehmann*, Angew. Chem. *80*, 38 (1968); Angew. Chem. internat. Edit. *7*, 74 (1968); *H.-D. Lehmann*, Dissertation, Universität Stuttgart 1968.

[174] *Y. V. Seifman, N. P. Gambaryan, L. A. Simonyan, R. B. Minasyan*, and *I. L. Knunyants*, Ž. obšč. Chim. *37*, 2476 (1967).

[175] *Ch. Lutz, I. Rommel, I. Lengyel*, and *J. Feeney*, Tetrahedron *22*, 1809 (1966).

[176] *L. A. Paquette* and *N. Horton*, Tetrahedron Letters *1968*, 2289.

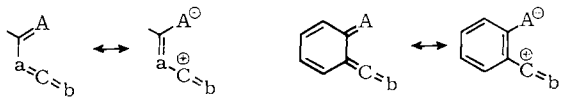
[177] *J. Ciabattoni* and *H. W. Anderson*, Tetrahedron Letters *1967*, 3377.

[178] *J. Ciabattoni* and *M. Cabell*, Tetrahedron Letters *1968*, 2693.

[179] *L. A. Paquette, T. J. Barton*, and *N. Horton*, Tetrahedron Letters *1967*, 5039.

[180] *W. Seeliger, E. Aufderhaar, W. Diepers, R. Feinauer, R. Nehring, W. Thier*, and *H. Hellmann*, Angew. Chem. *78*, 913 (1966); Angew. Chem. internat. Edit. *5*, 875 (1966).

[181] *W. Rohr, R. Swoboda*, and *H. A. Staab*, Chem. Ber. *101*, 3491 (1968).

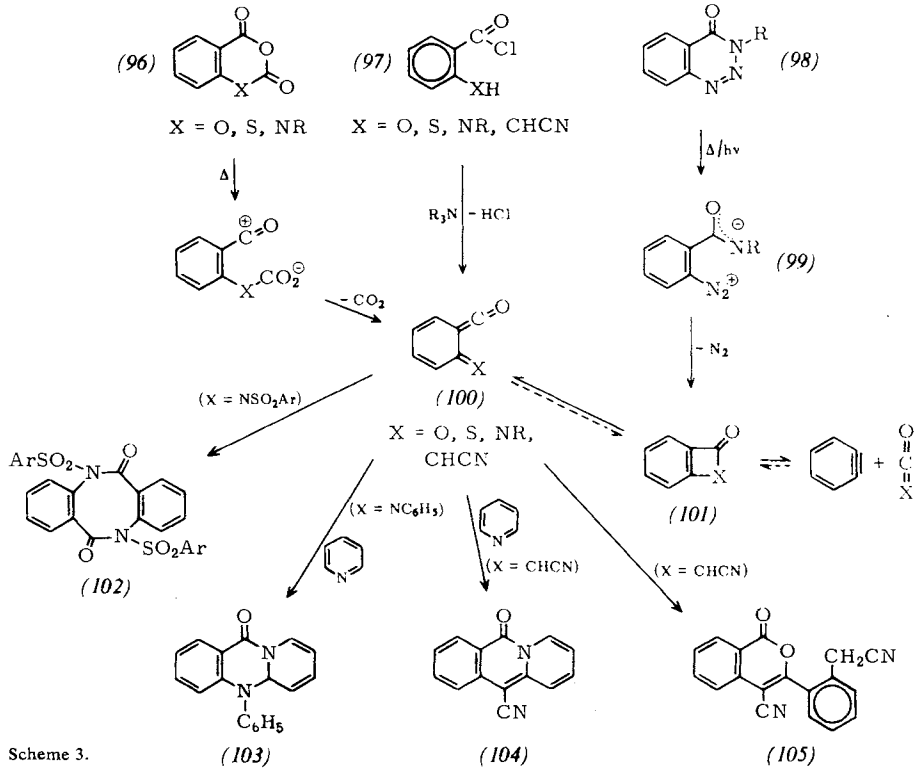


(94) (95)

Cycloadditions of ketenes, isocyanates, carbodiimides, ketones, azomethines, isonitriles, and electron-rich olefins to acylketenes, acyl and thioacyl isocyanates, acyl and imidoyl isothiocyanates [182], and acylsulfinylamines [183] to form six-membered rings (see [83]), some of which can be formulated as Diels-Alder reactions, nevertheless fit readily into the scheme *(47)* → *(48)* → *(49)* (important evidence is provided *e.g.* by the observation that thioacyl isocyanates, unlike other dienes, undergo cycloaddition to the C=N bond of imidazoline-4,5-diones [184]).

(100) is characterized by a tendency to dimerize [corresponding to the cycloaddition *(47)* + heterocumulene] and to undergo cycloadditions with heterocumulenes and with polar systems containing multiple bonds [83,173,185,186]. Examples are dimerizations to form *(102)* [188] and *(105)* [187]. Cycloaddition of pyridine yields *(103)* [188] (this compound, prepared from *N*-phenylanthraniloyl chloride and pyridine [190], was assigned a betaine structure) and *(104)* [187] (the primary adduct is dehydrogenated; the pyridine may be replaced *e.g.* by quinoline, isoquinoline, and 1-methylimidazole).

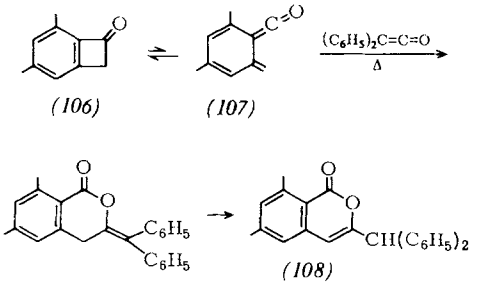
The slowness of the valence isomerization *(100)* ⇌ *(101)* is also shown by the failure of previous attempts to use benzocyclobutenones in the same way as benzocyclobutenes for cycloadditions [191]. The successful



Scheme 3.

Systems *(100)* of the quinoid type *(95)* can be obtained by elimination of CO_2, HCl, or N_2 from *(96)* to *(98)* [83,173,185–188]. Scheme 3 is an attempt to treat all the reactions from the same point of view. With *(96)* and *(97)* as starting materials, it was possible to detect *(100)*, but not *(101)* [*i.e.* the situation is similar to that found for *(60)*]. This indicates that the valence isomerization *(100)* ⇌ *(101)* is slower than the other secondary reactions of *(100)* [compare the isolation of a naphthazetinone having the constitution *(101)* [189]].

conversion [156] of dimethylbenzocyclobutenone *(106)* *via (107)* into the isocoumarin *(108)* confirms the view presented here for the behavior of polar diene systems toward heterocumulenes.



(106) (107) (108)

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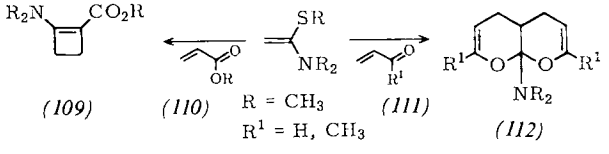
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Compounds of the type *(100)* may be expected, not only to isomerize into *(101)*, but also to undergo fragmentation into dehydrobenzene and a heterocumulene. Only one example of this is known at present, *i.e.* the decomposition of *o*-benzenediazoniumcarboxylate *via* a β-lactone to form dehydrobenzene[192] [similar to *(99)* → *(101)*]. Mention should also be made of the 1,6-dipolar cycloaddition of *o*-benzenediazoniumcarboxylate to dehydrobenzene[193].

The 2-diazoniumphenoxides ("*o*-quinone diazides") and α-diazoketones, which react with ketene imines and ketenes to give 1,4,5-oxadiazepines and γ-lactones respectively (cf.[194,195]), are formally also systems of the type *(47)*.

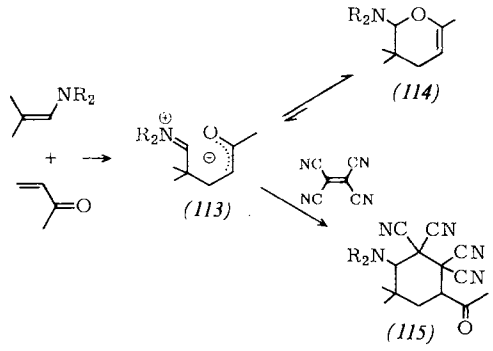
2.4. Diels-Alder Reactions

The question whether Diels-Alder reactions[40] and the decomposition of Diels-Alder adducts[196] are one-step or two-step reactions has been extensively discussed, particularly in connection with diradical intermediates. In addition to the vast majority of synchronous processes, however, there are also several examples (*e.g.* 5-cyano-1-methyl-1,2-dihydropyridine + acrylonitrile[197]; esters of phosphonous and phosphinous acids + 3-benzylidene-2,4-pentanedione[198]; 4-methyl-1,3-pentadiene + tetracyanoethylene[199]) in which dipolar intermediates must be considered. For example, the electronically closely related compounds *(110)* and *(111)* react with ketene *S,N*-acetals[55,57] to give *(109)* and *(112)* respectively. This means that either the activation energies of the 2 + 2 and 2 + 4 cycloadditions are very close to each other



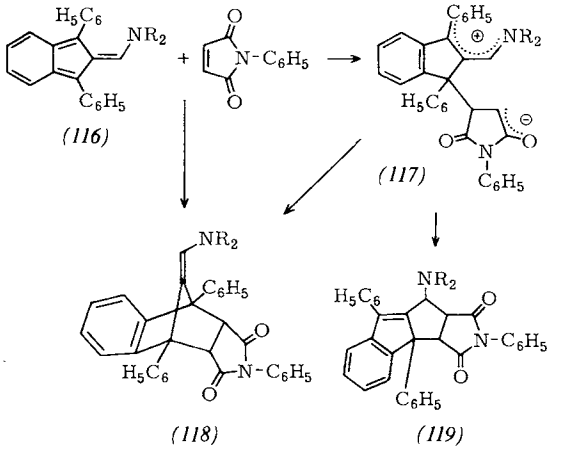
(109) *(110)* *(111)* *(112)*

or both reactions have a dipolar intermediate. The latter possibility is supported by the two-step cycloaddition of 3,4-dihydroisoquinolines to α,β-unsaturated ketones[200], and particularly by the reaction of dimethylaminoisobutene with vinyl methyl ketone[201], which leads *via (113)* to the six-membered ring adduct *(114)*. On reaction of *(114)* with tetracyanoethylene, the dipole *(113)* that is present in equilibrium is intercepted as *(115)*.



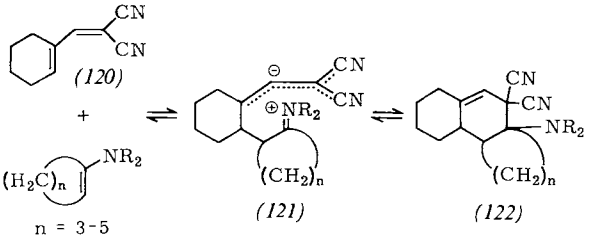
(113) *(114)* *(115)*

The isobenzofulvene *(116)* reacts with *N*-phenylmaleimide to give a mixture of *(118)* and *(119)*[202]. Whereas *(119)* can only be formed *via (117)*, the formation of *(118)* can be explained both as a "synchronous" Diels-Alder reaction and as a two-step cycloaddition *via (117)*. It is interesting to note that the 1,3-unsubstituted isobenzofulvene gives only an adduct corresponding to *(119)*. As a (10π + 2π) cycloaddition, the sequence *(116)* → *(117)* → *(119)* is reminiscent of the reaction of pyrrocoline with acetylenedicarboxylic ester[203].



(116) *(117)* *(118)* *(119)*

1,6-Dipolar intermediates *(121)* can be detected directly in the reaction of *(120)* with enamines[30,204]. The colorless Diels-Alder adducts *(122)* are formed at room temperature in apolar solvents and at about



(120) *(121)* *(122)*

−20 °C in polar solvents. At −40 °C, on the other hand, the reaction yields the yellow crystalline dipoles *(121)*, which give *(122)* when warmed [*(122)* reopens

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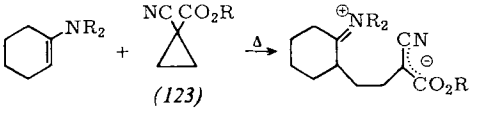
[203] *A. Galbraith, T. Small, R. A. Bairns,* and *V. Boekelheide,* J. Amer. chem. Soc. *83,* 453 (1961).

[204] Although ketene *S,N*-acetals behave similarly, the reaction stops at *(121)*, see ref. [30].

in polar solvents to form *(121)*, see also Table 1, reaction (8)]. It should be noted that the above-mentioned HMO model [107] correctly indicates the energetic advantage of the two-step route to *(122)* as compared with a one-step reaction. Evidence of two-step polar Diels-Alder reactions is also found in reactions of benzoyl isothiocyanate with *(3a)* [30].

2.5. Cycloadditions with Ring Opening

There are many cycloadditions in which 1,*x*-dipoles whose charge centers are not conjugated are formed by ring opening. Examples illustrating this principle include, in addition to the sequence *(114)* → *(113)* → *(115)*, the synthesis of *(124)* from pyrrolidinocyclohexene and *(123)* [205] [primary ring opening of *(123)*



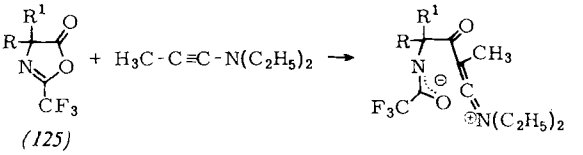
(123)



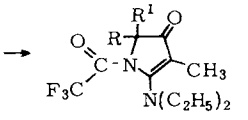
(124)

to form a carbanion-carbonium ion pair [206] must also be considered] as well as the addition of epoxides to oxazol-2-ines [180] and the reaction of oxazolones *(125)* with ynamines to form pyrrolones *(126)* [31].

Mention should also be made of the ring expansion of aziridinium salts with aldehydes, ketones, nitriles [207],

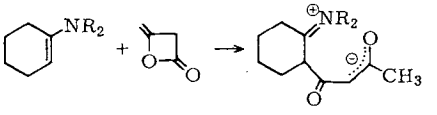


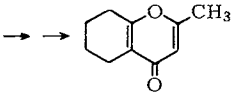
(125)



(126)

and nitrones [208] (this could be an example of a two-step 1,3-dipolar cycloaddition [38,39,209,210]) and the reaction of morpholinocyclohexene with diketene to form *(127)* [211] (for the formation of cyclohexane derivatives with the dimethylketene dimers, see [212]).





(127)

We are grateful to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for their support of our work in this field.

Received February 4, 1969 [A 693 IE]
German version: Angew. Chem. *81*, 348 (1969)
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Spectroscopic Investigation of Various Phosphorus-Sulfur Bonds

By J. Goubeau [*]

Dedicated to Professor H. Bredereck on the occasion of his 65th birthday

The results of spectroscopic investigations on phosphorus-sulfur compounds, and particularly the force constants, reveal several factors that decisively influence the bonding. The effects of hybridization, the other bonding partners and their electronegativities, the π-bonding components, and the ionic charge are discussed. It is shown that the P–S bond, unlike the P–O bond, never attains full double bond character, despite its great variability.

1. Introduction

It was shown in two earlier articles [1] that the force constants calculated from the vibration spectra provide more than qualitative information about the various bonds in a molecule. It has been deduced from a large volume of data, mainly on nitrogen compounds, that bond orders of 2 (double bonds) or more are to be expected if the sum of the Pauling electronegativities of two bonding partners is 5 or more and if their difference is not greater than 1.5.

To clarify the situation further, it was necessary to investigate the bonding of pairs of elements for which the sum of the electronegativities (Σx) is smaller than the limiting value of 5. An investigation of this nature was carried out on a broad basis by *Bürger* [2] on silicon-nitrogen compounds. This pair of elements has an electronegativity sum just below the limiting value ($\Sigma x = 4.8$), together with a relatively high electronegativity difference ($\Delta x = 1.2$). The highest bond order observed, 1.3, is in agreement with the rules proposed.

We have studied the pair of elements phosphorus and sulfur, for which the electronegativity sum (4.6) is again only slightly smaller than the limiting value indicated, but whose electronegativity difference $\Delta x = 0.4$ should be more favorable toward the formation of multiple bonds. Both elements belong to the second short period, so that d electrons must also be taken into account. This combination is particularly interesting because of the different oxidation states of phosphorus, the effects of which have also been studied. Since seriously weakened multiple bonds were to be expected for this pair of elements, all the factors that could influence the force constants had to be checked. The changes in P–S force constants due to:

1) hybridization,

2) inductive effects,

3) ionic charges, and

4) π bonds

are therefore reported in this article.

Nearly all the force constants given (k values in mdyne/Å) were calculated by the method described earlier [1]. Where bond orders are given, they correspond to the Siebert rule [3].

2. Effect of Hybridization

This effect was first observed for C–H bonds, whose force constants increase rapidly with increasing s component [4, 5]. A similar effect has also been found for various phosphorus compounds, if one assumes mainly p bonding in compounds of trivalent phosphorus, sp^3 hybridization in compounds containing tetracoordinate phosphorus, and sp^2 and pd hybridization in the equatorial plane and along the longitudinal axis, respectively, of the trigonal bipyramid in compounds of pentacoordinate phosphorus.

The force constants of several phosphorus compounds are compared from this point of view in Table 1. Examples have been chosen in which the part played by other effects is as small as possible. To facilitate comparison, the various force constants are given in the right-hand half of the table on the basis of a value of 100 for the force constant of the sp^3 hybrid. The values agree well among themselves, and also agree in their order of magnitude with the corresponding values for C–H bonds [5], particularly when one considers that the bonds of trivalent phosphorus are certainly not pure p bonds, since the bond angles at the phosphorus atom vary between 95 and 105 °C, indicating an appreciable and varying s component. A change from sp^3 to p is accompanied by a 6–21% decrease in the force constant, while a change from sp^3 to sp^2 results in a 5% increase. As expected, the greatest decrease (about 35%) in relation to sp^3 is found for the axial bond of the trigonal bipyramid (pd).

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Table 1. Dependence of the force constants of various phosphorus compounds on the hybridization of the phosphorus atom.

Hybridization	 pd	 p	 sp^3	 sp^2	pd	p	sp^3	sp^2
k(P–H)		3.10 [a]	3.30 [b]	3.59 [c]		94	100	109
k(P–CH_3)		2.77 [d]	3.05 [e]			91	100	
k(P–F)	4.52 [f]	5.19 [g]	6.34 [h]	6.38 [f]	71	82	100	101
k(P–Cl)	1.63 [i]	2.36 [j]	2.66 [k]	2.78 [i]	61	89	100	104
k(P–Br)		1.84 [l]	2.66 [m]			79	100	
k(P–OCH_3)		3.72 [o]	4.87 [p]			76	100	
Mean					66	85	100	105
Values for C–H bonds						75	100	105

The force constants were calculated from the spectra of the following compounds:
[a] PH_3; [b] $BH_3 \cdot PH_3$; [c] H_2PF_3; [d] $P(CH_3)_3$; [e] $SP(CH_3)_3$, $OP(CH_3)_3$; [f] PF_5; [g] PF_3; [h] OPF_3; [i] PCl_5; [j] PCl_3; [k] $SPCl_3$; [l] PBr_3; [m] $SPBr_3$; [o] $P(OCH_3)_3$; [p] $OP(OCH_3)_3$.

The only force constants available for the discussion of the effect of hybridization in phosphorus-sulfur compounds are those of the fully sulfur-substituted compounds $P(SCH_3)_3$, $SP(SCH_3)_3$, and PS_4^{3-} (see Table 2).

Table 2. Force constants of various phosphorus-sulfur compounds.

	p $P(SCH_3)_3$	sp^3 $SP(SCH_3)_3$	sp^3 PS_4^{3-}	p	sp^3
k(P–SCH_3)	2.06 2.22	2.56		81 78	100
k(S–P)		4.16	2.51		

Two values are given for $P(SCH_3)_3$, since rotational isomerism gives rise to two pairs of PS_3 stretching vibrations; both values were calculated for an all-*cis* model. The values of k(P–SCH_3) are themselves sufficient to demonstrate the effect of hybridization, since here again the change from sp^3 to p leads to a decrease of about 20%. The differences in the k(S–P) values are due to the effects of ionic charge and of π bonds (see Sections 4 and 5).

The experimental results available at present show that the force constant increases with increasing s component for all phosphorus compounds. The maximum changes are around 40%, and 20% in the case of phosphorus-sulfur bonds.

3. Effect of the Other Ligands

This effect is most easily demonstrated for series of compounds in which the sulfur, *e.g.* in $SP(SCH_3)_3$, is systematically replaced by other atoms. The simplest case is probably the replacement of the sulfur by oxygen, since the model is retained in full as regards its structure, so that satisfactory comparability of the values is to be expected. Two series of compounds are obtained, depending on whether just the three SR groups are replaced or these three groups and the sulfur atom substituted. The results of our calculations are shown in Table 3. Table 4 gives the same P–S and P–O force constants based on the values in $SP(SCH_3)_3$ and $OP(OCH_3)_3$ as standards (= 1.00).

Table 3. Force constants of the transition series $SP(SR)_3$ – $OP(OR)_3$.

	SPS_3	$SPOS_2$	SPO_2S	SPO_3
k(P–SCH_3)	2.56	2.76	3.23	
k(P–OCH_3)		3.90	4.17	4.59
k(S–P)	4.16	4.39	4.53	4.52
	OPS_3	$OPOS_2$	OPO_2S	OPO_3
k(P–SCH_3)	2.71	3.18	3.27	
k(P–OCH_3)		3.91	4.34	4.87
k(O–P)	8.71	9.05	9.38	9.83

Table 4. Force constants of the transition series $SP(SR)_3$ – $OP(OR)_3$ based on k(PS) in $SP(SCH_3)_3 = 1$ and k(PO) in $OP(OCH_3)_3 = 1$.

	SPS_3	$SPOS_2$	SPO_2S	SPO_3
k(P–SCH_3)	1.00	1.08	1.26	
k(P–OCH_3)		0.80	0.86	0.94
k(S–P)	1.00	1.05	1.09	1.08
	OPS_3	$OPOS_2$	OPO_2S	OPO_3
k(P–SCH_3)	1.06	1.24	1.28	
k(P–OCH_3)		0.80	0.89	1.00
k(O–P)	0.89	0.92	0.95	1.00

Each substitution of a sulfur atom by a more electronegative oxygen atom leads to an increase in all the force constants. This is true of the replacement both of the sulfur in the S–CH_3 groups and of the lone sulfur atom. The greatest changes (20–30%) occur for k(P–SCH_3) and k(P–OCH_3), whereas the S–P and O–P force constants change by only up to 10%.

If the SCH_3 groups in the two compounds $SP(SCH_3)_3$ and $OP(SCH_3)_3$ are replaced by the more electronegative chlorine atom (Table 5), it is again found that replacement of sulfur by oxygen leads to an increase of between 6 and 38% in all the force constants. The substitution of the SCH_3 groups by chlorine also leads in five out of six cases to a 13 to 21% increase in the force constant. However, k(P–SCH_3) decreases in the series $SP(SCH_3)_3$–$SPCl_3$, the major part of the decrease occurring with the introduction of the first chlorine atom. It is not yet certain whether this is due to failure of the calculation procedure as a result of strong coupling of νPCl with $\nu_s PS_2$ or to a real effect. The values of the P–Cl force constants are surpris-

Table 5. Force constants of the transition series $SP(SCH_3)_3$ – $SPCl_3$ and $OP(SCH_3)_3$ – $OPCl_3$.

	SPS_3	$SPClS_2$	$SPCl_2S$	$SPCl_3$	Δk (%)
k(P–SCH_3)	2.56	2.40	2.38		– 7
k(P–Cl)		2.36	2.45	2.66	+17
k(S–P)	4.16	4.40	4.60	4.89	+13
	OPS_3	$OPClS_2$	$OPCl_2S$	$OPCl_3$	
k(P–SCH_3)	2.71	2.93	3.28		+21
k(P–Cl)		2.66	2.75	3.00	+14
k(O–P)	8.71	9.23	9.68	10.24	+17
Δk(P–SCH_3) (%)	+6	+22	+38		
Δk(P–Cl) (%)		+13	+12	+12	

ingly low, and point to a distinct polar bonding component.

The only available example of tricoordinate phosphorus is the series $P(SCH_3)_3$ – PCl_3. As can be seen from Table 6, both force constants remain absolutely constant in this series. The same is found in the series PCl_3 – $P(OCH_3)_3$. The changes in both cases lie within the limits of error. Definite inductive effects are observed only in the series PCl_3 – PF_3, but they are generally smaller than for sp^3-hybridized phosphorus; p orbitals probably influence one another less than sp^3 orbitals. Other effects are probably also involved, since the P–SCH_3 force constants also exhibit anomalous behavior in the series $SP(SCH_3)_3$ – $SPCl_3$, if any importance is to be attached to variations of a few per cent.

Table 6. Force constants of the transition series $P(SCH_3)_3$ – PCl_3, PCl_3 – $P(OCH_3)_3$, and PCl_3 – PF_3.

	$P(SCH_3)_3$	$P(SCH_3)_2Cl$	$P(SCH_3)Cl_2$	PCl_3	Δk (%)
k(P–SCH_3)	2.06	2.03	2.04		–1
k(P–Cl)		2.36	2.32	2.36	±0
	PCl_3	$PCl_2(OCH_3)$	$PCl(OCH_3)_2$	$P(OCH_3)_3$	
k(P–Cl)	2.36	2.30	2.26		–4
k(P–OCH_3)		3.64	3.72	3.72	+2
	PCl_3	PCl_2F	$PClF_2$	PF_3	
k(P–Cl)	2.36	2.46	2.79		+19
k(P–F)		4.64	5.01	5.19	+12

Thus P–S force constants also depend on the electronegativity of the other bonding partners. Increasing electronegativity leads to increases of between 0 and 30% in the k values.

4. Effect of Ionic Charge

The force constants in $SP(SCH_3)_3$ and PS_4^{3-} are given in Table 2. Both species contain an sp^3-hybridized phosphorus atom, to which four sulfur atoms are attached; the main difference between them is the triple negative charge on the ion. k(S–P) in the anion is 2% lower even than k(P–SCH_3) in $SP(SCH_3)_3$, which has a value of 2.56. It would, however, be premature to conclude that the force constants are lowered by negative charge. Thus the change from $OP(OCH_3)_3$ to PO_4^{3-} is accompanied by a 10% increase in the force constant. The difference is probably due to very marked differences in the π-bonding components, as indicated by the bond orders (PS_4^{3-} 1.06, PO_4^{3-} 1.42).

We were again interested here by the changes resulting from the replacement of sulfur by the more electronegative oxygen. The force constants of the series PS_4^{3-} – PO_4^{3-} are given in Table 7. Comparison of these values with those in Table 3, which also refer to replacement of sulfur by oxygen, shows that while the directions of the changes are the same, they are smaller (14% as compared with 28%).

Table 7. Force constants of the transition series PS_4^{3-} – PO_4^{3-}.

	PS_4^{3-}	PS_3O^{3-}	$PS_2O_2^{3-}$	PSO_3^{3-}	PO_4^{3-}	Δk(%)
k(P–S)	2.51	2.60	2.60	2.86		+14
k(P–O)		6.03	6.11	5.84	6.20	+ 3

A question that arises in connection with these ions is whether the negative charges are located preferentially on the oxygen or (less likely) on the sulfur, or are uniformly distributed over the two types of atoms. In the first case the P–S bond in PSO_3^{3-} would be expected to exhibit a strong double-bond effect, *i.e.* to show a considerable increase in the S–P force constant (the same applying to the P–O constant in PS_3O^{3-} in the second case). These changes should be distinct even in $PS_2O_2^{3-}$. Since the force constants remain practically unchanged over the entire series, it can be concluded that the charges are fairly uniformly distributed over all four atoms.

The maximum effect of the ionic charge on the P–S force constant is probably of the order of 12%. Because of the small number of examples available, no general statement can be made about this effect, since it is probably also combined with π-bonding effects.

5. Effect of π Bonding

Compounds of the type $S-PX_3$ are particularly suitable for the investigation of this problem. In $S-P-(SCH_3)_3$, k(S–P) is greater than k(P–SCH_3) by 63% (Table 2). This difference is greater than any of the other force-constant differences discussed so far. Like the O–P bond in $O-PX_3$, the S–P bond must be assumed to have an appreciable π component. This conclusion was reached some time ago on the basis of the vibration spectra [6] and the interatomic distances [7]

[6] *H. Gerding, H. v. Brederode,* and *H. C. J. de Decker,* Recueil Trav. chim. Pays-Bas *61,* 19 (1942); *64,* 183, 191 (1945); *67,* 677 (1948); *H. Gerding* and *P. C. Nobel, ibid. 76,* 757 (1957); *A. R. Pitochelli* and *L. F. Audrieth,* J. Amer. chem. Soc. *81,* 4458 (1959); *A. Müller, H. Krebs, E. Niecke,* and *A. Ruoff,* Ber. Bunsenges. physik. Chem. *71,* 571 (1967).

[7] *A. Vos* and *E. H. Wiebenga,* Acta crystallogr. *8,* 217 (1955); *9,* 92 (1956); *S. van Houten* and *E. H. Wiebenga, ibid. 10,* 156 (1957); *Y. C. Leung* and *J. Waser, ibid. 10,* 574 (1957); *D. A. Wright* and *P. R. Penfold, ibid. 12,* 455 (1959).

Table 8. Stretching frequencies and force constants of $O-PX_3$ and $S-PX_3$.

	νPO (cm^{-1})	k(PO) (mdyne/Å)	% $k(OPF_3)$		νPS (cm^{-1})	k(PS) (mdyne/Å)	% $k(SPF_3)$
OPF_3	1395	11.89	100	SPF_3	695	5.21	100
$OPCl_3$	1290	10.24	86	$SPCl_3$	752	4.89	94
$OP(OCH_3)_3$	1283	9.83	82	$SP(OCH_3)_3$	620	4.52	87
$OPBr_3$	1261	9.74	82	$SPBr_3$	726	4.69	90
$OP(CH_3)_3$	1228	9.14	77	$SP(CH_3)_3$	567	3.33	64
$OP[N(CH_3)_2]_3$	1210	8.80	74	$SP[N(CH_3)_2]_3$	563	3.86	74
$OP(SCH_3)_3$	1202	8.71	73	$SP(SCH_3)_3$	700	4.16	80

in phosphorus-sulfur compounds. Calculation of the bond orders for the two force constants in $S-P-(SCH_3)$ by *Siebert*'s method[4] gives 1.16 (close to a single bond) for $P-SCH_3$ and 1.57, which is considerably higher than the value for a single bond, for S–P. The compound is in a state that lies between the two canonical structures:



Numerous investigations on the analogous oxygen compounds had shown that the frequency of the $O=P<$ vibration and the corresponding force constant decrease with decreasing electronegativity x of the other bonding partners[8]. Since a similar effect was also to be expected for the SP bond, a large number of compounds of this type were synthesized and examined spectroscopically, so that many SP force constants are available for discussion.

The stretching frequencies and force constants of some OPX_3 and SPX_3 molecules are compared in Table 8. The order found from the OP frequencies and force constants is retained in this table for the corresponding sulfur compounds. It must first be pointed out that the frequencies and force constants for the oxygen compounds show parallel variations; the above-mentioned dependence on electronegativity is found only to a rough approximation. The sulfur compounds, on the other hand, exhibit rather confusing behavior. Whereas the SP force constants again follow roughly the same order as for the oxygen compounds, the SP stretching frequencies follow no recognizable pattern. The low values of the frequency and force constant for $SP[N(CH_3)_2]_3$ and $SP(CH_3)_3$ are particularly interesting. Thus there is no simple dependence of the force constant on the electronegativity of the other bonding partners; the present general investigation gives a maximum change in the SP force constants of about 35%. The variations are similar in magnitude to those attributed to inductive effects (Section 3), and are also comparable with those of the OP force constants.

The unexpected behavior of the SP stretching vibrations is due to strong coupling with the other stretching vibrations of the molecule. In contrast to the OP vibration, which is situated well outside the range of the other stretching vibrations, and which may therefore be regarded as characteristic, the SP vibration lies in the middle of this range. In the case of the light bonding partners (F, OCH_3, $N(CH_3)_2$, CH_3) the $\nu_s PX_3$ vibrations which couple strongly with the νSP, are situated at higher frequencies and so displace νSP to lower frequencies (563–695 cm^{-1}). For the heavier partners Cl, SCH_3, and Br, the $\nu_s PX_3$ lie below νSP and displace νSP to higher frequencies (700–752 cm^{-1}). This coupling can, however, be largely compensated in the force constant calculation, as is shown by the results in Table 8, and the further discussion.

Figure 1 shows a plot of all the calculated SP force constants against the sum of the electronegativities of all three partners, the Pauling values being used for the atoms bonded directly to the phosphorus. Examination of the values for all the compounds SPX_3 now

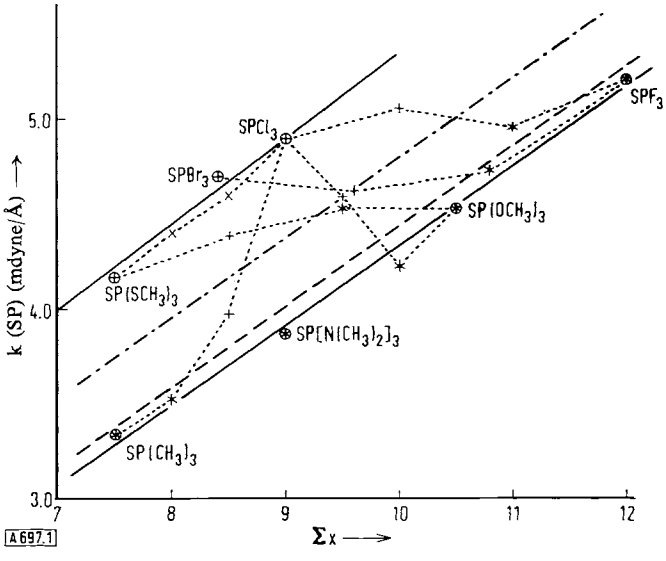


Fig. 1. SP force constants of compounds of the type $SP(X, Y)_3$ plotted against the sum of the Pauling electronegativities of the three other bonding partners.

⊛ : Three bonding partners from the first short period.

✳ : Two bonding partners from the first short period, and one from higher periods.

\+ : One bonding partner from the first short period, and two from higher periods.

⊕, × : Three bonding partners from higher periods.

reveals a remarkable effect: All the SP force constants for the compounds with the light atoms of the first short period lie on one straight line, and the values for compounds with the heavier atoms, including bromine, lie on another. The slopes of the two lines are roughly equal, indicating that the dependences of the S–P force constants on the electronegativity are the same. This result suggests that the procedure used to calculate the force constants cannot cope with the strong coupling

[8] *J. V. Bell, J. Heisler, H. Tannenbaum,* and *J. Goldenson,* J. Amer. chem. Soc. *76* 5185 (1954); *L. W. Daasch* Spectrochim. Acta *13,* 257 (1958); *L. C. Thomas* and *R. A. Chittenden* Spectrochim. Acta *20* 467 489 (1964).

of the SP vibration with the PX_3 vibrations, so that the observed discrepancy is due to the method of calculation. It must, however, be mentioned that the distance between the two straight lines is almost 1 mdyne/Å, corresponding to deviations that normally lie well outside the limit of error of the calculation process. Another possibility is that elements of the higher periods have a special effect on the SP force constant.

Further information is provided by compounds with mixed substituents of the type SPX_2Y or $SPXY_2$. A total of six series of this nature have so far been examined spectroscopically. One of these series, $SPCl_3$ – $SP(SCH_3)_3$, leads from heavy to heavy partner atoms. The k(SP) values for this series lie surprisingly close to the straight line for compounds with heavy atoms (cf. Table 5 and Fig. 1). The five other transitions lead from light to heavy partner atoms. If the dependence on electronegativity is assumed to be the same for the compounds with mixed substituents as for compounds containing only light or only heavy partner atoms, we obtain the average lines (---) for SP force constants with two light atoms and one heavy one and (–·–·) with two heavy atoms and one light one. The mean deviation from these average lines is ±0.15 mdyne/Å (≈4%), and so lies within the limit of error of the method. If these deviations were due to the calculation method, both types of compounds with mixed substituents should give approximately equal deviations midway between the two limiting lines. However, the nature of the deviations shows a pronounced dependence on the number of heavy atoms. The first heavy atom introduced leads to an average increase of 0.10 mdyne/Å, the next 0.37, and the third 0.50, giving a total increase of almost 1.0 mdyne/Å (20%). Thus elements from higher periods, which possess d electrons, more strongly favor the double bond form with $d\pi-p\pi$ interaction. It should be mentioned that the same effect is observed in the OP compounds. This indicates that there has been no failure of the calculation method.

Our examination shows a very strong dependence of the SP force constant on the electronegativity of the neighboring atoms. The values found lie between 5.21 (SPF_3) and 3.33 mdyne/Å ($SP(CH_3)_3$). The bond orders as found from these values by *Siebert*'s method lie between 1.89 and 1.33, while values between 2.44 and 1.88 are obtained for the OP bond orders. This comparison alone shows the very much smaller tendency toward double bond formation with the pair of elements phosphorus and sulfur. If the results are considered in conjunction with the rules given earlier (cf. Section 1), the limit given for the electronegativity sum is confirmed, since even in the most favorable case, a bond order of only 1.89 is obtained for S–P. This still corresponds to a very much higher double bond component than that found for the grouping Si–N. This is an excellent illustration of the strong influence of the electronegativity difference: ΔxSP = 0.4, ΔxSiN = 1.2. Thus SiN is well outside the limiting range for double bonds with respect to the sum and difference of the electronegativities, whereas SP is very close to this range.

6. Summary

P–S force constants of between 2.06 and 5.21 mdyne/Å are found for many phosphorus-sulfur compounds. The differences can be traced to four factors, which have been demonstrated separately in examples. The changes (maximum 40%) that accompany changes in hybridization are due to differences in the s components of the bonds, the force constant decreasing with decreasing s component. The other bonding partners also have a distinct influence on the force constant. In the case of tetracoordinate phosphorus, an increase in the electronegativity of the partners leads to a distinct increase (up to 30%) in the k(P–S) values. Practically no effect is observed with tricoordinate phosphorus. The force constant of the phosphorus-sulfur bond is decreased by transition from neutral molecules to negatively charged ions. Finally, it was found for many compounds of the type $S-PX_3$ that this bond exhibits partial double-bond character, which depends on the electronegativity of the other bonding partners. Thus the bond order in SPF_3 is 1.9, while that in $SP(CH_3)_3$ is 1.3. Bonding partners with d electrons also have an appreciable strengthening effect, as has also been found for the O=P bond.

I am grateful to the Deutsche Forschungsgemeinschaft and the Bundesministerium für wissenschaftliche Forschung for provision of the spectrographs, and to the Fonds der Chemischen Industrie for financial support of the work. Thanks are also due to Dr. Fritzowsky, Dr. Köttgen, Dr. Ombarek, Dr. Pohl, and Dipl.-Chem. Pulay for the preparation and spectroscopic examination of the compounds discussed and to Dr. Blaich, Dipl.-Chem. Lentz, Dipl.-Chem. Pulay, Dr. Sawodny, and Dr. Sirag Eldin for the calculation of the force constants.

Received: January 3, 1969 [A 697 IE]
German version: Angew. Chem. *81*, 343 (1969)
Translated by Express Translation Service, London

Excimers

By Th. Förster [*]

Dedicated to Professor H. Bredereck on the occasion of his 65th birthday

Excimers are molecular associates that exist only in excited electronic states. They are therefore detectable only in emission spectra, and particularly in fluorescence spectra. Despite their short lifetimes, they are responsible for many photophysical and photochemical effects.

1. Introduction

The concentration quenching of fluorescence is a phenomenon that has been known for a long time. It was discovered only recently, on the other hand, that instead of quenching, many fluorescent organic compounds exhibit a change in the fluorescence spectrum, *i.e.* a new component becomes evident in such a spectrum with increasing concentration. Since no corresponding change is observed in the absorption spectrum, the new fluorescence component must be ascribed to an associate formed only *after* absorption of light in the electronically excited state [1]. The term "excimers" has become widely accepted for associates of this type [2].

The fluorescent properties of crystals of many organic compounds and of macromolecular substances are due to excimers, as are the properties of some liquid scintillator systems. Excimers have also been detected as intermediates in many photochemical reactions, and it may be assumed that they are also involved in analogous radiochemical processes. An attempt will be made in this article to present a brief survey of existing knowledge in this field [3].

2. Excimer Formation of Pyrene in Solution

The role of the association of excited molecules as the cause of a change in the fluorescence spectrum with concentration was first recognized by us in the case of pyrene and some of its derivatives [4]; and the formation of excimers is still most easily demonstrated for pyrene.

Spectra of (oxygen-free) solutions of this compound at various concentrations in *n*-heptane at room temperature are shown in Figure 1. The structured spectrum observed at concentrations of 5×10^{-5} M and less is the fluorescence spectrum

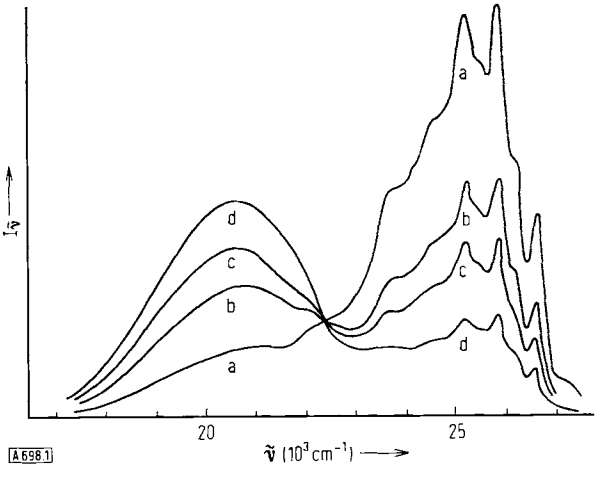


Fig. 1. Fluorescence spectra of pyrene in *n*-heptane. $t = 20$ °C, c (mole/l): 5×10^{-5} (a), 1.8×10^{-4} (b), 3.1×10^{-4} (c), 7.0×10^{-4} (d).

of monomeric pyrene, which extends from the UV to the violet region of the visible spectrum. An additional unstructured component appears at higher concentrations in the blue region, *i.e.* at longer wavelengths, and this component ultimately becomes the only one present. If, as in this example, the spectra are recorded for the same absorption of the exciting light, all the curves intersect at a single point. Such an "isoemissive" or "isostilbic" point [5] of an emission spectrum occurs if the spectrum consists of contributions due to only two components. It corresponds to the isosbestic point of an absorption spectrum, though the latter remains unchanged in the present case over the entire concentration range in which the fluorescence change occurs. Because of this validity of the Beer-Lambert law, as well as other observations, the blue fluorescence component is attributed to an associate that exists only in the excited electronic state, *i.e.* to an excimer. The absorption and fluorescence spectra of oxygen-free pyrene solutions remain unchanged on prolonged irradiation, and no stable photoproduct can be detected.

The mechanism of excimer formation can be deduced from the quantitative course of the fluorescence

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[1] *Th. Förster* and *K. Kasper*, Z. physik. Chem. N.F. *1*, 275 (1954).

[2] *B. Stevens* and *E. Hutton*, Nature (London) *186*, 1045 (1960). The term "excimer" should refer generally to electronically excited molecules whose physical and chemical properties differ appreciably from those of the same molecules in the ground state. However, the name has become commonly used for excited molecular associates, particularly dimers.

[3] Cf. *R. M. Hochstrasser*, Annu. Rev. physic. Chem. *17*, 466 (1966).

[4] *Th. Förster* and *K. Kasper*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *59*, 976 (1955).

[5] From στίλβειν: shine. I am grateful to Dr. *H. E. A. Kramer*, Stuttgart, for this suggestion.

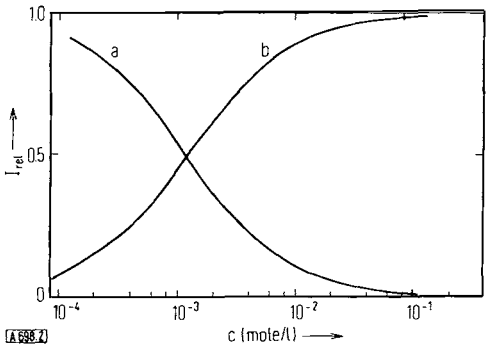
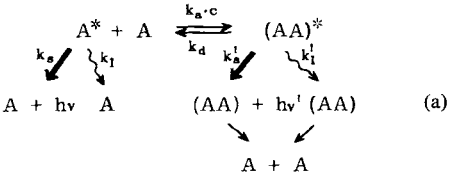


Fig. 2. Relative intensities of monomer component (a) and excimer component (b) of the fluorescence of pyrene in benzene. t = 20 °C. Half-value concentration $c_h = 1.2 \times 10^{-3}$ mole/l.

change. The concentration dependence of the intensities of the two fluorescence components for equal absorption is shown in Figure 2 for pyrene in benzene. The slopes of the curves correspond to a bimolecular mechanism for the formation of the excimer by combination of an electronically excited molecule A* (in the lowest excited singlet state) with an unexcited molecule A (in the singlet ground state). Together with the processes of fluorescence emission, the radiationless deactivation of the excited monomer and of the excimer, and the dissociation of the excimer to be discussed later, this leads to the following reaction scheme [4,6]:



⟶ : Normal ("adiabatic") reaction processes without alteration of existing excitation.
▬▶ : Radiation processes.
〰▶ : Radiationless ("diabatic") deactivation processes.

According to reaction scheme (a), the concentration dependences of the fluorescence quantum yields η and η' of the monomeric and excimeric components are

$$\eta = \eta_{max} / \left(1 + \frac{c}{c_h}\right) \quad (1) \qquad \eta' = \eta'_{max} / \left(1 + \frac{c}{c_h}\right) \quad (1')$$

i.e. a Stern-Volmer equation (1) for the monomer component and a corresponding inverse relation (1') for the excimer component. η_{max} and η'_{max} are the maximum quantum yields of the two components for very low and very high concentrations, respectively, and c_h is the half-value concentration which is common to both relations.

The relative quantum yields are identical with the relative intensities in Fig. 2. Their concentration dependences agree with equations (1) and (1'), the half-value concentration being $c_h = 1.2 \times 10^{-3}$ mole/l. The ratio of the quantum yields becomes

$$\frac{\eta'}{\eta} = \frac{\eta'_{max}}{\eta_{max} c_h} c \quad (2)$$

[6] *E. Döller* and *Th. Förster*, Z. physik. Chem. N.F. *34*, 132 (1962).

and thus increases in proportion to the concentration. Provided that the dissociation of the excimers can be ignored ($k_d = 0$), the quantities occurring in equations (1) to (2) are

$$\eta_{max} = \frac{k_s}{k_s + k_1} \quad (3) \qquad \eta'_{max} = \frac{k'_s}{k'_s + k'} \quad (3')$$

$$c_h = \frac{k_s + k_1}{k_a} \quad (4)$$

For $k_d = 0$, the decay of the monomer emission is purely exponential, with an average decay time $\tau = 1/(k_s + k_1 + k_a c)$. The excimer emission, on the other hand, follows a complicated bi-exponential course passing through a maximum, such as is also found in the formally analogous case of secondary products of a radioactive decay series.

The first confirmation of a time dependence of this type was provided by the different and concentration-dependent quenching of the two fluorescence components by oxygen [4,7]. *Birks, Dyson,* and *Munro* later managed to follow the emission from both components directly on flash-excitation [8]. The curves given in Figure 3 for pyrene in cyclohexane at a concentration slightly above the half-value concentration confirm the expected time characteristics.

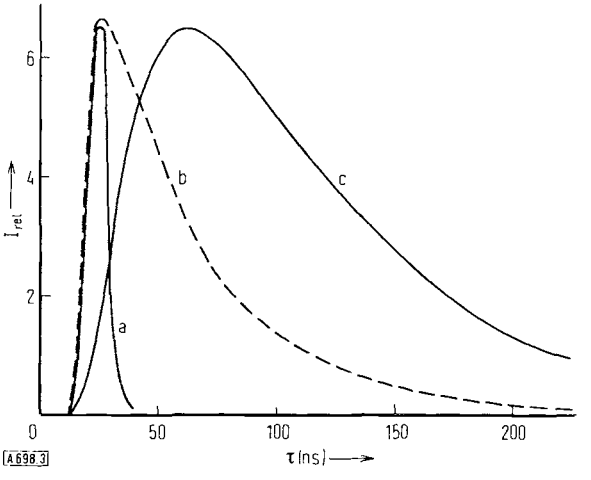


Fig. 3. Time dependence of excitation (a), monomer component (b), and excimer component (c) of pyrene in cyclohexane. $c = 5 \times 10^{-3}$ mole/l [8].

The association reaction that takes place during the brief excitation of the monomer has to be very fast, and hence diffusion-controlled. Both k_a and c_h should therefore depend on the viscosity of the solvent. The half-value concentrations measured in various inert solvents (aliphatic and aromatic hydrocarbons, alcohols) do in fact increase with increasing viscosity, though the strict proportionality expected from eq. (4) is not observed. This is due to the thermal dissociation of the excimers, which has not yet been taken into account.

This is obvious from the temperature dependences of the two fluorescence components, which are shown in Figure 4 for pyrene in liquid paraffin at a medium

[7] *K. Kasper*, Z. physik. Chem. N.F. *12*, 52 (1957).

[8] *J. B. Birks, D. J. Dyson,* and *I. H. Munro*, Proc. Roy. Soc. (London) *A 275*, 575 (1963).

concentration [6]. The opposing intensity variations of the two components above and below 80 °C are due to the fact that the formation of the excimer predominates at low temperatures, while its dissociation with reformation of the excited monomer predominates at high temperatures. This process is indicated in scheme (a), where it has been assigned the rate constant k_d. When it is taken into account, equations (1) to (3′) remain unchanged, but eq. (4) is replaced by the more general expression for the half-value concentration:

$$c_h = \frac{k_s + k_1}{k_a}\left(1 + \frac{k_d}{k_s' + k_1'}\right) \qquad (4')$$

If dissociation predominates ($k_d \gg k_s' + k_1'$), the half-value concentration no longer depends on k_a, alone, but on the ratio k_d/k_a; it is then determined by the excimer dissociation *equilibrium*, and is independent of the viscosity of the solvent.

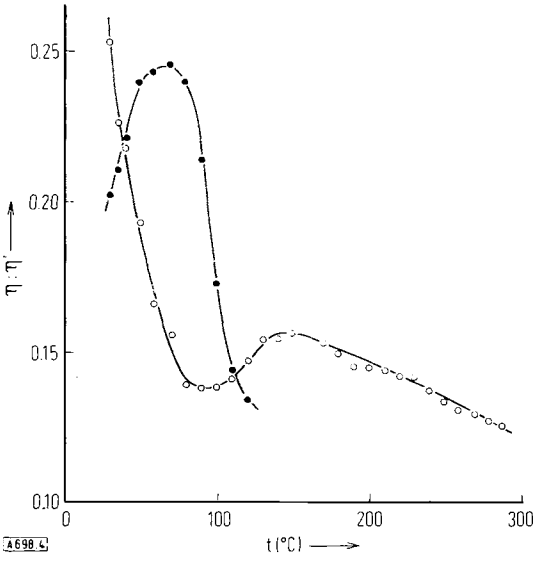


Fig. 4. Temperature dependence of the fluorescence of pyrene in liquid paraffin. $c = 5 \times 10^{-3}$ mole/l [6].
○: quantum yield of the monomer component, ●: of the excimer component.

If dissociation is appreciable, some of the excited monomers pass through the excimer stage, so that the decay of the monomeric component is no longer exponential. As dissociation equilibrium is approached the difference in the time dependences of the two components disappears [8a].

Figure 5 shows the temperature dependence of the half-value concentrations of pyrene in various inert solvents [9]. In the high temperature range (left), c_h increases with rising temperature and is practically independent of the nature of the solvent; in this range the excimer dissociation equilibrium is established. At lower temperatures c_h becomes diffusion-controlled, and increases with solvent viscosity.

These temperature functions can be used to find the kinetic and thermodynamic parameters of excimer formation. The most interesting quantity is the *enthalpy* of dissociation of the excimer, for which

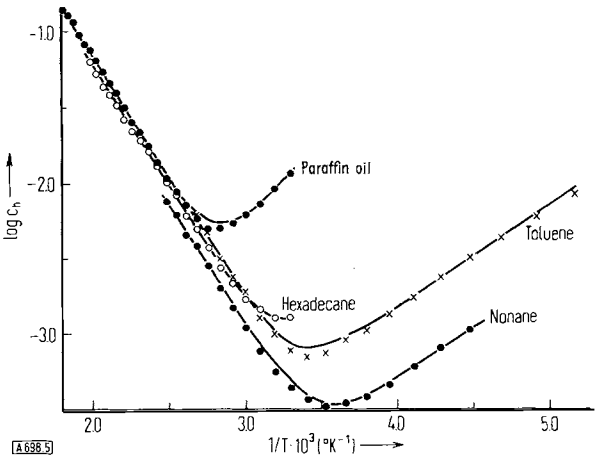


Fig. 5. Temperature dependence of the half-value concentration for the change in the fluorescence spectrum of pyrene with concentration [9].

values between 10 and 11 kcal/mole have been found in various solvents [6, 10]. With the aid of the fluorescence decay time, the *entropy* of dissociation of the excimer (based on unit concentrations) is found to be about 20 cal/deg·mole. These values indicate strong bonding and a rigid configuration for the excimer of pyrene.

3. Excimer Formation of other Aromatic Compounds

Following the discovery of excimer formation for pyrene (1954), it seemed that the ability to form excimers was confined to this hydrocarbon and a few of its derivatives such as 3-chloropyrene and the related benzo[*b*]pyrene, whose fluorescence change had already been observed by *Bandow* [11], but (as later by other authors [12]) had been attributed to ground state association. A weak excimer component was also found for some 9-alkylanthracenes [13], though not for anthracene itself. Another one was detected by *Berlman* for 2,5-diphenyloxazole and attributed to excimers [14].

Since 1962, changes in fluorescence spectra with concentration have also been observed (though only at lower temperatures or considerably higher concentrations than in the case of pyrene) for many aromatic compounds, *e.g.* benzene [15], naphthalene [16, 17], benz[*a*]anthracene [18, 19], perylene [19], anthanthrene [19],

[8a] *R. Speed* and *B. Selinger*, Austral. J. Chem. *22*, 9 1969).

[9] *Th. Förster* and *H. P. Seidel*, Z. physik. Chem. N.F. *45*, 58 (1965).

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[11] *F. Bandow*, Z. physik. Chem. *196*, 329 (1951).

[12] *N. O. Berg* and *G. Nordén*, Acta pathol. microbiol. scand. *36*, 193 (1955).

[13] *G. A. Tischenko*, *B. Ya. Sveshnikov*, and *A. S. Cherkasov*, Optika i Spektroskopija *4*, 631 (1958).

[14] *I. B. Berlman*, J. chem. Physics *34*, 1083 (1961).

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[16] *E. Döller* and *Th. Förster*, Z. physik. Chem. N.F. *31*, 274 (1962).

[17] *I. B. Berlman* and *A. Weinreb*, Molecular Physics *5*, 313 (1962).

[18] *J. B. Birks* and *L. G. Christophorou*, Nature (London) *194*, 442 (1962).

[19] *J. B. Birks* and *L. G. Christophorou*, Proc. Roy. Soc. (London), *A 274*, 552 (1963).

and a large number of derivatives [20–26], including substituted anthracenes [26a,b]. Anthracene itself does not give a fluorescence change, but exhibits concentration quenching; this is also due to the formation of an excimer, which does not however emit, but undergoes transformation into the stable dianthracene (cf. Section 11). *Birks* and *Christophorou* [22] have collected data on excimer formation of many aromatic compounds.

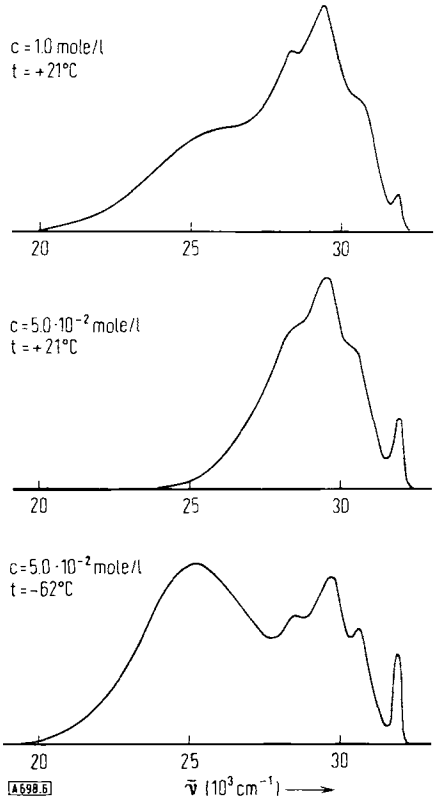


Fig. 6. Fluorescence spectra of naphthalene in toluene at various temperatures and concentrations [16].

As an example, Figure 6 shows the fluorescence spectra of naphthalene in toluene [16]. The excimer component is barely visible at room temperature even at very high concentrations, and emerges only at low temperatures. Domination of excimer fluorescence similar to that found in moderately concentrated pyrene solutions is observed only for a few liquid methylnaphthalenes [27–29].

The conditions for the occurrence of excimer fluorescence in the cases discovered later show that such excimers are less tightly bound, and that excimer dissociation occurs even below room temperature. Accordingly, the dissociation enthalpies are low, *e.g.* 5–6 kcal/mole for benzene [23] and for naphthalene [24,30,31]; alkyl substituents, which should sterically hinder excimer formation, reduce these values further. The dissociation entropies, on the other hand, are similar in magnitude to that of the pyrene excimer ($\approx$ 20 cal/deg·mole).

Despite the difference in the dissociation energies, the differences between the fluorescence maxima of the monomer and the excimer are almost as large in these cases as for pyrene, *i.e.* about 6000 cm^{-1}, which corresponds to an energy difference of 17 kcal/mole, and thus exceeds the dissociation energy of the pyrene excimer, and even more so than those of other aromatic excimers.

Figure 7 shows the potential-energy diagram, after *Stevens* and *Ban* [30], for a sandwich configuration of the excimer resulting from the mutual approach of the two components with their molecular planes parallel. According to this diagram the ground state of the excimer is *unstable*. This explains not only the diffuse character of excimer fluorescence, but also the failure of all attempts to find a corresponding component in the absorption spectrum without additional fixation of the excimer components.

The time characteristics of fluorescence have been studied for naphthalene [32], benz[*a*]anthracene [21],

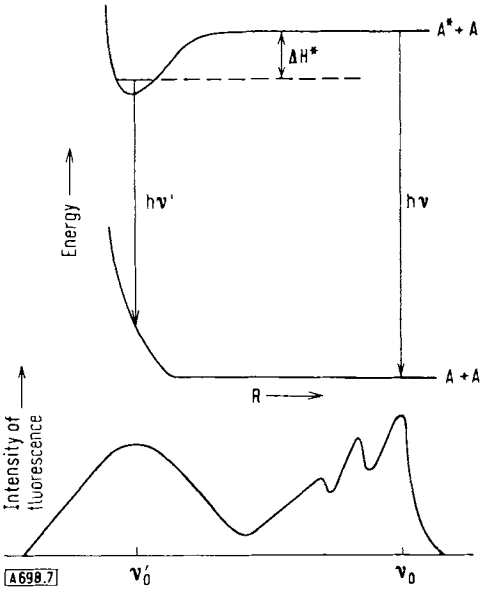


Fig. 7. Potential energy diagram for the formation of the excimer. R = distance between the molecular planes.

[20] *J. B. Birks* and *L. G. Christophorou*, Spectrochim. Acta *19*, 401 (1963).

[21] *J. B. Birks*, *D. J. Dyson*, and *T. A. King*, Proc. Roy. Soc. (London) *A 277*, 270 (1964).

[22] *J. B. Birks* and *L. G. Christophorou*, Proc. Roy. Soc. (London) *A 277*, 571 (1964).

[23] *J. B. Birks*, *C. L. Braga*, and *M. D. Lumb*, Proc. Roy. Soc. (London) *A 283*, 83 (1965).

[24] *J. B. Aladekomo* and *J. B. Birks*, Proc. Roy. Soc. (London) *A 284*, 551 (1965).

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[26] *S. S. Lehrer* and *G. D. Fasman*, J. Amer. chem. Soc. *87*, 4687 (1965).

[26a] *N. S. Bazilevskaya* and *A. S. Cherkasov*, Optika i Spektroskopija *18*, 58, 145 (1965); Optics and Spectroscopy *18*, 30, 77 (1965).

[26b] *J. B. Birks* and *R. L. Barnes*, Proc. Roy. Soc. (London) *A 291*, 556, 570 (1966).

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and derivatives of these compounds [33]. In the case of naphthalene, excimer dissociation attains complete equilibrium, and the same purely exponential decay is observed for both components.

4. Further Investigations on Excimers in Solution

In the equilibrium case, the change in the fluorescence spectra with concentration is controlled by the equilibrium of excimer formation; the dissociation enthalpy of the excimer can be found from the temperature dependence of this equilibrium. Similarly, the volume expansion connected with dissociation, or its negative, the volume contraction, occurring on formation of the excimer from the monomers, should be obtainable from the pressure dependence of the effect.

The fluorescence properties of aromatic compounds in solution depend on pressure even in the absence of any molecular association, but appreciable variations occur only at pressures above 10 kbar. The intensity ratios of the monomer and excimer components, on the other hand, vary at much lower pressures. The direction of this variation depends on whether excimer formation is diffusion- or equilibrium-controlled [34,35]. In the former case, *e.g.* for pyrene below room temperature, the excimer component is found to decrease, but this is merely due to the pressure-induced increase in solvent viscosity. On the other hand, for naphthalene and other compounds where the dissociation equilibrium is established, the excimer component increases with pressure [36] (cf. Fig. 8).

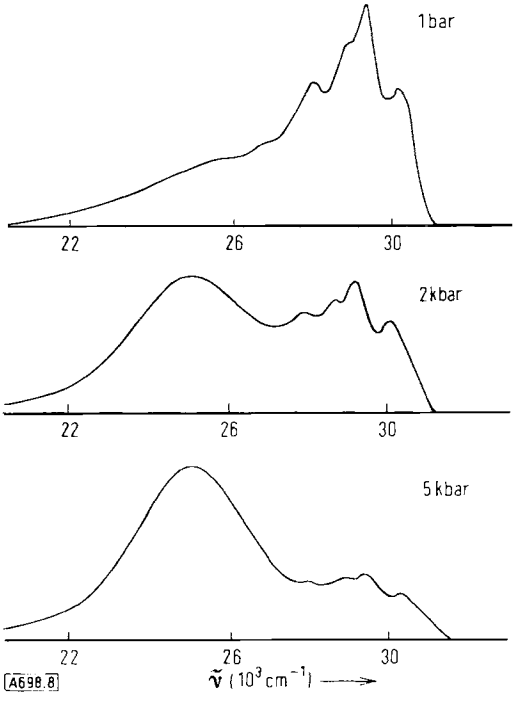


Fig. 8. Fluorescence spectrum of 1,6-dimethylnaphthalene in *n*-heptane at various pressures. t = 20 °C; c = 0.32 mole/l [30].

The pressure dependences of naphthalene-excimer formation in a series of different solvents gave almost identical values of 16 cm³/mole for the volume contraction. This contraction is considerable if compared to twice the molar volume of naphthalene in the crystalline state (224 cm³/mole). If a sandwich structure is assumed, the distance between the two molecular planes in the excimer can be estimated from the volume contraction to be about 3.0 Å [36].

Aromatic hydrocarbons can be solubilized in water by suitable detergents; they solve in the lipid phase, which has a well defined micelle structure under suitable conditions. In such solutions of aromatic hydrocarbons, the extent of excimer formation should be governed, not by the overall concentration of the aromatic compound in the solution, but by its local concentration in the lipid phase. It is in fact found that 2-methylnaphthalene, whose fluorescence change in homogeneous solutions corresponds to a half-value concentration of about 1 mole/l, has a similar value with cetyldimethylbenzylammonium chloride as the detergent [37]; on the other hand, pyrene in the same system has a half-value concentration of 2.6×10^{-2} mole/l, which is greater by a factor of 20 than that in a comparable homogeneous solution. This deviation is due to the size of the micelles, which must contain at least two molecules of the aromatic compound if the excimer is to be formed. Estimation of the micelle size on this basis leads to values similar to those found by the usual methods.

5. Intramolecular Excimers

Larger molecules in which two or more aromatic residues are flexibly linked to each other by aliphatic carbon atoms should be capable of forming intramolecular excimers, and their fluorescence spectra should contain an excimer component that is independent of concentration. According to *Hirayama* [38], this is the case with di- and triphenylalkanes whose phenyl groups are joined by aliphatic chains containing exactly *three* carbon atoms. The fluorescence spectra of two such compounds are shown in Figure 9; the intensity ratios of the two components in these cases depend on the solvent, but not on the concentration. Their absorption spectra are normal and resemble those of ethylbenzene or of diphenylalkanes with shorter or longer connecting methylene chains that are incapable of excimer formation because of steric or statistical factors. Solutions of polystyrene and of polyvinylnaphthalene, in which the aryl groups are again linked by aliphatic chains of three carbon atoms, give fluorescence spectra containing both monomer and excimer components at room temperature [39]. At 77 °K, polystyrene shows only the monomer component, probably owing to an activation barrier to the formation of the excimer.

[33] *J. B. Birks* and *T. A. King*, Proc. Roy. Soc. (London) *A 291*, 244 (1966); *N. S. Bazilevskaya, L. A. Limareva, A. S. Cherkasov*, and *V. I. Shirokov*, Optika i Spektroskopija *18*, 354 (1965); Optics and Spectroscopy *18*, 202 (1965).

[34] *Th. Förster, C. O. Leiber, H. P. Seidel*, and *A. Weller*, Z. physik. Chem. N.F. *39*, 265 (1963).

[35] *H. P. Seidel* and *B. K. Selinger*, Austral. J. Chem. *18*, 977 (1965).

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[37] *Th. Förster* and *B. Selinger*, Z. Naturforsch. *19a*, 38 (1964).

[38] *F. Hirayama*, J. chem. Physics *42*, 3163 (1965).

[39] *M. T. Vala, J. Haebig*, and *St. A. Rice*, J. chem. Physics *43*, 886 (1965).

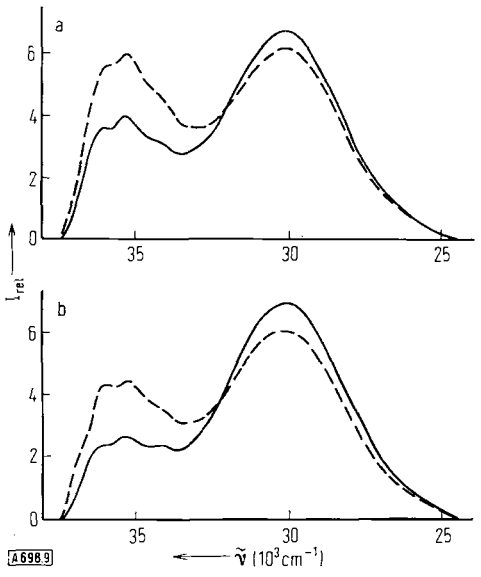


Fig. 9. Fluorescence spectra of 1,3-diphenylpropane (a) and 1,3,3-triphenylpentane (b) in cyclohexane (——) and 1,4-dioxane (---) [38].

Nucleic acids and synthetic di- and polynucleotides also exhibit excimer fluorescence, though their absorption spectra are monomolecular [40].

In paracyclophanes, two phenyl groups are linked by methylene chains in the *p,p'* position [39,41,42]. The fluorescence spectrum of [4,4]-paracyclophane (in solution at room temperature) shows only the excimer component, while those of [4,5]- and [6,6]-paracyclophanes contain practically no excimer component; all these compounds have normal absorption spectra. [2,2]-Paracyclophane exhibits pure excimer fluorescence, but its absorption spectrum is also different from those of its homologs. In this case it appears that even in the unexcited state, the distance between the two phenyl groups is appreciably shorter than that of closest approach between freely mobile groups.

6. Excimer Fluorescence in Crystals and Stable Aggregates

The fluorescence of crystalline pyrene is blue and structureless, and its maximum (4600 Å) hardly differs from that of the long-wave component in solution (4760–4780 Å). This fluorescence is also due to excimers. In this connection, *Ferguson* [43] recalled attention to the fact that in the crystal lattice of pyrene, the molecules are arranged in parallel pairs with an interplanar distance of 3.53 Å [44]. According to *Stevens* [45] a general relationship exists between fluorescence and the crystal structure of aromatic compounds. Naphthalene, anthracene, phenanthrene, and other "elongated" molecules favor structures of an A type, in which adjacent molecules are oriented almost perpendicular to one another. The fluorescence spectra of such crystals are not very different from those of dilute solutions, and may be regarded as monomer spectra. "Disk-shaped molecules", on the other hand, favor structures of a B type, in which the molecules are either arranged in *pairs*, as in pyrene, benzo[*g,h,i*]perylene, and perylene (α-form), or *stacked* in columns in the crystal lattice, as in perylene (β-form), coronene, ovalene, and benzo[*b*]pyrene (monoclinic form). Excimer fluorescence occurs only in crystals of the B type, in whose lattices adjacent molecules have an arrangement similar to that in the excimer. Nevertheless, this arrangement is by no means the same, as is shown by the absorption spectra of type B crystals, which (apart from a slight Davydov splitting) are very similar to the solution spectra. Thus here too the excimer configuration is achieved only after light absorption, with further approach of two molecules that were already adjacent. The observation that α-perylene no longer exhibits excimer fluorescence at very low temperatures [46] could be explained by a freezing of this configuration change.

The monomer fluorescence exhibited by many crystalline aromatic compounds in agreement with their lattice type changes at high pressures (10 to 50 kbar) into a structureless band at a longer wavelength. This has been observed for crystals of naphthalene [47–49], anthracene [48–50], phenanthrene [49], benz[*a*]anthracene [50], chrysene [50], and naphthacene [51]. The structureless band is generally interpreted as excimer fluorescence, though the red shift in relation to the monomer emission is not always as large as in solution. In the case of pyrene [52] and α-perylene crystals [53], which exhibit excimer fluorescence even at normal pressure, this fluorescence shifts to still longer wavelengths as the pressure is increased.

Many observations suggest that the excimer fluorescence is emitted preferentially by lattice defects, which act as traps and capture the initially delocalized excitation energy. In addition to their excimer fluorescence, microcrystals of pyrene exhibit a weak monomer component, which is attributed to surface defects [54]. For crystals that give excimer emission only at high pressures, the fluorescence change is frequently irreversible, so that after return to normal pressure the spectrum still has an excimer component, which disappears only after a relatively long time or on annealing. The degree of reversibility seems to depend both on the size of the crystal and on the irradiation at

[40] *J. Eisinger, M. Guéron, R. G. Schulman,* and *T. Yamane,* Proc. nat. Acad. Sci. USA *55*, 1015 (1966).
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[45] *B. Stevens,* Spectrochim. Acta *18*, 439 (1962).
[46] *J. Tanaka,* Bull. chem. Soc. Japan *36*, 1237 (1963).
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[48] *P. F. Jones* and *M. Nicol,* J. chem. Physics *43*, 3759 (1965).
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[52] *H. W. Offen* and *R. R. Eliason,* J. chem. Physics *43*, 4096 (1965).
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high pressure [49]. An extreme case of a disordered lattice exists in solids having amorphous structures, which are obtained in the case of organic substances by condensation from the vapor at low temperatures. Films of anthracene prepared in this way at −70 °C exhibit excimer fluorescence, which changes into monomer fluorescence on crystallization [55, 56].

Excimer formation appears from these observations to concern parallel pairs of adjacent molecules within the crystal rather than the crystal as such. One should therefore also expect excimer fluorescence from *isolated* pairs of molecules having a similar configuration. According to *Ferguson*, such "sandwich dimers" can be produced from supercooled solutions of the aromatic compounds in vitreously solidifying solvents by controlled heating and recooling [57], and, in the case of anthracene and some of its derivatives, also by photolytic decomposition of the stable photodimers [58]. The controlled heating method yields sandwich dimers of pyrene [57] and perylene [59], whose absorption and fluorescence spectra differ considerably from those of the monomeric compounds, but are similar to those of the crystals. Obviously, these sandwich dimers too emit only after further approach of their components.

Sandwich dimers of 9- and 9,10-disubstituted anthracenes, which also give excimer fluorescence, have also been obtained by one or other of these methods [60,61]. The dimers of anthracene itself are particularly interesting. In agreement with its crystal type (A), anthracene gives only monomer fluorescence both in solution and in the crystalline state. Different dimers are obtained by controlled heating and by photolysis of dianthracene, the first resulting in monomer fluorescence and the second in excimer fluorescence [62]. It can be concluded from the absorption spectra that only the latter has a sandwich configuration, whereas the molecular planes in the other dimer are inclined at about 55° to each other. The sandwich dimer and the 55°-dimer also differ very markedly in their fluorescence decay times at 77 °K (≈ 200 and ≈ 10 ns respectively) [63]. It has been deduced from fluorescence decay times that deformed anthracene crystals contain lattice defects corresponding to the 55°-dimer [64].

7. Excimers from Triplet States or Free Radicals

The formation of excimers is not restricted to the combination of a singlet excited monomer with an unexcited monomer (Scheme (a)). They can also be formed *via* two monomers in metastable triplet states (denoted by (†) to distinguish them from singlet excited states (*)):

$$A^{\dagger} + A^{\dagger} \rightarrow (AA)^{*} \; [\rightleftarrows A^{*} + A] \qquad (b)$$

To produce a singlet excimer, the excitation energies of the two triplet molecules, which would not be sufficient alone, are added together.

An excimer formed in accordance with Scheme (b) should be evident in the spectrum of "delayed fluorescence", *i.e.* an emission that has the same spectrum as fluorescence, but a longer decay time because of the time spent in the triplet state.

The first indication of process (b) came from the observation by *Stevens* and *Hutton* that on flash excitation, the excimer component of pyrene in solution persists over several milliseconds [2]. *Parker* and *Hatchard* [65] later found that this is due to a separate, slowly decaying, low-intensity component, which is superimposed on the normal fluorescence, and is proportional to the square of the excitation intensity. This *biphotonic* nature of the process led to its interpretation by the reaction scheme (b).

The monomer component also appears with that of the excimer in delayed fluorescence. The ratio of the two components varies with temperature and concentration in a manner similar to, but not exactly the same as, that in prompt fluorescence. [66–68]. At higher temperatures, the excited monomer (as indicated in (b)) is regenerated by dissociation of the excimer, but with the excimer component predominant because of incomplete equilibration. The singlet excited monomer may also be formed directly by an energy transfer process between the two separate triplet molecules [69]:

$$A^{\dagger} + A^{\dagger} \rightarrow A^{*} + A \qquad (b')$$

At low temperatures and correspondingly high solvent viscosities, process (b′) and the monomer component predominate in delayed fluorescence. This process involves electron *exchange* between the two molecules, and so takes place only over short distances, though not necessarily so short as the distance for excimer formation by process (b).

The concurrent processes (b) and (b′) are considered together in the Parker-Stevens mechanism of delayed fluorescence. A different mechanism, according to which excimer and singlet excited monomer are formed *via* an intermediate higher excited excimer state, has been proposed by *Birks* [70–72] and further discussed by other authors [73–75].

[55] *H.-H. Perkampus* and *L. Pohl*, Z. physik. Chem. N.F. *39*, 397 (1963).

[56] *H.-H. Perkampus* and *L. Pohl*, Z. physik. Chem. N.F. *40*, 162 (1964); *H. H. Perkampus* and *K. Kortüm*, *ibid. 54*, 73 (1967).

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Excimer components have also been found in the delayed fluorescence of solutions of naphthalene [76], benzo[*b*]pyrene [66], benz[*a*]anthracene [71], and phenanthrene [77]. In delayed as well as in prompt fluorescence, the emission of less strongly bound excimers is confined to a narrow temperature range, in which the approach of the triplet molecule is sufficiently fast, but the dissociation of the excimer is not yet too pronounced.

Excimers should be formed not only by electron exchange between two molecules in triplet states but also by electron *transfer* between a radical-anion and a radical-cation (both in their unexcited states):

$$A^- + A^+ \rightarrow (AA)^* \qquad (c)$$

The excimer emission then appears as *chemiluminescence*. With radical-anions and radical-cations produced by alternating current electrolysis under potentiostatic conditions, *Chandross*, *Longworth*, and *Visco* [78] obtained chemiluminescence spectra with monomer and excimer components as well from several aromatic hydrocarbons. A subsequent quantitative investigation of the concentration dependence of the two components for 9,10-dimethylanthracene in dimethylformamide confirmed reaction scheme (a), though participation of other processes cannot be ruled out [79].

8. Unsymmetrical Excimers

Just as dissimilar molecules can form stable associates and complexes, they should also be capable of forming excimers. The existence and stability of unsymmetrical excimers whose components differ in their excitation energies, ionization potentials, or electron affinities is important to the problem of the bonding mechanism in excimers.

Aromatic compounds having very similar constitutions, and differing *e.g.* only in the position of the alkyl substituents, should produce unsymmetrical as well as symmetrical excimers in mixed solutions, though their structureless fluorescence spectra would be difficult to identify. Mixed excimers of this type *e.g.* between anthracene and 9-alkyl- or 9,10-dialkylanthracenes [80,81], between pyrene and 1-methylpyrene [82,83], and in other systems of the same kind have been detected by specific excitation of one component or by measurement of the total excimer fluorescence as a function of composition. The formation enthalpies of mixed excimers have also been determined [84]. The combination of formation and rapid dissociation of mixed excimers represents a mechanism for the transfer of excitation energy from one component to the other. A non-fluorescent or weakly fluorescent component can thus quench the fluorescence of the other, as has been observed *e.g.* in the case of 9,10-dialkylanthracenes by 9-bromo- or 9-acetylanthracenes [85–87]. The mixed excimer of anthracene and 9,10-diphenylanthracene can also be detected in delayed fluorescence; obviously, it is formed from the triplet states of the two partners in accordance with (b) [88].

The formation of unsymmetrical excimers between molecules of aromatic compounds having essentially different excitation energies is less obvious. Investigations on solid solutions of perylene in pyrene [89] and on mixed solutions of both compounds in a liquid solvent [90] have revealed changes in the fluorescence spectra, but no typical excimer bands have been found.

More favorable conditions for the formation of unsymmetrical excimers are provided by molecules having very different ionization potentials and electron affinities. Pairs of this type tend to form *electron donor-acceptor complexes* [91] (EDA or charge-transfer complexes) in the solid state or even in solution, where they give rise to broad structureless absorption bands in addition to those of the components. Besides these stable complexes, others have been discovered that exist only in the fluorescing excited state. For example, the fluorescence of pyrene (acceptor) in dilute benzene solution is replaced by a structureless component at a longer wavelength on addition of dimethylaniline (donor) [92,93]. Since this phenomenon is analogous to excimer formation [94–96], the terms *heteropolar* exci-

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[93] *H. Leonhard* and *A. Weller*, Ber. Bunsenges. physik. Chem. *67*, 791 (1963).

[94] *N. Mataga*, *T. Okada*, and *K. Ezumi*, Molecular Physics *10*, 203 (1966).

[95] *N. Mataga*, *K. Ezumi*, and *T. Okada*, Molecular Physics *10*, 201 (1966).

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mers or *hetero*-excimers are used [97]. The fluorescence effect in this case and the well-known quenching of fluorescence by non-absorbing impurities are related in the same manner as the concentration-induced fluorescence change and concentration quenching.

Hetero-excimers have been found with numerous aromatic hydrocarbons as acceptors and several aromatic amines as donors in nonpolar solvents [95,96]. The excimer band shows a red shift with increasing electron affinity of the acceptor and with decreasing ionization potential of the donor. For the same donor, a linear relation is found between the wave number of the band maximum and the electron affinity or the reduction potential of the acceptor [98]. In most of the cases studied the acceptor was the lower excitation energy so that it becomes primarily excited under usual conditions. Nevertheless, there are also examples for the opposite case [99]. The fluorescence of a heterotriple complex has also been reported [100]. Nonspecific solvent effects may lead to spectral effects similar to those of the formation of hetero-excimers but should be interpreted differently [101].

Unlike the fluorescence of symmetrical excimers, that of hetero-excimers exhibits an appreciable solvent dependence. The spectrum shifts toward the red with increasing dielectric constant of the solvent, as is to be expected in view of the polar nature of hetero-excimers [94,102,103]. The fluorescence yield and the decay time decrease simultaneously, which has to be interpeted by a solvent dependence either of the electronic structure of the excimer [104] or of its formation and decomposition kinetics [105].

9. Triplet Excimers

A question of considerable theoretical interest is whether molecules in metastable triplet states form triplet excimers with molecules in singlet ground states:

$$A^{\dagger} + A \rightarrow (AA)^{\dagger} \qquad (d)$$

These should appear as an additional component in the phosphorescence spectrum, the properties of which are similar to those of the excimer component in the fluorescence spectrum. Diffuse regions in the low-temperature phosphorescence spectra of some halogenobenzenes in the crystalline state [106] and in solution in organic glasses [107] have been interpreted in this way. The hitherto clearest evidence of the existence of triplet excimers has been found in alcoholic solutions of naphthalene, for which an excimer-like component is superimposed on the monomer phosphorescence over a narrow temperature range around 180 °K [108].

10. Origin of the Excimer Binding Energy

The electronic state of a symmetrical singlet excimer could obviously be described by a resonance hybrid with uniform distribution of the excitation energy over both components:

$$A^*A \leftrightarrow AA^* \qquad (e)$$

We therefore assumed at first that the stability of the pyrene excimer was due to excitation (or exciton) resonance between the two configurations in formula (e) [1]. Greater stability is then to be expected if the state of the excimer is derived, not from the lowest-energy state ^1L_b (77 kcal/mole) of the monomer, but from the state ^1L_a, which is only slightly higher (86 kcal/mole) and also has a very high oscillator strength ($f = 0.35$) [109,110]. States with even higher energies have also been considered [110a].

A second hypothesis for the state of the excimer was proposed by *Ferguson* [43], who interpreted it as a charge-transfer state. A resonance hybrid can again be formulated for a symmetrical excimer:

$$A^+A^- \leftrightarrow A^-A^+ \qquad (f)$$

According to this hypothesis, the energy of the excimer should depend on the difference between the ionization potential and the electron affinity of the monomer. A good correlation exists between this difference and the position of the excimer emission [77,111]; however, since the correlation with the position of the ^1L_a state is equally good [112], it is impossible to decide in favor of one of the two hypotheses.

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The first quantum chemical calculations on excimers from parallel molecules of naphthalene, pyrene, *etc.* were performed by *Konijnenberg* [113] and by *Murrell* and *Tanaka* [114] by the semi-empirical PPP method. These calculations showed that with acceptable values of the parameters involved, and particularly of the distance between the two molecules within the excimer, the position of the excimer band can be reproduced only if both excitation- and charge resonance are taken into account.

This corresponds to a combination of (e) and (f) and to a more general formulation of the excimer state as a resonance hybrid:

$$A^*A \leftrightarrow AA^* \leftrightarrow A^+A^- \leftrightarrow A^-A^+ \qquad (g)$$

Depending on the particular case, either the neutral or the ionic configurations may predominate. The formulation (g) can likewise be applied to unsymmetrical and hetero-excimers.

Quantum chemical calculations have been carried out for the excimers of anthracene and perylene as well as for those of naphthalene and pyrene [114, 115]. In addition to highly symmetrical sandwich configurations (D_{2h}), less symmetrical ones have also been discussed [116, 117]. Similar calculations for the benzene excimer, the treatment of which includes the paracyclophanes, have also been carried out for configurations of lower symmetry [118–120].

Besides the PPP method, simpler and less conventional semi-empirical methods have also been used, several of them based on orbitals extending over both components of the excimer [112, 121].

Most of these calculations give only the excitation energy of the excimer as a function of its geometrical configuration. The latter itself, and particularly the equilibrium distance between the planes of the two excimer compounds, can only be deduced from the agreement of calculated and experimental values for the position of the excimer band. Values between 3.0 and 3.6 Å were obtained in every case.

Quantum chemical calculations of the actual energy states, *i.e.* the potential surfaces of the excimer and its unstable ground state, have been carried out only for a few examples, *e.g.* benzene [122] and naphthalene [123], by simplified semi-empirical methods. The potential surface of the ground state of the benzene excimer has also been used for the calculation of the spectral distribution of its emission [124].

11. Excimers as Intermediates in Photochemical Reactions and Photophysical Processes

Photochemical reactions, apart from trivial exceptions, are chemical reactions proceeding from excited electronic states. Excimers occur as intermediates in photochemical dimerizations in which an excited and an unexcited molecule form a stable dimer whose components are linked by principal valences. The best-known example is the photodimerization of anthracene with formation of dianthracene. This reaction, which proceeds from the excited singlet state state [125, 126], was assumed to occur *via* an electronically excited associate [127, 128], later to be identified as the excimer [126, 129]. Very probably, the photochemical reaction is the reason for the concentration *quenching* of fluorescence at room temperature; instead of emitting, the excimer undergoes transformation to the stable photodimer. At lower temperatures [55, 56] or in the presence of bulky substituents [62, 129] in position 9 or 10, this transformation is suppressed, so that excimer fluorescence occurs.

It is also very probable that the photodimerizations of naphthacene, pentacene [130], and 2-alkoxynaphthalenes [131, 132] occur *via* excimers. The (unsensitized) photodimerization of acenaphthylene [133] is known to involve two different mechanisms, one of which leads to the *syn* dimer and the other to the *anti*. A mechanism proposed for the formation of the *syn* dimer proceeds *via* the excimer [134].

The photodimerization of thymine is of interest in biology, and particularly in genetics, since it is involved in the inactivation of deoxyribonucleic acid by UV irradiation. Excimers are also assumed to participate in this process [135, 136].

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An important photophysical process is the intermolecular transfer of electronic excitation energy, which plays an important part in the function of the widely used liquid scintillators. These consist of an aromatic solvent, generally toluene, with a dissolved substance that fluoresces at longer wavelengths, *e.g.* 2,5-diphenyloxazole (PPO). Their function depends on the transfer of excitation energy initially produced in the solvent to the solute. This could occur as a radiationless process between separated molecules [137]. However, since excimers are rapidly and reversibly formed in toluene and other common solvents [138, 139], processes such as

$$A^* + A \rightleftarrows (AA)^* \rightleftarrows A + A^* \qquad (h)$$

which are evidently analogous to the Grotthus proton transfer process, must also be considered [140, 141]. This may be a useful principle in the search for new scintillator systems [142]. Excimers also appear to be involved in the transfer of electronic excitation from host to guest molecules in crystals under high pressure [143].

Thanks are due to the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft for their generous support of the work in this field carried out in the author's institute.

Received: January 16, 1969 [A 698 IE]
German version: Angew. Chem. *81*, 364 (1969)

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A New Type of Corrin Synthesis

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Work towards a synthesis of vitamin B_{12} has inspired a new type of corrin synthesis. The key step is a light-induced 1,16-hydrogen transfer leading to an antarafacial ($\pi \rightarrow \sigma$)-cycloisomerization of a seco-corrinoid metal complex. The construction of the seco-corrinoid ligand system is achieved by coupling monocyclic ring precursors in their enamide or enamine form through the methods of sulfide-contraction via oxidative coupling and of iminoester-enamine condensation.

The structural and functional uniqueness of vitamin B_{12} and B_{12}-coenzymes continues to stimulate chemical research on corrins in a number of laboratories [1]. One of the important contributions to the synthetic aspects of the field has recently come from *A. W. Johnson* and his collaborators [1c] through their synthesis of corrinoid complexes from tetrapyrrolic precursors. In addition, the continuing investigations in the Harvard and ETH (Zürich) laboratories towards a synthesis of vitamin B_{12} have produced results of a methodological [2] and theoretical [3] nature which, among other things, have induced the development of a new type of corrin synthesis. This is exemplified by the synthesis of (±)-palladium(II)-15-cyano-1,2,2,7,7,12,12-heptamethyl-*trans*-corrin perchlorate *(20)*.

The concept of corrin synthesis used in our previous work [4] requires the construction of two bicyclic intermediates *(1)* and *(2)* containing the A/D- and B/C-moieties respectively, followed by coupling of the C

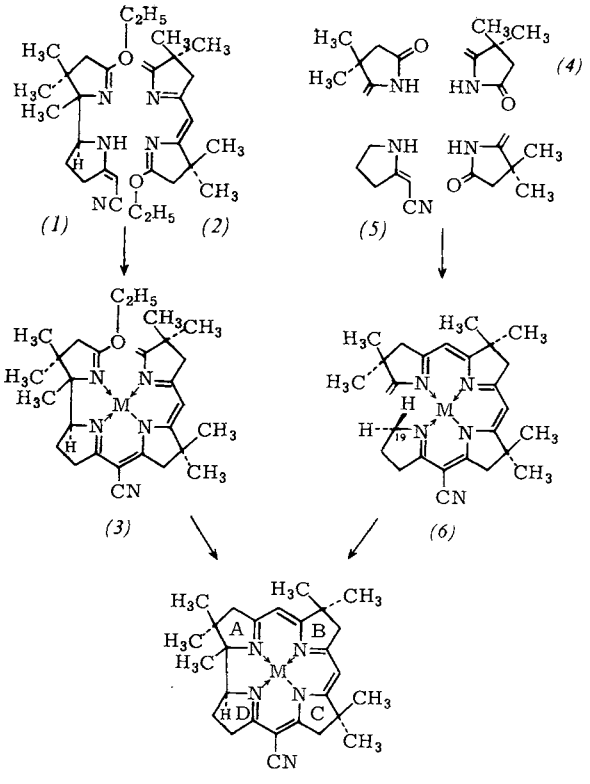
[*] Dr. Yasuji Yamada, Dr. D. Miljkovic, P. Wehrli, Dipl.-Ing.-Chem. ETH, Dr. B. Golding, P. Löliger, Dipl.-Ing.-Chem. ETH, Dr. R. Keese, K. Müller, Dipl.-Ing.-Chem. ETH, and Prof. A. Eschenmoser
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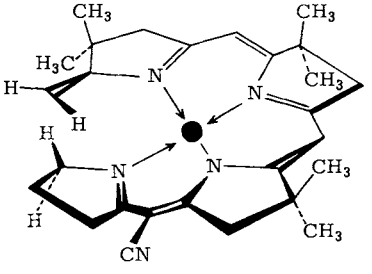
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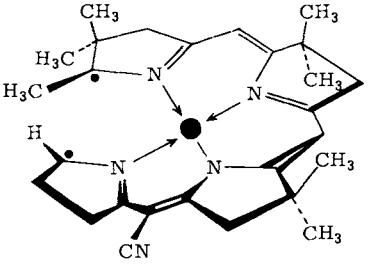
Scheme 1.

and D rings in an iminoester-enamine condensation, and finally by an A/B-cyclization of type *(3)*→*(7)* within a robust [5] transition-metal complex. Inherent in this concept is the configurational problem which arises in the preparation of the A/D-component. In contrast, a cyclization between the rings A and D to the macrocyclic ligand is a characteristic of the conversion of tetrapyrrolic precursors to tetradehydro-corrins [1c,6]. An A/D-cyclization, though mechanistically completely different, is likewise the key step in the new corrin synthesis; namely, a light-induced 1,16-hydrogen transfer leading to a constitutionally and configurationally specific cycloisomerization of a seco-corrionid metal complex *(6)* to the corresponding trans-corrin complex *(7)*. The possibility of incorporating such an "all-or-nothing" process into the planning of a multistep project illustrates once again the new dimension bestowed on organic synthesis by the heuristic concept of sigmatropic rearrangements propounded by *R. B. Woodward* and *R. Hoffmann* [7].

Models of metal complexes *(6)* display the ligand system coiling around the metal ion and one of the ring D methylene hydrogens in position 19 lying directly underneath (or above) the exocyclic methylidene group of ring A; this is the case the more one tries to hold all four ligand nitrogen atoms in a common plane with the coordination center [cf. *(6a)*]. The models also suggest that such planoid complexes optimally fulfill the geometrical prerequisites for an antarafacial sigmatropic 1,16-hydrogen transfer from carbon 19 of ring D to the methylene carbon at ring A. The formal primary product of such a presumably



(6a)



(6b)

endothermic [8] process would be a 15-center 16-electron-π-system *(6b)*, which is separated from the *trans*-corrin complex *(7)* by a correspondingly exothermic, antarafacial electrocyclic 1,15-(π→σ)-isomerization.

Fig. 1 shows the symmetry of the two HMO's π_8 and π_9 [9] which, in the sense of a Woodward-Hoffmann frontier orbital analysis [7], are relevant to both antarafacial processes, namely the 1,16-hydrogen transfer and the 1,15-(π→σ)-isomerization. The prognosis is: whereas the latter process is symmetry allowed in the ground state, the hydrogen transfer would have to be induced photochemically (if it could be induced at all). So far, the experimental findings are in accord with this prognosis.

A second feature of the new type of corrin-synthesis is the construction of vinylogous amidine systems from thiolactams and enamides by oxidative coupling followed by sulfide-contraction. The method has developed from the problem of preparing a B/C-component for a synthesis of vitamin B_{12} [10,11,2b] and represents

[5] With the exception of the method for the synthesis of metal-free corrins (see *A. Fischli* and *A. Eschenmoser*, Angew. Chem. *79*, 865 (1967); Angew. Chem. internat. Edit. *6*, 866 (1967).

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[8] No classical Kekulé structure can be formulated for the π-system of *(6b)* if one neglects 1,3-σ bonds. The HMO-model of the *(6b)*-chromophore puts two π-electrons in a non-bonding orbital (see [9]).

[9] The data of Fig. 1 result from a simple HMO-treatment of the corresponding 16- and 15-center π-systems neglecting metal ions. The following set of parameters has been used: $\beta_{CN} = 0.8\ \beta_{CC}$, $\alpha_N = \alpha_C + 1.5\ \beta_{CC}$ (symmetry invariant in the range $\alpha_C \leqslant \alpha_N \leqslant \alpha_C + 2\ \beta_{CC}$); *A. Streitwieser:* Molecular Orbital Theory for Organic Chemists. John Wiley, New York 1961.

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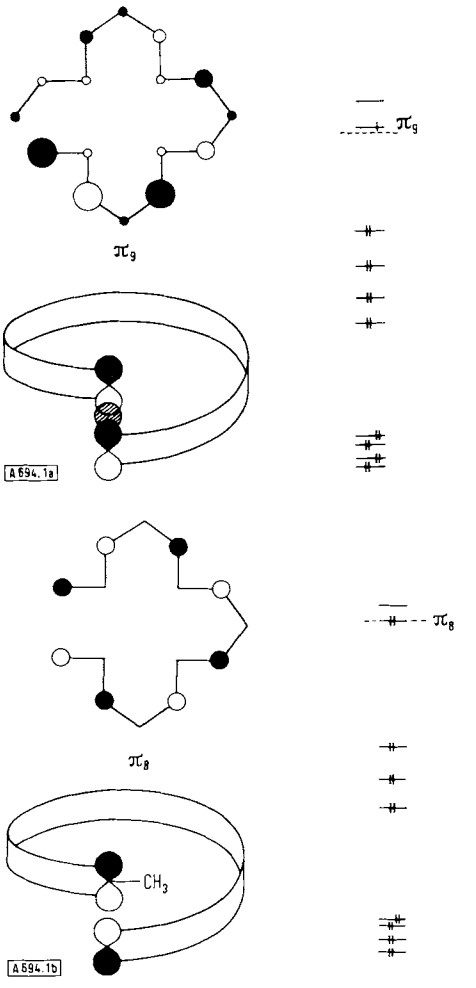
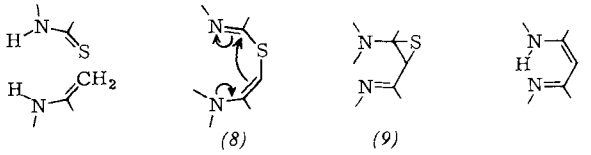


Fig. 1. a) Symetry of the HMOs π_9 and b) π_8.

formally an intramolecular version of the iminoester-enamine condensation method.

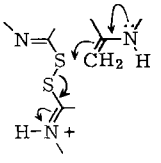
The condensation centers of both the lactam thiocarbonyl carbon and the enamide methylidene carbon are first oxidatively linked by a sulfide-bridge [cf. *(8)*]. An intramolecular thioiminoester condensation in the presence of a phosphorus thiophile leads then to the vinylogous amidine system. The simplest mechanistic pathway includes an intermediate formation of the corresponding episulfide derivative *(9)*; the transfer of sulfur to thiophiles with concomitant carbon-carbon double bond formation is a well-known property of episulfides [12].



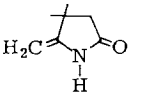
(8) *(9)*

[12] A possibility which cannot be ruled out consists of the formation of both the π-, as well as the σ-(C,C)-bond within a (>S=P<) complex. The sulfide-contraction method formally belongs to a group of reactions loosely defined in the literature as "Sulfur Extrusion Reactions"; see *J. D. Loudon* in *N. Kharash*: The Chemistry of Organic Sulfur Compounds, Pergamon Press, London 1961, Vol. *I*, 299. On the desulfurization of episulfides with thiophilic phosphorus compounds, see *N. P. Neureiter* and *F. G. Bordwell*, J. Amer. chem. Soc. *81*, 578 (1959); *D. D. Denney* and *M. J. Boskin*, *ibid. 82*, 4736 (1960); *M. Sander*, Chem. Reviews *66*, 326 (1966). On the application of the sulfide-contraction method to the preparation of metal-free corrins see [5].

Reaction with benzoyl peroxide has proved to be the simplest method for oxidative coupling of thiolactams and enamides. The identified intermediate in the coupling reaction is the readily formed bis-imidoyl-disulfide [13] which undergoes an acid-catalyzed electrophilic substitution at the methylidene carbon of the enamide; thereby the liberated equivalent of thiolactam is reconsumed by further oxidation. In a variation of this procedure, the isolated disulfide can be coupled with the potassium salt of the enamide [14].



The sulfide-contraction procedure and the iminoester-enamine condensation are preparatively complementary methods which allow the construction of the corrin chromophore from cyclic precursors in either their enamide or enamine form. The experimental realization of this concept is exemplified by the synthesis of seco-corrinoid complexes *(6)* starting from the simple monocyclic precursors *(4)* and *(5)*; The following Scheme [16] surveys the results of this synthesis together with those so far obtained on the cycloisomerization problem (*i.e. (6)→(7)*).

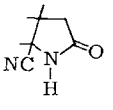


(4)

preparation see [4a, 17, and 11]

↓ 90%

1,1 KCN/1,1 $KHCO_3/H_2O$/1 h/RT – 50 °C



(10) [11]

m.p. 196 °C (from CH_2Cl_2-cyclohexane) 3420^m, 2230^w, 1712^s cm^{-1} ($CHCl_3$); 1.13(s/3H), 1.38(s/3H), 1.55(s/3H), 2.02 **2.30/2.41**/2.69 (AB/$J \approx$ 17 Hz/2H) 7.5(s, broad/1H) ppm ($CDCl_3$).

↓ 82%

1.2 P_2S_5 susp. in benzene/6 h/80 °C

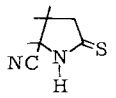
[13] See *F. Hodosan*, Bull. Soc. chim. France *1957*, 633; *F. Hodosan* and *N. Serban*, *ibid. 1960*, 133.

[14] A modification of the sulfide-contraction method, which can be applied to the preparation of vinylogous amides (and vinylogous amidines) has been developed independently at Harvard University [2a] and the ETH Zürich [1e, 2b, 15]. Thus, secondary thiolactams can quite generally be alkylated on sulfur by α-bromoketones or α-bromocarboxylic esters; the alkylation products undergo a base-induced desulfurization in the presence of a thiophilic phosphorus compound with concomitant contraction to a C-acyl-enamine. (Sulfide-contraction method *via* alkylative coupling.) An analogous observation had previously been made by *E. Knott*, (J. chem. Soc. (London) *1955*, 916).

[15] *P. Dubs*, Dissertation, ETH Zürich, 1969.

[16] The Scheme lists the spectral data of the compounds in the following order: λ_{max} values of the UV.-spectrum (log ε – values in brackets; sh = shoulder), selected bands from the IR.-spectrum (s = strong, m = medium, w = weak intensity), the signals of the proton resonance spectrum in δ-values referred to δ (tetramethylsilane) = 0 ppm, and finally, selected peaks of the mass spectrum (% intensity in brackets). The yields apply to crystalline, spectroscopically pure material. Correct analytical data have been obtained for all compounds formulated in the scheme. RT = Room temperature.

[17] *R. Scheffold*, Dissertation, ETH Zürich, 1963; *E. Bertele*, Dissertation, ETH Zürich, 1963.

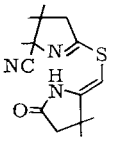


(11) [11]

m.p. 124 °C (from CH_2Cl_2-hexane);
269 nm (4.2) (C_2H_5OH);
3400^m, 3140^m, 2235^{ww}, 1470^s cm^{-1} ($CHCl_3$);
1.11(s/3H), 1.37(s/3H), 1.60(s/3H), 2.56/**2.85**/**2.89**/3.17 (AB/$J \approx$ 17 Hz/2H), 8.9(s, broad/1H) ppm ($CDCl_3$).

↓ 72%

1.3 *(4)* + 1.1 dibenzoylperoxide/benzene/RT/24 h

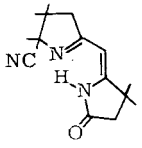


(12)

m.p. 132 °C (from CCl_4; *ca.* 1 Mol cryst.-CCl_4);
259 nm (4.1) (C_2H_5OH);
3420^m, 2235^{ww}, 1725^s, 1655^s, 1577^s cm^{-1} ($CHCl_3$);
1.08(s/3H), 1.33(s/3H), 1.37(s/6H), 1.50 (s/3H), 2.43(s/2H), 2.63/2.65(2s/2H), 5.35 (s/1H), 8.2(s, broad/1H) ppm ($CDCl_3$).

↓ 84%

5(C_6H_5)$_3$P/under N_2/130 °C/1 h

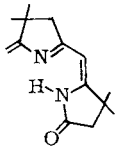


(13)

m.p. 127 °C (from CH_2Cl_2-hexane);
M.W. found 261 (in CH_2Cl_2);
292 nm (4.3) (C_2H_5OH);
3230^w (broad), 2250^{ww}, 1743/1727^s, 1650^s, 1567^s cm^{-1} ($CHCl_3$);
1.05(s/3H), 1.33(s/9H), 1.53 (s/3H), 2.40(s/2H), 2.30/**2.58**/**2.62**/2.90 (AB/$J \sim$ 17 Hz/2H), 5.04(s/1H) ppm ($CDCl_3$);
233 (7%), 232 (40%/M^+–HCN), 218 (15%), 217 (100%/M^+–HCN–CH_3).

↓ 88%

2.8 $(CH_3)_3COK$/$(CH_3)_3COH$/80 °C/1 h

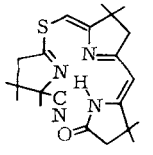


(14)

m.p. 159 °C (from CH_2Cl_2-hexane);
see [4a, 17, and 11]

↓ 51% [18]

1.0 disulfide *(11a)* + 1.0 $(CH_3)_3COK$/$(CH_3)_3COH$-benzene (8:5)/RT/5.5 h

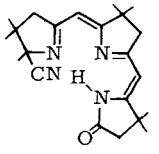


(15) [11]

m.p. 165 °C (from CH_2Cl_2-hexane);
277(4.3), 294(sh/4.0), 360(4.3) nm (C_2H_5OH);
3240^w (broad), 2240^{ww}, 1745/1728^s, 1640^s, 1575^m, 1523^s cm^{-1} ($CHCl_3$);
1.08(s/3H), 1.23(s/6H), 1.33(s/9H), 1.51 (s/3H), 2.41(s/2H), 2.66(s/4H), 5.15 (s/1H), 6.31(s/1H), *ca.* 11 (broad/1H) ppm ($CDCl_3$);
399 (18%), 398 (68%/M^+), 248 (100%).

↓ 82%

1.9 (C_6H_5)$_3$ P/1.2 (C_6H_5)$_3$ P·BF_3/benzene/3 h/80 °C



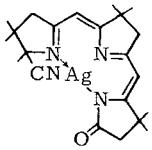
(16) [11]

m.p. *ca.* 170 °C (from cyclohexane);
255 (4.50), 365 (4.29) nm (C_2H_5OH);
3200^w (broad), 2230^{ww}, 1740^s/1725^m (sh), 1640^s, 1620^s, 1610^m(sh), 1560^m, 1500^{ss} cm^{-1} ($CHCl_3$);
1.12(s/3H), 1.22(s/6H), 1.34(s/9H), 1.57 (s/3H), 2.40(s/2H), 2.63(s/2H), 3.03(s, broadened/2H); 5.19(s/1H), 5.68(s/1H), *ca.* 11 (very broad/1H) ppm ($CDCl_3$);
367 (23%), 366 (78%/M^+), 324 (100%).

↓ ca. 95%

1.7 Ag_2O/benzene (N_2)/1 h/RT

[18] Yield in experiments carried out by Dr. *L. Ellis*.

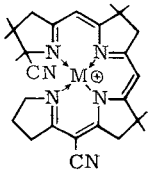


(17)

m.p. 182 °C(from hexane-benzene (20:1));
M.W. found 486 (in CH_2Cl_2/25 °C);
274(sh/4.36), **284**(4.50), 307(sh/3.83), 322 (3.66), 414(sh/4.15), **440**(4.28), 467(sh/4.11) nm (C_2H_5OH);
1715^s, 1605^s, 1540^s, 1518^s, 1490^s cm^{-1} (CCl_4);
1.06/1.29/1.31/1.37/1.39/1.43/1.81 (7 CH_3-s), 2.29/2.69(2 CH_2-s), 2.50/**2.65**/**3.02**/3.18 (AB/$J \approx$ 16 Hz/2H), 5.00(s/1H), 5.10(s/1H) ppm (CCl_4);
475 (7%), 474 (25%), 473 (7%), 472 (25%/M^+(^{107}Ag)), 324 (100%).

↓ 68% [21]

a) 1.8 (C_2H_5)$_3O^+BF_4^-$/0.5 ethyl diisopropylamine/CH_2Cl_2/3 h/RT(N_2) →
+3.8 (5)/24 h/RT(N_2);
b) 3.2 $Ni(ClO_4)_2$/CH_3CN →
2.1 $NaOC_2H_5$/RT



(18a)

$ClO_4^\ominus$

M = Ni^{II}: m.p. *ca.* 280 °C (dec.) (from CH_2Cl_2-methyl acetate);
270(4.20), 310(sh/4.14), 323(4.23), 467 (4.21) nm (C_2H_5OH);
2219^m, 1630^w, 1614^w, 1588^s, 1549^m, 1515^s cm^{-1} ($CHCl_3$);
1.22/1.34/1.38/2.14(4 CH_3-s), 1.49/1.52 (2s/9H), 1.9–2.5(m/2H), 2.8–3.4(2s+m/8H), *ca.* 3.8/4.4(2m/2H), 5.98/6.09(2s/2H) ppm ($CDCl_3$);
512 (2%/M^+–H), 497 (7%/M^+–H–CH_3), 485 (15%/M^+–H–HCN), 470 (100%/M^+–HCN–CH_3).

↓ 89%

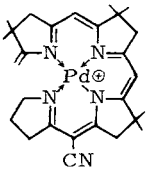
a) *(18a)* + KCN/CH_3OH/10 min/RT;
b) Pd(II)-acetate/CH_2Cl_2–C_2H_5OH/$NaOC_2H_5$/RT/10 min.

(M = Pd^{II}) *(18b)*

M = Pd^{II}: m.p. *ca.* 295 °C (dec.) (from CH_2Cl_2-methyl acetate);
262(4.22), 306(sh/4.24), **316**(4.37), 350 (sh/3.80), 367(3.88), 389(sh/3.83), 448 (sh/4.21), **469**(4.31) nm (C_2H_5OH);
2219^m, 1627^w, 1609^w, 1584^s, 1546^m, 1513^s cm^{-1} ($CHCl_3$);
1.27/1.34/1.43/1.56(4 CH_3-s), 1.53(s/9H), 1.9–2.7(m/2H), 2.9–3.5(2s+m/8H), *ca.* 4.0/4.4(2m/2H), 6.07/6.20(2s/2H) ppm ($CDCl_3$);
560 (3%/M^+(^{106}Pd)–H), 545 (11%/M^+–H–CH_3), 533 (23%/M^+–H–HCN), 518 (100%/M^+–H–HCN–CH_3) and corresponding isotope peaks.

↓ 84%

ca. 10 $(CH_3)_3COK$/$(CH_3)_3COH$/6 h/80 °C



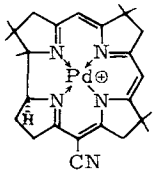
(19)

$ClO_4^\ominus$

m.p. *ca.* 240 °C (dec.) (from CH_2Cl_2-methyl acetate);
261(4.17 T) **320**(4.40), 364(sh/3.80), 384 (3.91), 407(3.91), **468**(4.17) nm (C_2H_5OH);
2220^m, 1627^m, 1610^m, 1586^s, 1540^m, 1517^s cm^{-1} ($CHCl_3$);
1.33/1.44/1.51/1.52(4s/18H), 1.8–2.4 (m/2H), 2.9–3.4(2s+m/8H), 3.8–4.2 (m/1H), 4.2–4.6(m/1H), 4.85/4.91 (2 d/$J \approx$ 2 Hz/H_2C=C◇), 6.13/6.29(2s/2H) ppm ($CDCl_3$);
533 (39%/M^+(^{106}Pd)–H), 518 (100%/M^+(^{106}Pd)–H–CH_3), 503 (14%), 488 (21%), 473 (11%), 458 (16%) + corresponding isotope peaks; suppl. peak at 548 (M^+–H+O?).

>95% (spectroscopically) 89% (cryst. isolated)

hν (sunlight) in CH_2Cl_2 (c = $5.1 \cdot 10^{-3}$ mole/l) in evacuated pyrex flask/RT/4 h

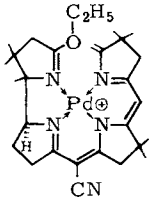


(20) $ClO_4^{\ominus}$

m.p. *ca.* 320 °C (dec.) (from methyl acetate);
249(4.24), **308**(4.48), 352(3.72), 371(3.93), 392(4.00), **445**(4.32), 458(sh/4.27), 463 (sh/4.26) nm (C_2H_5OH);
2221^m, 1623^m, 1583^s, 1542^m, 1502^{ss} cm^{-1} ($CHCl_3$);
1.25/1.26/1.36/1.47/1.50/1.53/1.54 (7 CH_3-s), 1.8–2.7(m/2H), 2.8–3.8(s + AB + m/8H), 4.6–4.9(m/1H), 6.12/6.40 (2s/2H) ppm ($CDCl_3$);
533 (24%/M^+(^{106}Pd)–H), 518 (100%/M^+–H–CH_3), 503 (7%), 488 (17%), 473 (6%), 458 (8%) + corresponding isotope peaks; suppl. peak at 548 (*ca.* 3%/M^+–H+O?).

↑ 83%

ca. 20 $(CH_3)_3COK/(CH_3)_3COH/N_2$/40 h/136–145 °C.

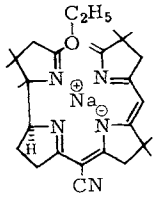


(3b) $ClO_4^{\ominus}$

m.p. *ca.* 215 °C (dec.) (from methanol);
246(4.19), 257(sh/4.05), 280(sh/4.09), 289 (4.11), 304(sh/4.01), 325(3.73), 343(3.69), 421(4.22) nm (C_2H_5OH);
2218^m, 1625^s, 1614^s, 1603^s, 1550^w, 1537^s cm^{-1} ($CHCl_3$);
inter alia 5.61/5.06/4.57(3 vinylproton-s), 4.1–4.6(m/3H/–O–CH_2–; >CH–N=) *etc.* ppm ($CDCl_3$);
551 (*ca.* 2.5%/M^+(^{106}Pd)–C_2H_5), 426 (100%/M^+–$C_9H_{16}NO$ (ring A)) + corresponding isotope peaks.

↑ 52%

1.04 Pd(II)-acetate in C_2H_5OH/CH_2Cl_2/10 min/RT



(3a) preparation see [4c, 19, and 20]

↑

(1) + (2)

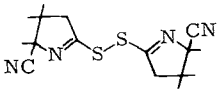
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(11)

Appendix

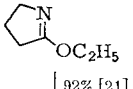
↓ 92%

0.53 benzoylperoxide/K_2CO_3 susp. in $(CH_3)_3COH$/0 °C/RT/*ca.* 12 h.



(11a)

m.p. 119 °C (from CCl_4/0 °C) log $\varepsilon_{223\,nm}$ 3.85 (C_2H_5OH);
2240^w, 1585^s cm^{-1} ($CHCl_3$);
1.12(s/6H), 1.37(s/6H), 1.53(s/6H), 2.78 (s broadened/4H) ppm ($CDCl_3$);
334 (15%/M^+), 239 (61%), 225 (15%), 183 (37%), 169 (37%), 168 (83%), 167 (92%/$M^+/2$), 166 (100%).



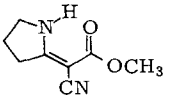
4 methylcyanoacetate (without solvent), 24 h/100 °C.

↓ 92% [21]

[19] *A. Fischli*, Dissertation, ETH Zürich, 1968.

[20] *I. Felner-Caboga*, Dissertation, ETH Zürich, 1967.

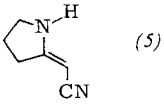
[21] Yield in experiments carried out by *H. Wild*.



m.p. 137 °C (from ether);
267 nm (4.33);
3350^m, 2210^s, 1675^s, 1597^s cm^{-1} ($CHCl_3$);
2.0–2.3(m/2H), 2.95(t/$J \approx$ 8 Hz/2H), 3.72(s+t/$J \approx$ 8 Hz/5H), 9.0(s broad/1H) ppm ($CDCl_3$).

↓ 88%

1 N NaOH/H_2O/20 min/100 °C/ → conc. HCl/0 °C.



(5)

m.p. 73 °C (from hexane);
267 nm (4.28);
3460^m/3340^m, 2195^s, 1625^s cm^{-1} ($CHCl_3$);
1.8–2.3(m/2H), 2.4–3.0(m/2H),3.3–3.65 (m/2H), 3.70/4.00 (2 triplettoid s/each *ca.* 0.5 H), 5.6 (s broad/1H) ppm ($CDCl_3$) (mixture of *cis*/*trans* diastereoisomers *ca.* 1:1).

Coupling of two molecules of the monocyclic enamide *(4)* by the sulfide-contraction process requires protection of the highly nucleophilic carbon-carbon double bond of the potential thioamide partner. This protection is best provided by the cyanide group which can easily be introduced in alkaline medium [22] and which survives the conditions of the subsequent reactions; eventually it can be cleanly expelled from vinylogous imidines by strong base. In contrast to the enamide *(4)* itself, the cyanolactam *(10)* can be converted without difficulty to the corresponding thiolactam *(11)* by the classical P_2S_5 method [23].

Under the conditions of the oxidative coupling, the enamide *(4)* is practically inert towards benzoyl peroxide; thus the oxidative dimerization of the thiolactam *(11)* to the disulfide *(11a)* and its coupling with the enamide *(4)* to form the mixed sulfide *(12)* can be combined in a single procedure. However, the disulfide *(11a)* can also be isolated in high yield as a labile, yet crystalline compound from reaction of the thiolactam *(11)* with half a mole of benzoylperoxide in the absence of the enamide *(4)* (see appendix to Scheme 2) [24].

The constitutional type *(12)* [25] of the coupling products obtained in this way has been verified by analytical and spectroscopic data on crystalline samples in a number of cases including the present one. Although it is usually possible to isolate these sensitive compounds, it is preparatively preferable to desulfurize the crude coupling products directly after removal of benzoic acid by means of an organic polymer base or solid potassium carbonate. Simple heating of compound *(12)* with triphenylphosphine produces the

[22] This enamide-protection method was first used in another connection by *R. B. Woodward* and *A. Wick* (unpublished). The addition of CN^- in alkaline medium doubtless occurs not to the enamide (4) directly, but rather to the N-acyl-ketimine isomer; see the addition of nitromethane to (4) in basic medium [4d].

[23] *W. Walter* and *K. D. Bode*, Angew. Chem. *78*, 517 (1966); Angew. Chem. internat. Edit. *5*, 447 (1966).

[24] A detailed description of reaction sequences of type *(11)*→*(12)*→*(13)* can be found in *P. Löliger*, Dissertation, ETH Zürich, 1968, p. 76–104.

[25] The configuration at the (–S–C=C) double bond is arbitrarily formulated.

vinylogous amidine *(13)* in high yield, together with triphenylphosphinesulfide. Treatment of the amidine *(13)* with potassium *tert*-butoxide (CN^--elimination from the presumably doubly deprotonated derivative) leads to the familiar bicyclic lactam *(14)*, previously prepared in other ways [4, 5, 26]. This lactam is the product of a formal carbonyl-methylidene self-condensation of the monocyclic enamide *(4)*, a process which points in a most direct way towards the structure of the corrin chromophore. The sulfide-contraction method is one which experimentally simulates such a transformation.

The repetition of this process adds another vinylogous amidine unit to the bicyclic lactam *(14)* to form the tricyclic analog *(16)*. In this more complicated case, the base-induced version of the oxidative coupling had to be used [NH-deprotonation of the lactam *(14)* and reaction with the isolated disulfide *(11a)*]. The crystalline tricyclic sulfide *(15)* [25] can be desulfurized in the desired way by heating with triphenylphosphine alone; however, the preparatively important observation has been made that boron trifluoride drastically catalyzes the sulfide-contraction in this case. This catalytic effect is mechanistically ambiguous; the working hypothesis was that coordinative bridging of the flanking nitrogen atoms would result in a steric acceleration of contraction.

Experiments towards the addition of the fourth ring *via* an enamine-iminoester condensation led to an instructive experience. In contrast to the bicyclic analog [4], the direct *O*-alkylation of the tricyclic lactam *(16)* with triethyloxonium tetrafluoroborate proved to be preparatively useless, because presumably indiscriminate *O*- and *N*-alkylation occurred. This difficulty is overcome in the corresponding silver complex *(17)*, in which the sp^2-electron pairs of at least two of the three nitrogen atoms are blocked towards alkylation by digonal coordination with the silver ion. Alkylation of the silver complex and subsequent reaction with the ring component *(5)* [27] in its free enamine form produce the tetracyclic condensation product which is conveniently isolated from the reaction mixture in the form of its magnificently crystalline diamagnetic nickel(II) complex *(18a)*. Cyanide ions remove the nickel(II) with great ease, thus allowing the preparation of complexes of other metal ions, *e.g.* of the crystalline palladium(II) complex *(18b)*. The cyanide protecting-group is removed by deprotonation with potassium *tert.*-butoxide to yield the seco-corrinoid palladium(II) complex *(19)*. The constitution of this diamagnetic complex is convincingly verified by analytical and spectroscopic data, particularly by its transparently interpretable proton resonance spectrum. The same is true for the spectroscopically similar and again diamagnetic nickel(II) complex which can be prepared analogously from *(18a)*.

Ultraviolet light from a mercury high pressure lamp, or simply sunlight, transform oxygen-free solutions of the palladium(II) complex *(19)* in pyrex vessels at room temperature into the (±)-palladium(II)-15-cyano-1,2,2,7,7,12,12-heptamethyl-*trans*-corrin complex *(20)* without detectable by-products. The constitution and configuration of the crystalline cyclization product are beyond doubt: the UV-, IR-, NMR- and mass-spectra are identical with those of a complex which was prepared for the purpose of comparison by the classical synthetic route *(3a)*→*(3b)*→*(20)*. The trans-configuration of the A/D ring junction is likewise beyond doubt, since (±)-dicyano-cobalt(III)-15-cyano-1,2,2,7,7,12,12-heptamethyl-*trans*-corrin, synthesized previously from the same intermediate *(3a)* [4d], has recently been characterized by an X-ray structure determination carried out by *P. Galen-Lenhert* [28].

Under reaction conditions which almost quantitatively convert the palladium(II) complex *(19)* into the *trans*-corrin complex *(20)*, no reaction of the corresponding nickel(II) complex could be detected spectroscopically. The same holds for the irradiation of the nickel complex at higher temperature (*e.g.* in triglyme at 150 °C). In the first instance, X-ray structural analysis will have to provide information as to whether or not it is justified to correlate this drastic reactivity difference with a corresponding difference in the geometry of the two seco-corrinoid complexes. It is well known that the palladium(II) ion has a stronger tendency towards a planar coordination than the nickel(II) ion [29]. Finally, no UV-spectroscopic indication for the occurence of a thermally-induced cycloisomerization *(6)*→*(7)*, of either the palladium complex *(19)* or the related nickel complex, has been obtained so far.

The fact of the cycloisomerization *(19)*→*(20)* (surprising as it is, after all) does lend substance to the reaction mechanism *(6a)*→*(6b)*→*(7)* envisaged in the planning stage of the work, but, of course, it does not confirm it. In particular, the light-induction and the observed nickel-palladium reactivity difference pose a series of questions which are not answered yet. The experimental study of these and other questions is proceeding.

This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung. We thank Dr. D. St. C. Black for translation of the German manuscript.

Received: January 23, 1969 [A 694 IE]
German version: Angew. Chem. *81*, 301 (1969)

[26] *A. P. Johnson, P. Wehrli, R. Fletcher,* and *A. Eschenmoser,* Angew. Chem. *80*, 622 (1968); Angew. Chem. internat. Edit. *7*, 623 (1968).

[27] The choice of this ring component was conditioned by the intention to aim at a corrin derivative which eventually can be identified by direct comparison. For the preparation of (5) see the appendix to Scheme 2.

[28] We thank Prof. *P. Galen-Lenhert* for communication of his unpublished results.

[29] See *e.g.* the difference in behaviour of the nickel(II)- and the palladium(II)-complexes of the bicyclic lactam *(14)* in the synthesis of the corphin system [26].

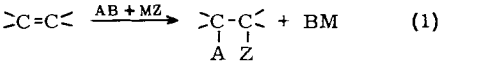
Conjugated Additions in Hydrogen Fluoride

By L. S. German and I. L. Knunyantz [*]

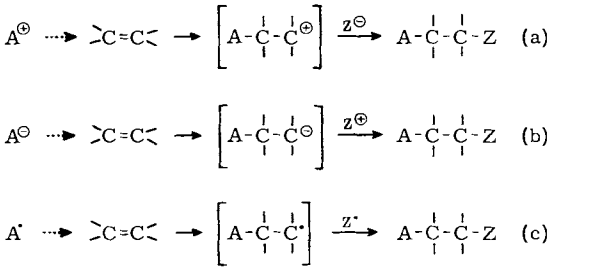
Fluorine and another substituent can be added in a single step to compounds having CC double bonds in anhydrous hydrogen fluoride. It is possible in this way to obtain e.g. α-fluorinated β-halogeno, β-alkyl, β-nitro, and β-amino compounds, and also (in some cases by secondary reactions) fluorinated ethers, alcohols, esters, and carboxylic acids, β-fluoro alcohols can be obtained by conjugated "hypofluorination" in the presence of oxenium ions.

1. Introduction

Fluorinated organic compounds containing functional groups can be obtained by several methods. For example, the desired number of fluorine atoms may be introduced into a (simple) organic molecule, followed by a functional group, or a compound that already contains a functional group may be fluorinated. Among the methods for the simultaneous introduction of fluorine and a functional group, conjugated addition to olefins with the aid of fluoride ions occupies a special place. "Conjugated" additions are additions in which two substituents that were not connected to each other in the starting compounds are added to the double bond [eq. (1)].

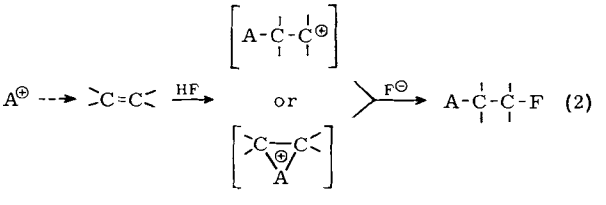


(1)



(a) (b) (c)

These reactions may proceed by (a) electrophilic, (b) nucleophilic, or (c) free radical mechanisms. In reactions of the ionic type, the attacking species A need not carry a full charge; AB could be a polar molecule containing sufficiently electrophilic [case (a)] or nucleophilic centers [case (b)].



(2)

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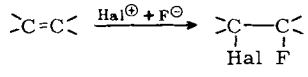
The present article will deal with electrophilic conjugated additions in which the intermediate cation is stabilized by fluoride ions from hydrogen fluoride [case (a) with MZ = HF, eq. (2)].

In this process the hydrogen fluoride also acts as an electrophilic catalyst. The acidity of the medium can, if desired, be increased by addition of SbF_5 or BF_3, or decreased by addition of metal fluorides, ethers, *etc.*

The ease with which the acidity of the solvent (and hence the electrophilicity of the process) can be altered, the high concentration of fluoride ions per unit volume, and the ready availability of hydrogen fluoride permit the use of the latter as a specific bifunctional medium (catalyst-reagent) in conjugated additions.

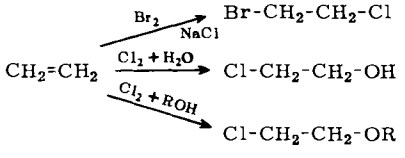
2. Synthesis of Organofluorine Compounds

2.1. Halogenation



(3)

Conjugated halogenation is a classic example of a conjugated addition [1]. The method has been used for the preparation of halogeno ethers, vicinal dihalogenoalkanes with different halogen atoms, *etc.*



(4)

The first attempts to use fluoride ions in conjugated halogenations were unsuccessful. Thus the reaction of elementary bromine with ethylene in hydrofluoric acid led only to 1,2-dibromoethane [2]. The reaction of chlorine with ethylene in saturated $NaHF_2$ solution, which leads to 1-chloro-2-fluoroethane, was described

[1] *E. Biilmann*, Recueil Trav. chim. Pays-Bas *36*, 313 (1916); *J. Conant* and *E. Jackson*, J. Amer. chem. Soc. *46*, 1727 (1924); *A. Francis*, *ibid.* *47*, 2340 (1925); *P. Bartlett* and *D. Tarbell*, *ibid.* *58*, 466 (1936).

[2] *A. I. Titov* and *F. L. Maklyaev*, Ž. obšč. Chim. *24*, 1631 (1954).

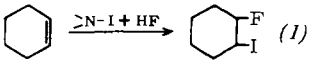
in 1954[3]. Other applications of the method and its reproducibility were not, however, reported.

The conjugated addition of bromine and fluorine to double bonds of steroids was achieved independently by two groups of investigators in 1959, by reaction of the steroid with *N*-bromosuccinimide and HF in CH_2Cl_2/tetrahydrofuran[4,5].

$$\geq C{=}C\leq \xrightarrow{\geq N\text{-}Br + HF} \underset{Br\ F}{\geq C{-}C\leq} \text{ - trans} \qquad (5)$$

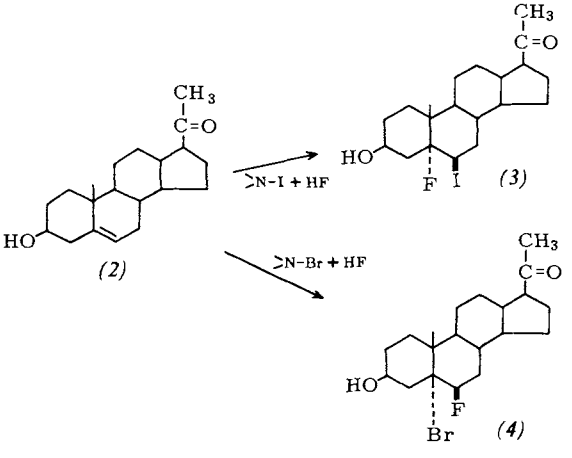
This method has become very widely used for the synthesis of steroids containing fluorine, particularly 6-fluoro steroids having a hormone action. The favor in which this reaction is held is due to its high selectivity and its stereospecificity, giving only *trans* addition products (for further examples see[6–10]).

The addition of chlorine and fluorine to double bonds of steroids has been effected in a number of solvents with *N*-chlorosuccinimide/HF[8,9,11]. Vicinal fluoroiodohydrocarbons can be readily obtained by treatment of olefins with *N*-iodosuccinimide/HF in tetrahydrofuran; for example, *(1)* is obtained in 73% yield[11].



(1)

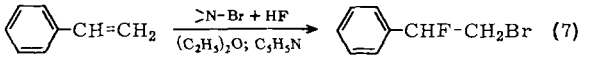
A number of anomalies have been observed in the conjugated iodination of steroids containing double bonds. Thus the reaction of *N*-iodosuccinimide and HF with Δ^5-steroids such as *(2)* yields 5α-fluoro-6β-iodo compounds such as *(3)*, whereas bromine and fluorine add to *(4)* in the reverse sense[12].



The conjugated addition of bromine and fluorine to 1-alkenes (molar quantities of *N*-bromosuccinimide, excess of HF, diethyl ether as the solvent) gives 1-bromo-2-fluoroalkanes in 70–80% yield, together with insignificant amounts of 2-bromo-1-fluoroalkanes[13]. Reaction with the solvent yields brominated ethers $RCH(OC_2H_5)CH_2Br$ as by-products. Branched olefins, such as 2-ethyl-2-butene, do not react so readily.

$$R\text{-}CH{=}CH_2 \xrightarrow[(C_2H_5)_2O]{\geq N\text{-}Br + HF} \begin{matrix} R\text{-}CHF\text{-}CH_2Br \\ + \ R\text{-}CHBr\text{-}CH_2F \end{matrix} \qquad (6)$$

The conjugated halogenation of styrene under the usual conditions yields an appreciable quantity of tarry products, but this quantity can be greatly reduced by addition of pyridine.



(7)

As is usual in electrophilic additions to allyl halides, both possible orientations are found in the conjugated bromination of allyl bromide.

$$CH_2{=}CH\text{-}CH_2Br \xrightarrow{\geq NBr + HF} \begin{matrix} CH_2Br\text{-}CHF\text{-}CH_2Br & 22\% \\ CH_2Br\text{-}CHBr\text{-}CH_2F & 32\% \end{matrix} \qquad (8)$$

The esters of some α,β-unsaturated acids[14,15], as expected, give exclusively the esters of the α-bromo-β-fluoro carboxylic acids on bromination.

$$\begin{matrix} R\text{-}CH{=}CH\text{-}COOCH_3 \\ \downarrow \geq N\text{-}Br + HF \\ R\text{-}CHF\text{-}CHBr\text{-}COOCH_3 \\ R = H,\ C_6H_5 \end{matrix} \qquad (9)$$

Diethyl maleate and diethyl fumarate react similarly[14]. A new synthesis of methyl α-fluoroacrylate *(5)*[14,15] was achieved by conjugated addition of "BrF" to the CC double bonds of allyl trichloroacetate.

Apart from *N*-bromosuccinimide and *N*-bromoacetamide, 1,3-dibromo-5,5-dimethylhydantoin and 1-bromo-3,5,5-trimethylhydantoin[15] have also been successfully used as brominating agents in conjugated additions. 1,3-Dibromo-5,5-dimethylhydantoin has the advantage that it is readily soluble in ether/HF.

The conjugated chlorination of some olefins and halogenoolefins in anhydrous HF with chlorine or

[3] *C. Thomas*, US-Pat. 2673884 (1954); Chem. Abstr. *49*, 4007 (1955).

[4] *A. Bowers*, J. Amer. chem. Soc. *81*, 4107 (1959).

[5] *C. Robinson, L. Finckenor, E. Olivero*, and *D. Gould*, J. Amer. chem. Soc. *81*, 2191 (1959).

[6] *D. Gould, M. Reimann*, and *L. Finckenor*, US-Pat. 3009938 (1959); Chem. Abstr. *56*, 7396 (1962).

[7] *A. Bowers, L. Ibanez, E. Denot*, and *R. Becerra*, J. Amer. chem. Soc. *82*, 4001 (1960).

[8] *H. Reimann* and *D. Gould*, US-Pat. 3009932 (1961); Chem. Abstr. *56*, 10245 (1962).

[9] *H. Reimann* and *D. Gould*, US-Pat. 3009929 (1961); Chem. Abstr. *56*, 11672 (1962).

[10] *H. Hess, S. Figor, G. Hughes*, and *W. Moreland*, US-Pat. 3042696 (1962); Chem. Abstr. *57*, 15205 (1962).

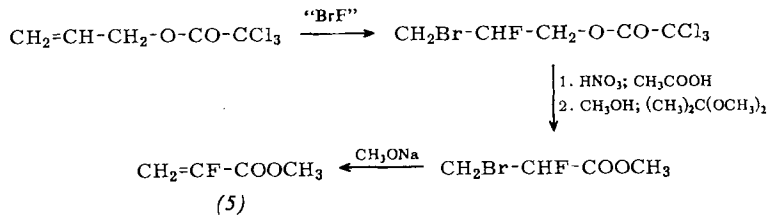
[11] *H. Reimann* and *D. Gould*, US-Pat. 3009928 (1961); Chem. Abstr. *56*, 6049 (1962).

[12] *A. Bowers, E. Denot*, and *R. Becerra*, J. Amer. chem. Soc. *82*, 4007 (1960).

[13] *F. Pattison, D. Peters*, and *F. Dean*, Canad. J. Chem. *43*, 1700 (1965).

[14] *A. Bose, K. Das*, and *T. Jacob*, Chem. and Ind. *1963*, 452; *A. Bose, K. Das*, and *P. Funke*, J. org. Chemistry *29*, 1202 (1964).

[15] *F. Dean* and *F. Pattison*, Canad. J. Chem. *43*, 2415 (1965).



(5)

hexachloromelamine was investigated in 1966 [16]. Thus when chlorine and ethylene are passed simultaneously into an excess of anhydrous hydrogen fluoride at −20 to −30 °C, some 1-chloro-2-fluoroethane is obtained by conjugated "chlorofluorination", together with 1,2-dichloroethane formed by addition of chlorine. 1,1-Dichloroethylene reacts similarly.

$$\begin{aligned} CH_2{=}CH_2 &\xrightarrow{Cl_2 + HF} CH_2Cl{-}CH_2F \quad 17\% \\ &\quad + \\ &\quad CH_2Cl{-}CH_2Cl \quad 75\% \\ CH_2{=}CCl_2 &\xrightarrow{Cl_2 + HF} CH_2Cl{-}CCl_2F \quad 21\% \\ &\quad + \\ &\quad CH_2Cl{-}CCl_3 \end{aligned} \qquad (10)$$

The formation of two chlorination products can probably be explained by the fact that ionization of the chlorine molecule ($Cl_2 \rightarrow Cl^+ + Cl^-$) is negligible in anhydrous HF, and the unionized chlorine molecule adds as a whole to the double bond. The yield of chlorofluoroalkane should therefore be increased by an increase in the Cl^+ concentration; it did in fact increase slightly when HF containing urea was used. The intermediate *N*-chlorination products of urea might transfer chlorine in this case.

Chlorofluoroalkanes can be obtained in 60–65% yield by the addition of an olefin to a mixture of hexachloromelamine and HF at or slightly above atmospheric pressure [16]. Examples of suitable olefins are ethylene, propene, 1,1-dichloroethylene, and 1,1-difluoroethylene, as well as methyl acrylate. The chlorofluorination of cyclohexene proceeds readily in HF/hexachloromelamine/diethyl ether.

The addition to unsymmetric olefins is oriented strictly in accordance with the polarity of the double bond, as is to be expected of an ionic process.

$$\begin{aligned} CH_3{-}CH{=}CH_2 \\ CF_2{=}CH_2 \\ CH_2{=}CH{-}COOCH_3 \end{aligned} \xrightarrow{>NCl + HF} \begin{aligned} CH_3{-}CHF{-}CH_2Cl \\ CF_3{-}CH_2Cl \\ CH_2F{-}CHCl{-}COOCH_3 \end{aligned} \qquad (11)$$

The conjugated halogenation of olefins in the presence of HF probably proceeds in the same way as other conjugated additions. The first step is the attack of the Cl^+, Br^+, or I^+ ion on the π bond of the olefin to form a three-membered 'onium complex with the halogen. The second step is the nucleophilic attack of the fluoride ion on this complex, with formation of the *trans* adduct as usual.

$$>C{=}C< \xrightarrow{Hal^\oplus} >C(\overset{\oplus}{Hal})-C< \xrightarrow{F^\ominus} >C(Hal)-C(F)< \qquad (12)$$

Hal = Cl, Br, I

The positive ion formed from the olefin and the halogen cation is capable of an electrophilic attack on the aromatic nucleus [16]. Thus the reaction of hexachloromelamine with a mixture of ethylene and benzene in the presence of HF yields 8% of β-chloroethylbenzene, together with 1-chloro-2-fluoroethane and mono- and dichlorobenzenes. The possibility that β-chloroethylbenzene is formed in a secondary reaction, such as the alkylation of benzene by initially formed 1-chloro-2-fluoroethane, has been ruled out by special experiments, which showed that benzene is not alkylated by either 1-chloro-2-fluoroethane or 1,2-dichloroethane under the conditions of the reaction.

The competing electrophilic attack of Cl^+ on the aromatic nucleus could be responsible for the low yield of β-chloroethylbenzene. At lower olefin concentrations and with higher π-electron densities on the aromatic molecule than on the olefin, the reaction generally yields halogenobenzenes.

2.2. Nitration

$$>C{=}C< \xrightarrow{NO_2^\oplus + F^\ominus} >C(NO_2)-C(F)<$$

The first example of a conjugated nitration of olefins was the reaction of a 10% solution of HNO_3 in HF with 1,1-dichloroethylene at −10 °C. Other olefins also react under these conditions [17].

$$\begin{aligned} CH_2{=}CCl_2 \\ CHCl{=}CCl_2 \\ CH_2{=}CHCl \\ CF_2{=}CF_2 \\ CH_3{-}CH{=}CH_2 \end{aligned} \xrightarrow{HNO_3 + HF} \begin{aligned} NO_2{-}CH_2{-}CCl_2F \\ NO_2{-}CHCl{-}CCl_2F \\ NO_2{-}CH_2{-}CHClF \\ NO_2{-}CF_2{-}CF_3 \\ NO_2CH_2{-}CHF{-}CH_3 \end{aligned} \qquad (13)$$

It was later found that the reaction rate depends only slightly on the excess of HF, but is strongly dependent on the nature of the double bond in the olefins [18–21]. Thus the nitrofluorination of 1,1-dichloroethylene and of 1,1-difluoroethylene is sufficiently fast even at −60 °C, whereas the reaction of trifluoroethylene under these conditions is slower by a factor of six. Fluoronitroalkanes are formed only slowly from tetrafluoroethylene and from chlorotrifluoroethylene at 10–20 °C, and increased pressures and temperatures are necessary for the successful nitrofluorination of hexafluoropropene. The relative rates and the reaction order confirm the ionic and electrophilic nature of the process.

If the double bond in the olefin is not sufficiently polar, nitrofluorination yields two isomeric fluoronitro-

[16] *I. L. Knunyantz* and *L. S. German*, Izvest. Akad. Nauk SSSR, Ser. chim. *1966*, 1065.

[17] *A. I. Titov*, Doklady Akad. Nauk SSSR *149*, 330 (1963). Akad. Nauk SSSR, Otdel. chim. Nauk *1963*, 1946.

[18] *I. L. Knunyantz, L. S. German*, and *I. N. Rozhkov*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1963*, 1946.

[19] *I. L. Knunyantz, B. L. Dyatkin, L. S. German, I. N. Rozhkov*, and *V. A. Komarov*, Ž. vses. chim. Obšč. im. D.I. Mendeleeva *8*, 709 (1965).

[20] *I. L. Knunyantz, L. S. German*, and *I. N. Rozhkov*, Ž. vses. chim. Obšč. im. D.I. Mendeleeva *10*, 599 (1965).

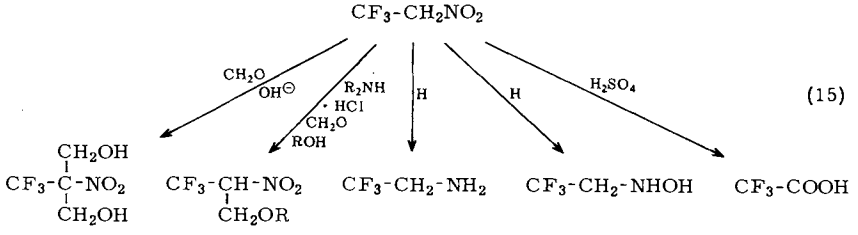
[21] *I. L. Knunyantz, L. S. German*, and *I. N. Rozhkov*, Russ. Pat. 152235 (1962).

alkanes. Examples are the reactions of allyl chloride and chlorotrifluoroethylene [18].

$$CH_2{=}CH{-}CH_2Cl \xrightarrow{HNO_3+HF} \begin{matrix} NO_2{-}CH_2{-}CHF{-}CH_2Cl \\ + \\ CH_2F{-}CH(NO_2){-}CH_2Cl \end{matrix} \quad (14)$$

$$CF_2{=}CFCl \xrightarrow{HNO_3+HF} \begin{matrix} CF_2Cl{-}CF_2NO_2 \\ + \\ CF_3{-}CFCl{-}NO_2 \end{matrix}$$

Many organofluorine compounds can be prepared from the resulting fluoronitroalkanes [21–26] [for examples see eq. (15)].

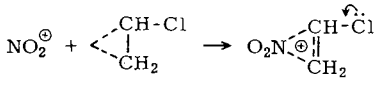


(15)

The nitrofluorination of ethylene followed by acid hydrolysis of the resulting β-fluoronitroethane to form monofluoroacetic acid could be of industrial interest [20, 21].

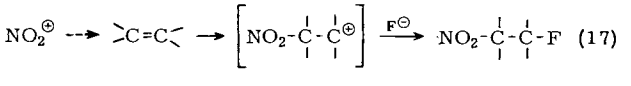
Nitrofluorination of methyl acrylate gives methyl 3-fluoro-2-nitropropionate, which can be converted into methyl 3-hydroxy-2-nitropropionate. Reduction of this last compound followed by hydrolysis yields DL-serine [26].

The nitrofluorination, as illustrated here for the case of chloroethylene, probably proceeds by formation of a three-membered transition complex and subsequent ring opening by fluoride ions [17]. An alternative is suggested in eq. (17).



(16)

$$\xrightarrow{F^{\ominus}} O_2N{-}CH_2{-}CHClF$$



(17)

It would probably be possible to decide between these two possibilities by nitrofluorination of *cis-trans* isomeric olefins. If the reaction proceeds *via* a transition complex in accordance with eq. (16), it should lead only to *trans* addition, whereas eq. (17) does not permit stereospecific addition.

[22] *I. L. Knunyantz, L. S. German,* and *I. N. Rozhkov,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1963*, 1950.

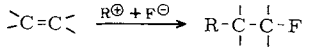
[23] *I. L. Knunyantz, L. S. German,* and *I. N. Rozhkov,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1964*, 1630.

[24] *I. L. Knunyantz, L. S. German, I. N. Rozhkov,* and *B. L. Dyatkin,* Izvest. Akad. Nauk SSSR, Ser. chim. *1966*, 250.

[25] *I. L. Knunyantz, L. S. German, B. L. Dyatkin,* and *I. N. Rozhkov,* Russ. Pat. 168307 (1965); Chem. Abstr. *62*, 16053 (1965).

[26] *I. N. Rozhkov,* Dissertation, Institute of Elementoorganic Compounds of the Academy of Sciences of the USSR, Moscow 1963.

2.3. Alkylation



The HF-catalyzed alkylation of olefins has been extensively studied in connection with the industrial production of paraffins from higher olefins. Higher alkyl fluorides were formed as undesirable by-products. Some of the reactions described could be interpreted as typical conjugated "fluoroalkylations".

Thus 1-fluoro-3,3-dimethylbutane was obtained in 26% yield, together with a large quantity of polymeric products, from isobutylene and ethylene in HF [27]. 2-Methyl-1-butene similarly gives 1-fluoro-3,3-dimethylpentane.

tert-Butyl and *tert*-amyl alcohols have also been successfully used in the conjugated fluoroalkylation of ethylene [28].

$$CH_3{-}\underset{\underset{R}{|}}{\overset{\overset{CH_3}{|}}{C}}{-}OH + CH_2{=}CH_2 \xrightarrow{HF} CH_3{-}\underset{\underset{R}{|}}{\overset{\overset{CH_3}{|}}{C}}{-}CH_2{-}CH_2F \quad (18)$$

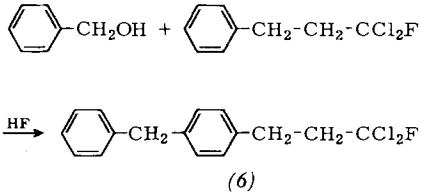
$$R = CH_3,\ C_2H_5$$

Alcohols having labile hydroxyl groups react under mild conditions with 1,1-dichloroethylene in HF to form halogeno hydrocarbons containing CCl_2F groups [29].

$$ROH + CH_2{=}CCl_2 \xrightarrow{HF} R{-}CH_2{-}CCl_2F \quad (19)$$

R = *tert*-butyl, *tert*-amyl, benzyl, α-phenethyl

Benzyl alcohol gives *p*-(3,3-dichloro-3-fluoropropyl)-diphenylmethane *(6)* as a by-product, formed by electrophilic benzylation of the initially formed dichlorofluoropropylbenzene.



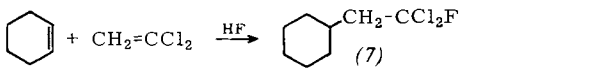
(6)

Cyclohexene reacts with 1,1-dichloroethylene to form (2,2-dichloro-2-fluoroethyl)cyclohexane *(7)*.

[27] *C. Linn* and *L. Schmerling,* US-Pat. 2451843, (1948); Chem. Abstr. *43*, 2628 (1949).

[28] *C. Linn* and *L. Schmerling,* US-Pat. 2539668 (1951); Chem. Abstr. *45*, 5710 (1951).

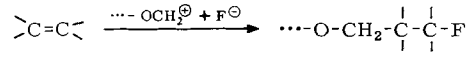
[29] *L. S. German* and *I. L. Knunyantz,* Izvest. Akad. Nauk SSSR, Ser. chim. *1967*, 675.



(7)

The conjugated fluoroalkylation of olefins in the presence of anhydrous HF can generally be described by a carbonium ion mechanism. However, the course of the reaction is influenced by complex formation and solvation, which are characteristic of hydrogen fluoride solutions; in the alkylation of some aromatic compounds in the presence of HF, no free carbonium ions could be detected. Thus the reaction of benzene with optically active *sec*-butanol in HF yields *sec*-butylbenzene, which is also active[30]. Kinetic studies on the alkylation of toluene with *tert*-butyl chloride in HF were also incompatible with the intermediate formation of *tert*-butyl cations[31]. The carbonium ion concept can, however, be successfully applied in most cases, with the reservation that the carbonium ion need not exist as a kinetically independent species.

2.4. Hydroxymethylation and Related Processes



The electrophilic α-hydroxyalkylation of olefins (Prins reaction) is often used for the synthesis of compounds such as 1,3-glycols, 1,3-dioxolanes, and halogeno carboxylic acids[32]. The Prins reaction in HF offers a convenient route to organofluorine compounds containing oxygen. The reaction of tetrafluoroethylene with formaldehyde in anhydrous hydrogen fluoride[33]

$$CF_2=CF_2 \xrightarrow[50\,^\circ C]{(CH_2O)_x + HF} CF_3-CF_2-CH_2OH + CF_3-CF_2-CH_2-O-CH_2F \qquad (19a)$$

yields pentafluoropropanol and the corresponding fluoromethyl ether, as well as a number of by-products[34]. When 80% hydrofluoric acid or a mixture of HF with H_2SO_4 is used, only pentafluoropropanol is obtained. Hexafluoropropene reacts similarly[35].

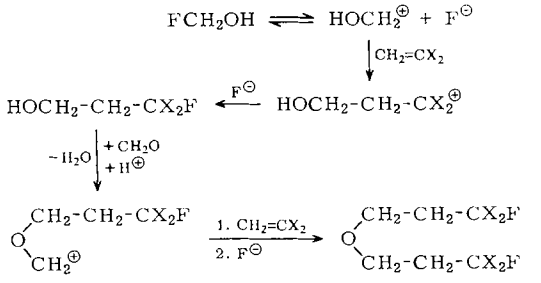
$$CF_3-CF=CF_2 \xrightarrow{(CH_2O)_x + HF} (CF_3)_2CF-CH_2OH \qquad (20)$$

1,1-Difluoroethylene, 1,1-dichloroethylene, and 1-chloroethylene react readily with a 15% solution of paraformaldehyde in HF to give symmetrical fluoro ethers[36,37] (a similar process was described in[34]).

$$2\,CH_2=CXX^1 \xrightarrow{(CH_2O)_x + HF} (CFXX^1-CH_2-CH_2)_2O \qquad (21)$$

(a), X=X¹=Cl; *(b)*, X=X¹=F; *(c)*, X=H, X¹=Cl

According to[34], the reaction of HF with paraformaldehyde yields fluoromethanol and symmetrical difluorodimethyl ether. Hydrogen fluoride, as a strong acid, facilitates dissociation of the fluoromethanol into a hydroxymethyl cation, which carries out an electrophilic attack on the double bond of the olefin[*], and a fluoride ion.



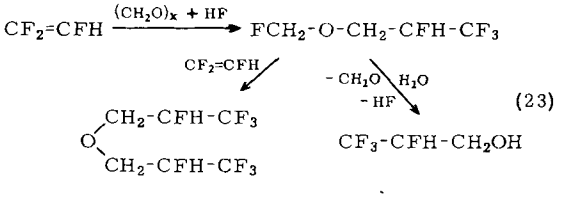
Whereas fluoromethyl pentafluoropropyl ether is formed as the principal product according to eq. (19), a second olefin molecule is inserted into the C–F bond of the fluoromethyl group in the case of halogeno olefins containing hydrogen.

This abnormal behavior can probably be explained by the difference in the ease of dissociation of the C–F bond in fluoromethyl ethers of the type $CX_3-CH_2-CH_2-O-CH_2F$ (X = halogen) and in perfluoro alcohols with unfluorinated CH_2OH groups. For example the pentafluoroethyl group in $C_2F_5-CH_2-O-CH_2F$ reduces the basicity of the ether oxygen, so that the dissociation at the C–F bond is also reduced[**]. If the polyhalogenoalkyl group is situated farther away from the oxygen atom, its inductive effect is much weaker and the fluoromethyl group can readily dissociate at the C–F bond.

$$CF_3-CF_2-CH_2-O-CH_2F \not\longrightarrow CF_3-CF_2-CH_2-O-CH_2^+ + F^- \qquad (22)$$

$$CF_3-CH_2-CH_2-O-CH_2F \longrightarrow CH_3-CH_2-CH_2-O-CH_2^+ + F^-$$

It should be mentioned that the reaction with trifluoroethylene yields 2,3,3,3-tetrafluoropropanol as well as the symmetrical ether[37]. The alcohol is probably formed by hydrolysis of the intermediate fuoromethyl ether.



After condensation of 1,1-dichloroethylene with CH_2O in HF, the ester *(8)* and the ether *(9)* were isolated. The formation of these compounds can be described by eq. (24).

[30] *R. Burwell* and *S. Archer*, J. Amer. chem. Soc. *64*, 1032 (1942).

[31] *J. Simons* and *J. Sprauer*, J. Amer. chem. Soc. *64*, 648 (1942).

[32] *W. Barendrecht*, Chem. Weekbl. *54*, 404 (1958).

[33] *V. Weinmayr*, US-Pat. 2992276 (1961); Chem. Abstr. *55*, 23347 (1961).

[34] *V. Weinmayr*, J. org. Chemistry *28*, 492 (1963).

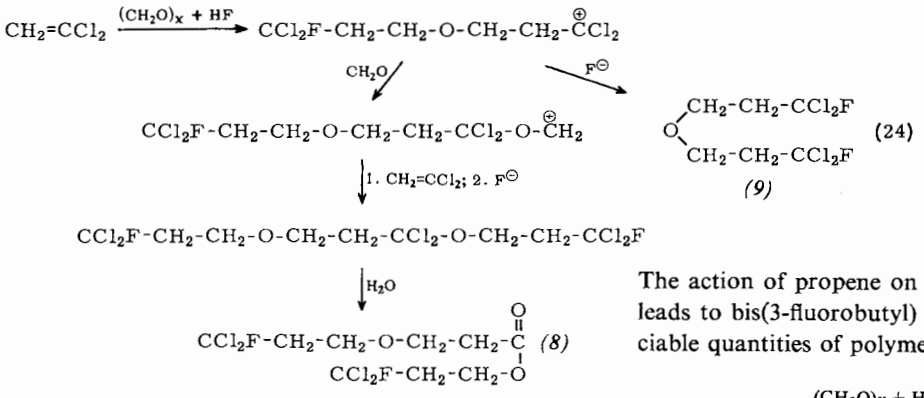
[35] *V. Weinmayr*, US-Pat. 2999884 (1961); Chem. Abstr. *56*, 325 (1962).

[36] *I. L. Knunyantz* and *L. S. German*, Russ. Pat. 154857 (1962); Chem. Abstr. *60*, 5337 (1964).

[37] *L. S. German* and *I. L. Knunyantz*, Ž. vses. chim. Obšč. im. D.I. Mendeleeva *11*, 354 (1966).

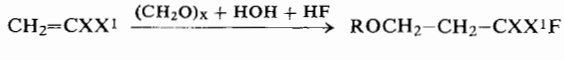
[*] Bis(fluoromethyl) ether can also dissociate at the C–F bond, but this does not appreciably influence the condensation scheme.

[**] The condensation of $C_2F_5-CH_2-O-CH_2F$ with $CF_2=CF_2$ is possible only at high temperatures and under pressure.



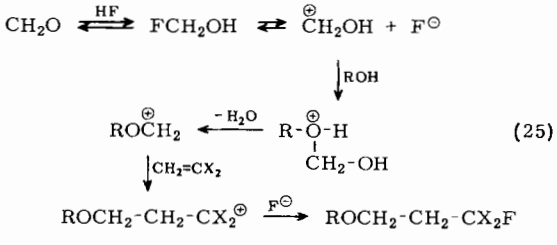
The cation with the charge on the dichloromethyl group can thus not only be stabilized by fluoride ions but can also carry out an electrophilic attack on the carbonyl oxygen in formaldehyde.

A hypothesis on the intermediate formation of fluoro alcohols in the condensation of formaldehyde with halogenoolefins containing hydrogen in HF was later verified [38, 39]. According to this hypothesis this reaction in the presence of aliphatic alcohols yields only unsymmetrical ethers.



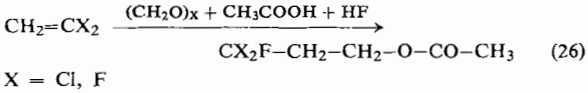
R = CH_3, C_2H_5, C_4H_9, $ClCH_2$–CH_2
X=X¹=F; X=X¹=Cl; X=Cl, X¹=H

We proposed the scheme shown in eq. (25) for this reaction.



Many alcohols (excluding benzyl and allyl alcohols, which readily dissociate in HF) can take part in condensations of olefins with formaldehyde.

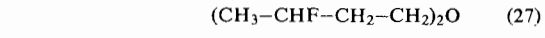
1,1-Dichloroethylene and 1,1-difluorethylene can be acetoxymethylated [38].



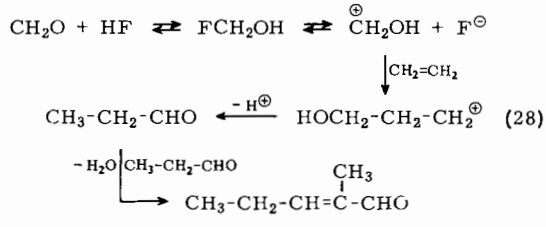
X = Cl, F

These esters are formed in the same manner as the unsymmetrical ethers [see eq. (25)]. Direct reaction of the halogeno olefins with formaldehyde to form a symmetrical ether containing fluorine competes effectively with ester-formation.

The action of propene on paraformaldehyde and HF leads to bis(3-fluorobutyl) ether, together with appreciable quantities of polymeric products [40].

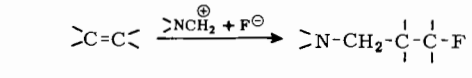


The reaction of ethylene with paraformaldehyde and HF in solution yields about 43% of 2-methyl-2-pentenal [40]. We believe that the reaction proceeds in accordance with eq. (28).

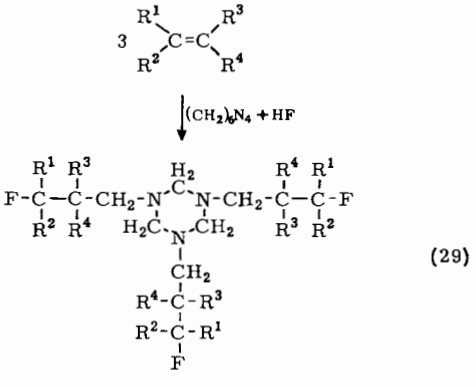


How does the β-hydroxypropyl cation change into (protonated) propionaldehyde? In our opinion a hydride ion migrates from the α to the γ position of the cation. The driving force for the isomerization is the tendency of the system to form a stable oxonium ion.

2.5. Aminomethylation



In conjugated aminomethylation in anhydrous HF with hexamethylenetetramine, chloroolefins and fluoroolefins react under mild conditions to give *sym-*



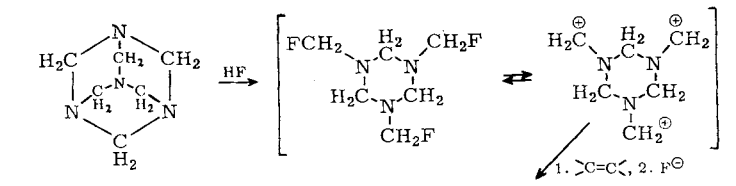
(29)

(a), $R^1 = R^2 = Cl$, $R^3 = R^4 = H$
(b), $R^1 = R^2 = F$, $R^3 = R^4 = H$
(c), $R^1 = R^2 = R^3 = F$, $R^4 = H$
(d), $R^1 = R^2 = R^3 = R^4 = F$

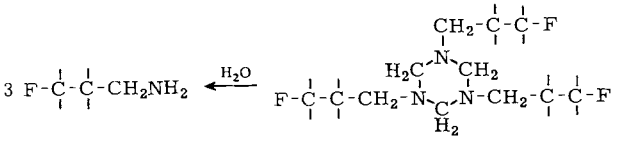
[38] *L. S. German* and *I. L. Knunyantz*, Ž. vses. chim. Obšč. im. D.I. Mendeleeva *11*, 356 (1966).

[39] *L. S. German* and *I. L. Knunyantz*, Russ. Pat. 154858 (1962); Chem. Abstr. *60*, 6749 (1964).

[40] *L. S. German* and *I. L. Knunyantz*, Izvest. Akad. Nauk SSSR, Ser. chim. *1967*, 677.



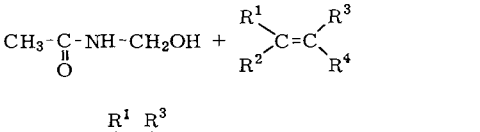
(30)



hexahydrotriazines containing *N*-polyhalogenoalkyl groups [41,42].

The hydrolysis of the *sym*-hexahydrotriazines readily yields the amines; moreover, this reaction also proceeds during the conjugated aminomethylation. We propose the course shown in eq. (30). The indicated cleavage of hexamethylenetetramine in anhydrous HF has actually been established [43].

Acetamidomethylation of halogenoolefins in HF solution yields *N*-(polyhalogenopropyl)acetamides [42]. The reaction proceeds *via* protonation at the nitrogen, elimination of water, and addition of the halogenoolefin and the fluoride ion.

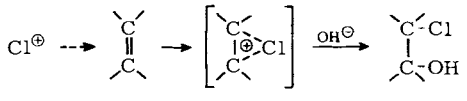


(31)

(a), $R^1 = R^2 = Cl$, $R^3 = R^4 = H$
(b), $R^1 = R^2 = F$, $R^3 = R^4 = H$
(c), $R^1 = R^2 = R^3 = F$; $R^4 = H$
(d), $R^1 = R^2 = R^3 = R^4 = F$

2.6. Conjugated Hypofluorination

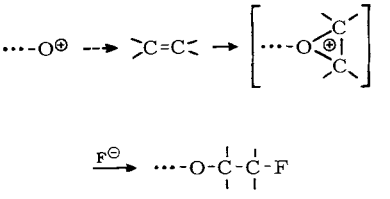
The chlorination and bromination of olefins in alkaline media are widely used methods for the preparation of β-halogeno alcohols. The conjugated hypohalogenation is generally assumed to follow eq. (32).



(32)

Hypofluorination by this scheme is impossible, since the fluorine molecule does not dissociate into the ions ($F_2 \rightarrow F^+ + F^-$) under the usual conditions.

One possibility for ionic hypofluorination could be the reaction of an olefin with an oxenium ion in the presence of a fluoride-ion generator. This reaction was carried out in 1966 with 1,1-dichloroethylene and 1,1-difluoroethylene, which were treated with a solution of CrO_3 in anhydrous HF [44].



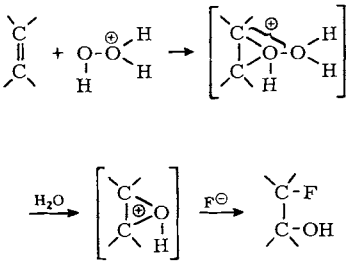
(33)

We believe that the initially formed chromyl difluoride carries out an electrophilic attack on the double bond of the olefin.

$$CX_2{=}CH_2 \xrightarrow{1.\ CrO_3 + HF,\ 2.\ H_2O} CX_2F{-}CH_2OH \qquad (34)$$

X = F or Cl

Hydrogen peroxide reacts in the same way as chromyl fluoride with halogenoolefins in HF. It is known that in strongly acidic media, H_2O_2 forms the conjugate acid $H_3O_2^+$, which is an OH^+ donor. The reaction of H_2O_2 and olefins in HF solution can thus be formulated in accordance with eq. (35).



(35)

The reaction of 1,1-dichloroethylene with 85 to 90% H_2O_2 in anhydrous HF gives 2,2-dichloro-2-fluoroethanol in 7% yield [45].

$$CCl_2{=}CH_2 \xrightarrow{H_2O_2 + HF} CCl_2F{-}CH_2OH \qquad (36)$$

The yield can be improved to 25–30% by addition of acetic anhydride. Dichlorofluoroethyl acetate is formed as a by-product.

The reaction should proceed more readily in more strongly acidic solution. The overall yield of dichlorofluoroethanol and its acetate is in fact increased to 42% in the presence of catalysts for electrophilic reactions (*e.g.* BF_3 or SbF_5). Similarly, 2-chloro-2-fluoroethanol

[41] *I. L. Knunyantz, L. S. German,* and *A. V. Podol'ski,* Russ. Pat. 180606 (1965); Chem. Abstr. *65,* 12219 (1966).

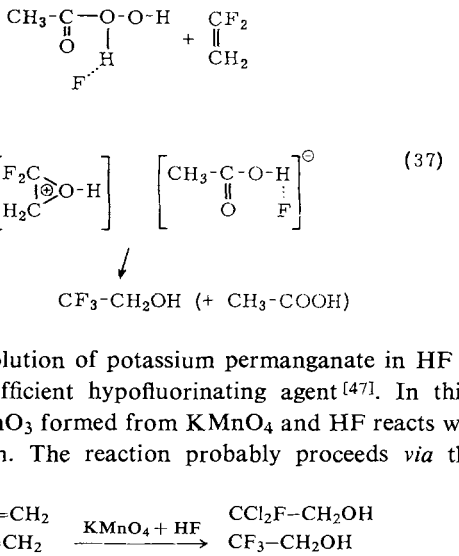
[42] *A. V. Podol'ski, L. S. German,* and *I. L. Knunyantz,* Izvest. Akad. Nauk SSSR, Ser. chim. *1966,* 1575.

[43] *L. S. German, I. L. Knunyantz,* and *A. V. Podol'ski,* Chim. geterocikličceskich Soedinenij *1966,* 938.

[44] *L. S. German* and *I. L. Knunyantz,* Doklady Akad. Nauk SSSR *166,* 602 (1966).

[45] *L. S. German, G. G. Belen'ki,* and *I. L. Knunyantz,* Doklady Akad. Nauk SSSR *171,* 1333 (1966).

and its acetate are obtained in a total yield of 30% from vinyl chloride. 1,1-Difluoroethylene can be hypofluorinated with freshly prepared peroxyacetic acid in the presence of HF[46].



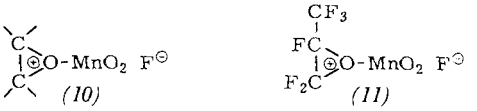
A solution of potassium permanganate in HF is also an efficient hypofluorinating agent[47]. In this case $FMnO_3$ formed from $KMnO_4$ and HF reacts with the olefin. The reaction probably proceeds *via* the ion

$$\begin{array}{l} CCl_2{=}CH_2 \\ CF_2{=}CH_2 \\ CHCl{=}CH_2 \end{array} \xrightarrow{KMnO_4 + HF} \begin{array}{l} CCl_2F{-}CH_2OH \\ CF_3{-}CH_2OH \\ CHClF{-}CH_2OH \end{array} \qquad (38)$$

[46] *G. G. Belen'ki, L. S. German,* and *I. L. Knunyantz,* Ž. obšč. Chim. *37*, 1687 (1967).

[47] *G. G. Belen'ki, L. S. German,* and *I. L. Knunyantz,* Izvest. Akad. Nauk SSSR, Ser. chim. *1967*, 2780.

(10), which can be stabilized in the reaction with perfluoroolefins ($CF_2{=}CF_2$ and $CF_3{-}CF{=}CF_2$) by cleavage not only of the C–O but also of the O–Mn



bond. The reaction of $KMnO_4$ and HF with perfluoropropene leads to a 30% yield of hexafluoromethyloxirane[47,48].

The presence of such a large number of fluorine atoms in the olefin molecule leads to a decrease in the electron density on the oxygen atom in the complex *(11)*. This explains the ease of cleavage of the oxygen-metal bond.

Other perhalogenoethylenes give only acyl fluorides of the perhalogenoacetic acids on hypofluorination.

$$\begin{array}{l} CF_2{=}CFCl \\ CF_2{=}CCl_2 \\ CFCl{=}CFCl \end{array} \xrightarrow{KMnO_4 + HF} \begin{array}{l} CF_2Cl{-}COF + CF_3{-}COF \\ CFCl_2{-}COF + CF_2Cl{-}COF \\ CF_2Cl{-}COF + CFCl_2{-}COF \end{array}$$

Received: March 29, 1968 [A 689 IE]
German version: Angew. Chem. *81*, 321 (1969)
Translated by Express Translation Service, London

[48] *G. G. Belen'ki, L. S. German,* and *I. L. Knunyantz,* Izvest. Akad. Nauk SSSR, Ser. chim., *1968*, 554.

Crystal Structure Analysis by Neutron Diffraction I[**]

By Georg Will[*]

Neutron diffraction is a valuable complement to X-ray diffraction methods for the determination of crystal structures. A description of the principles of the method is followed by specific examples of the additional information obtained from neutron diffraction experiments: in the structural analysis of benzene, oxalic acid dihydrate, vitamin B_{12}, ferrites, metal cyanides and carbides; and in studies of hydrogen bonding, ferroelectric effects, and thermal vibrations in crystals. Anomalous dispersion in neutron diffraction is also discussed.

1. Introduction

Together with X-ray diffraction, neutron diffraction is one of the most important methods for studying the crystal structure and constitution of molecules. However, whereas X-ray structure analyses are now carried out in many laboratories[1], the use of neutron diffraction is at present very limited. The main reasons for this are the great expense involved in neutron diffraction experiments and the small number of suitable nuclear reactors. With the construction of high-flux reactors[2] having neutron fluxes of the order of 10^{15}

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Mineralogisch-Petrologisches Institut und Museum
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[**] Part I: Neutron diffraction at atomic nuclei. – Part II: "Neutron diffraction and magnetic structure" will appear shortly in this journal.

[1] X-ray structure analysis and its application to problems of molecular constitution have been discussed in this journal on a number of occasions: *e.g. W. Hoppe*, Angew. Chem. *69*, 659 (1957); *G. Habermehl, ibid. 75*, 78 (1963); *M. F. Perutz, ibid. 75*, 589 (1963); *I. C. Kendrew, ibid. 75*, 595 (1963); *W. Hoppe, ibid. 77*, 484 (1965); *78*, 289 (1966); Angew. Chem. internat, Edit. *4*, 508 (1965); *5*, 267 (1966).

[2] The HFBR high-flux reactor at Brookhaven National Laboratory (USA) has a flux density of $\approx 6 \times 10^{14}$ neutrons/cm² sec. A similar reactor with a flux density of $\approx 5 \cdot 10^{15}$ neutrons/cm² sec is under construction at Grenoble (France) as a joint Franco-German project. For comparison, the flux density of the FR2 research reactor at the Kernforschungszentrum Karlsruhe is 4×10^{13} neutrons/cm² sec.

neutrons/cm^2 · sec and higher, it can be forseen that neutron diffraction will become increasingly important as an investigational technique. It does not compete with X-ray diffraction but is a valuable complement to it, and a neutron diffraction study is generally an extension of an X-ray investigation to answer specific questions which are difficult to solve from the X-ray data alone.

The neutron is an uncharged elementary particle. Its most important characteristics are as follows: Mass: $m_n = 1.008922$ atomic mass units (Dalton), Spin: $I_n = 1/2$, Magnetic moment: $\mu_n = 1.91319$ nuclear magnetons (μ_N).

According to de Broglie's equation:

$$\lambda = \frac{h}{mv} \qquad (1)$$

a beam of neutrons can be considered to have wave properties in the same way as a beam of electrons. The wave nature of the neutron was demonstrated in 1936 by diffraction experiments on MgO crystals by *Halban* and *Preiswerk* [3] and *Mitchell* and *Powers* [4]. The neutron sources for these experiments were Ra–Be specimens. However, it was not until the development of nuclear reactors in the years following 1942 that there were neutron sources of high enough intensity for the neutron itself to be used as a probe for studying the properties of solids. The first neutron crystal diffractometer was installed at Oak Ridge in the USA in 1946, and neutron diffraction was first used as an experimental tool by *Wollan* and *Shull* in 1948 [5]. Soon after this an antiferromagnetic spin configuration could be detected in MnO [6] using the magnetic moment associated with the neutron as an atomic probe for the first time.

2. Principle of the Method

2.1. Production of a Neutron Beam

At present practically the only sources of thermal neutrons are nuclear reactors in which fast neutrons are produced by fission and are then slowed down by a moderator (hydrogen, deuterium, or graphite). The velocity distribution of the neutron beams in the reactor is therefore Maxwellian with a maximum at about 2.2×10^5 cm/sec, corresponding to 1.8 Å. The equations for converting velocity v (cm/sec) or energy E (eV) into wavelength λ (Å) are

$$\lambda \mathrel{\hat{=}} \frac{3.956 \times 10^5}{v} \mathrel{\hat{=}} \frac{0.286}{\sqrt{E}} \qquad (2)$$

Wavelengths of the order of the interatomic distances are required to achieve resolution of the atoms in the crystals by neutron diffraction experiments. The wavelengths normally used lie within the range of about 1.0 to 1.1 Å, and thus do not originate from the maximum of the Maxwell curve. (The radiation from the Cu–K_α line, which is frequently used in X-ray structure analysis, has a wavelength of 1.54 Å.) The monochromatic neutron beam required for diffraction experiments is generally produced with the aid of a "monochromator crystal", by means of which a narrow wavelength band can be separated from the continuous neutron spectrum by Bragg reflection at the plane (hkl) according to $\lambda = 2d \sin\Theta$. However, the planes of higher order also reflect beams at the same angle 2Θ, particularly the plane of second order (2h, 2k, 2l) which reflects a beam of wavelength $\lambda/2$ [7]. This wavelength contamination is kept small by accepting a loss of intensity and working in the region of the high-energy branch of the Maxwell distribution curve rather than at its maximum. The residual $\lambda/2$ component for 1.05 Å, a frequently used wavelength, is about 1%. This wavelength is often preferred because ^{239}Pu has a resonance absorption line at 0.526 Å, so that it can be used as a $\lambda/2$ filter.

The most common monochromators are single crystals of copper or lead. It is possible to obtain sufficiently large single crystals of these metals which also have a good mosaic spread, the factor which ultimately determines the intensity yield. Single crystals of germanium have also been used in recent times. The structure of these crystals enables a primary beam free from a $\lambda/2$ component to be obtained by the space group extinction. However, the germanium crystals available at present suffer from the disadvantage of small mosaic spread.

2.2. Principles of Neutron Diffractometers

Fig. 1a shows a twin neutron diffractometer [8]. Fig. 1b is a schematic presentation, which is common to all such installations.

A single reactor channel is used to operate two diffractometers. Two primary beams of different wavelengths are separated out from the "white" neutron beam by two differently positioned single crystal monochromators. The two beams reach the two diffractometers from different directions (the figure shows a four-circle single-crystal diffractometer and a two-circle powder diffractometer).

The finite width of the wavelength band produced (half-width ≈ 0.04 Å) raises fundamental difficulties. It causes the width of the reflection peaks to increase very rapidly at large scattering angles 2Θ, and this results in considerably reduced resolution at high scattering angles, particularly in neutron diffraction studies on polycrystalline materials. The practical

[3] *H. Halban* and *P. Preiswerk*, C. R. hebd. Séances Acad. Sci. *203*, 73 (1936).

[4] *D. P. Mitchell* and *P. N. Powers*. Physic. Rev. *50*, 486 (1936).

[5] *E. O. Wollan* and *C. G. Shull*, Physic. Rev. *73*, 830 (1948).

[6] *C. G. Shull* and *J. S. Smart*, Physic. Rev. *76*, 1256 (1949).

[7] Cf. *e.g. G. Will, S. J. Pickart, H. A. Alperin*, and *R. Nathans*, J. Physics Chem. Solids *24*, 1679 (1963).

[8] Neutron diffraction experiments are at present conducted at three sites in the Federal Republic of Germany: at Munich (1 diffractometer), Karlsruhe (2 twin diffractometers), and Jülich (1 twin diffractometer). There have been many descriptions of the construction of neutron diffractometers: *e.g.* in *G. E. Bacon, J. C. Smith* and *C. O. Whitehead*, J. sci. Instruments *27*, 330 (1950); *D. G. Hurst, A. J. Pressesky*, and *P. R. Tunnicliffe*, Rev. sci. Instruments *21*, 705 (1950); *G. Lutz*, Z. Kristallogr., Kristallgeometr., Kristallphysik, Kristallchem. *114*, 232 (1960); Kerntechnik *2*, 391 (1960); For a further description see also *P. A. Egelstaff*: Thermal Neutron Scattering. Academic Press, London 1965, p. 98.

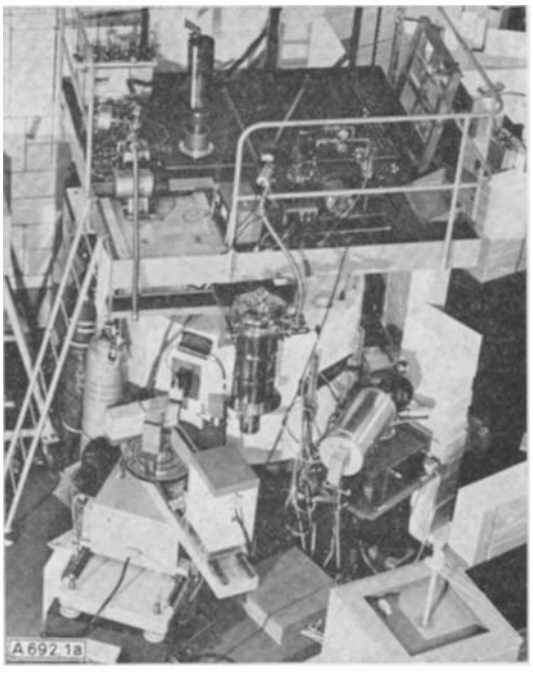


Fig. 1a. Twin neutron diffraction installation of the Technische Hochschule Darmstadt in front of the FR2 research reactor at the Kernforschungszentrum, Karlsruhe (cf. Fig. 1b). A ^{235}U fission chamber as a beam monitor which is used for both diffractometers, can be seen at the channel exit.

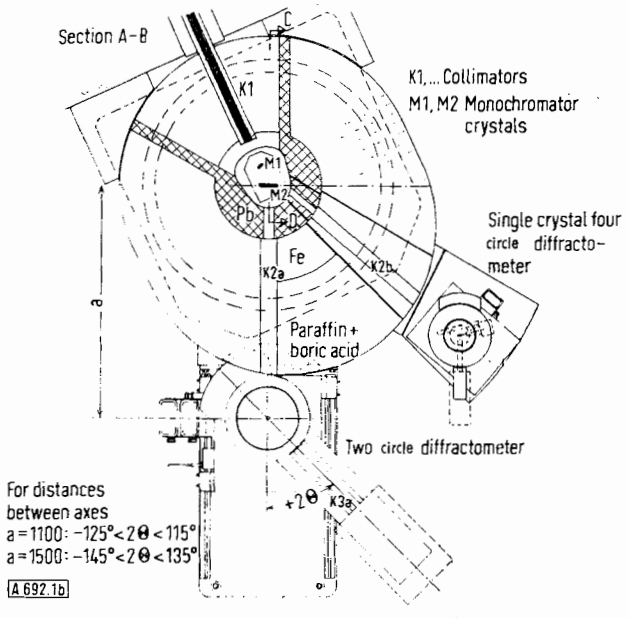


Fig. 1b. Schematic representation of the beam in the twin neutron diffraction installation shown in Fig. 1a. The "white" beam from the reactor is directed by a collimator K_1 to two differently positioned single-crystal monochromators M_1 and M_2, which deflect monoenergetic neutron beams to the two diffractometers [8a].

limit to the range of the measurements with the arrangement shown is therefore reached at a scattering angle of approximately 60–70° (because of the shorter wavelength ($\approx$1.0 Å), this is comparable to a scattering angle of about 100–120° in an X-ray Cu–K_α diagram). The resolution could be improved by having a large angle take-off (up to 90°) between the "white" and monochromatic beams [9], but such an arrangement is seldom possible because of the severely limited space available around reactors.

Neutron diffractometers are very similar to the instruments used for X-ray structure analysis. Depending on their application, we can distinguish single-crystal and powder diffractometers.

The four-circle single-crystal diffractometer shown in Figure 1 differs from an X-ray instrument only in having a heavy neutron counter (the weight resulting from the necessary screening) in place of an X-ray counter [10]. The instrument shown operates on the principle of the Eulerian cradle, which enables the crystal to be rotated about three axes – φ, χ, and ω – to any desired orientation in space. The counter can be rotated about a fourth axis – the 2Θ axis – to satisfy the Bragg reflection condition. The angle settings and data output are program-controlled (in this example with punched tape). The recent tendency is for these instruments to be controlled by small digital computers or by on-line operation with large computers.

Strictly speaking, powder diffractometers are one-circle instruments, since only the 2Θ circle is freely variable, while the Θ circle is coupled in the ratio of 2:1. The construction of these instruments is analogous to that of the Debye-Scherrer powder diffractometers used in the X-ray technique, but they are more robust to enable ancillary equipment such as furnaces and cryostats or magnets (to align the magnetic moments in the sample) to be attached to it.

Because of the high penetration of neutrons the temperature range from about 1.5 K° to about 1100 °C can be covered without difficulty in neutron diffraction experiments.

Figure 2 shows the Debye-Scherrer neutron diffraction diagram for Mg_2Si as an example of the form in which the results are recorded [11]. The neutron flux measured in the neutron counter was transmitted to a linear recorder parallel to the punched tape output. The intensity of the neutron beam is very low compared to the intensities produced by X-ray tubes, and the times required for neutron diffraction measurements are therefore rather long (about one hour per degree).

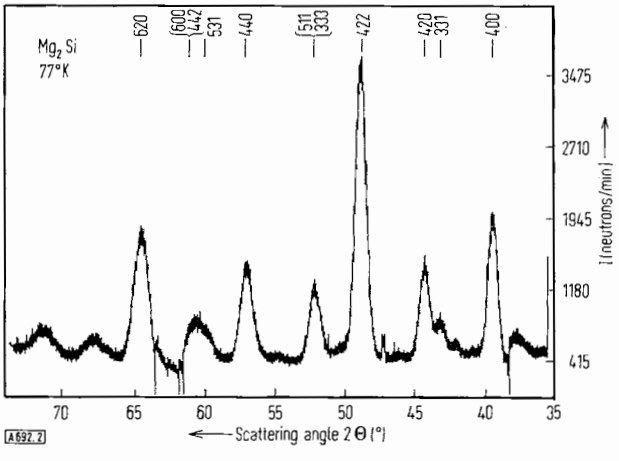


Fig. 2. Debye-Scherrer neutron diagram of Mg_2Si at 77 °K.

2.3. Detection of Neutrons

Since neutrons are uncharged, they can be detected only indirectly by collision processes or nuclear reactions. Until now mainly BF_3 counters have been used

[8a] *U. König*, Dissertation, Technische Hochschule Darmstadt 1967.

[9] *B. T. M. Willis*, Acta crystallogr. *13*, 763 (1960); *H. Dachs* and *H. Stehr*, Z. Kristallogr., Kristallgeometr., Kristallphysik, Kristallchem. *117*, 135 (1962); *H. Stehr*, *ibid.* *118*, 263 (1963).

[10] For a detailed description of these automatic four-circle diffractometers the reader is referred to the extensive literature on X-ray structure analysis. Cf. *e.g. W. Hoppe*, Angew. Chem. *77*, 484 (1965); Angew. Chem. internat. Edit. *4*, 508 (1965).

[11] *G. Will*, unpublished.

in neutron diffraction experiments, the neutrons being recorded by means of the reaction:

$^{10}B(n, \alpha)^{7}Li$

High-pressure ^{3}He counters[12] operating at about 10 atm are also highly suitable as neutron detectors (their advantage is the very compact construction: 100% absorption with a length of only 3 cm), but have not yet found general acceptance. Uranium fission chambers have a special application as intensity monitors for the primary beam; these counters use the nuclear fission process in ^{235}U and are employed to balance variations in the neutron flux due to fluctuations in the reactor output.

Shull[13] developed a method of neutron photography in which ^{6}LiF and ZnS are used as a fluorescent screen. On neutron capture, ^{6}Li produces α-particles which in turn produce fluorescence in the ZnS, and these flashes are recorded on highly sensitive polaroid film. In principle it is therefore possible to photograph Laue and Debye-Scherrer diffraction patterns but these photographs can be evaluated quantitatively only with the aid of calibration curves. The method is therefore used only for alignment purposes; the exposure required for photographing the direct beam is about 5–10 sec. (A Laue photograph, of a germanium crystal, shown in[13] was exposed for 4 min. Development time is about 1 min. Limit of detection is about 15 neutrons per mm^2).

2.4. Physical Principles of Neutron Diffraction

The interaction of neutrons with matter when a beam of neutrons is incident on a crystal is determined essentially by two processes of approximately the same order of magnitude:

(a) interaction between the neutron and the atomic nuclei through the nuclear forces;

(b) magnetic interaction between the magnetic moment of the neutron and the magnetic moment of the unpaired electrons (in paramagnetic ions or atoms) through a classical dipole interaction. These interactions are of the order of 10^{-12} to 10^{-13} cm.

The nuclear scattering interaction between neutrons and matter is described by the "nuclear scattering length" b (measured in fermis; 1f = 10^{-13} cm). The scattering cross section σ (measured in barns; 1 barn $\equiv$ 10^{-24} cm^2) is related to the nuclear scattering length by the expression $\sigma = 4\pi b^2$. For comparison, the electromagnetic interaction between X-rays and the electric charges on shell electrons is of the order of 10^{-11} cm (1 electron $\triangleq$ 0.282×10^{-12} cm).

Whereas the scattering of X-rays increases in proportion to the atomic number Z, no such simple rule holds for the scattering of neutrons by nuclei, which can be represented by two processes: (1) the scattering of a plane wave at a rigid sphere (hard sphere or potential scattering), which increases with volume and thus with $\sqrt[3]{A}$ (where A is the mass number of the nucleus; cf. Fig. 3). More important than potential scattering is resonance scattering, in which the neutrons are captured and re-emitted by excited nuclei. This results in a random distribution of nuclear scattering amplitudes through the periodic system, depending on the nuclear energy levels (Fig. 3). Because of this resonance scattering different isotopes of the same element may exhibit marked differences in scattering power (isotope-specific scattering amplitudes): *e.g.* ^{58}Ni: b = 14.4 f, ^{60}Ni: b = 3.0 f, ^{62}Ni: b = −8.7 f; or ^{1}H: b = −3.78 f, ^{2}H: b = 6.5 f.

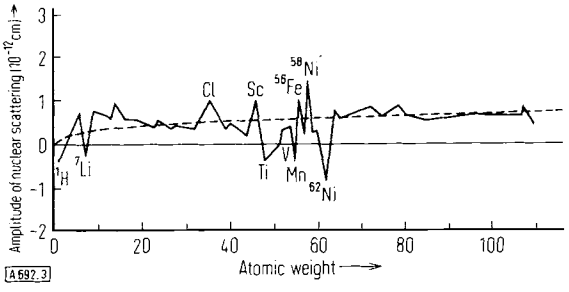


Fig. 3. Nuclear scattering amplitudes as a function of atomic weight. The monotonic curve for "potential scattering" of neutrons by the nuclei is shown by the dotted line.

Under certain conditions, namely when the neutron energy is smaller than the resonance energy of the nucleus, the resonance term in the scattering formula can be negative[14], and if at the same time the contribution of resonance scattering exceeds the potential scattering, the resultant nuclear scattering length b becomes negative. This means that there is no phase difference between the incident and scattered waves (a positive sign of b indicates a phase change of 180°, in analogy to X-ray scattering). The Fourier peaks for such nuclei with negative b values are thus negative in Fourier diagrams. Important nuclei with negative scattering lengths are ^{1}H: −3.78 f, Li (natural mixture): −1.8 f, ^{55}Mn: −3.6 f, ^{51}V: −0.5 f.

The nuclear scattering lengths, which are necessary for evaluation of diagrams must be determined by diffraction experiments on crystals having a simple structure, preferably an NaCl structure, because the energy levels of nuclei are not known with sufficient accuracy for theoretical calculations. The nuclear scattering lengths for natural isotope mixtures are made up of the contributions of the separate isotopes in proportion to their occurrence. The negative scattering length of lithium is thus principally determined by the isotope ^{7}Li with b = −2.1 f.

In contrast to X-ray scattering, which is strongly angle-dependent (atomic diameter $\approx$ 10^{-8} cm), the scattering

[12] *W. R. Mills, R. L. Caldwell,* and *I. L. Moragn,* Rev. sci. Instruments *33*, 126 (1962).

[13] *S. P. Wang, C. G. Shull,* and *W. C. Phillips,* Rev. sci. Instruments *33*, 126 (1962); *S. P. Wang* and *C. G. Shull,* J. physic. Soc. Japan *17*, Suppl. B-II, 340 (1962); *H. G. Smith,* Rev. sci. Instruments *33*, 128 (1962).

[14] The scattering of a neutron at an atomic nucleus was first treated by *G. Breit* and *L. E. Wigner,* Physic. Rev. *49*, 519 (1936), and is described by the Breit-Wigner formula – cf. *G. E. Bacon*: Neutron Diffraction. Clarendon Press, Oxford (1962).

of neutrons by nuclei does not depend on the angle of scattering (nuclear diameter $\approx 10^{-13}$ cm). The atomic form factor used in X-ray structure analysis is therefore unknown in neutron nuclear scattering, although magnetic scattering of neutrons is angle-dependent and is described by a magnetic form factor.

3. Evaluation of the Data

Crystal structure analysis with neutrons is very similar to an X-ray structure analysis. The intensity of a neutron wave scattered at a lattice plane (hkl) is proportional to the square of the crystallographic structure factor F_{hkl} for this plane, for which the following relation holds:

$$F_{hkl} = \sum_i b_i \, e^{2\pi i(hx_i + ky_i + lz_i)} \tag{3}$$

(the summation is carried out over all atoms i). This expression differs from the structure factor in X-ray diffraction only in the substitution of the nuclear scattering lengths b_i, which do not depend on the angle of scattering, for the angle-dependent atomic form factors f_i. The values of the structure factor F can therefore be determined from the measured reflection intensities by the same methods as in X-ray diffraction and Fourier series can be calculated.

$$\rho(xyz) = \frac{1}{V} \sum_{h=-\infty}^{+\infty} \sum_{k=-\infty}^{+\infty} \sum_{l=-\infty}^{+\infty} F_{hkl} \, e^{2\pi i(hx+ky+lz)} \tag{4}$$

Fourier inversion of the experimental structure factors with the correct signs or phases yields Fourier diagrams completely analogous to the electron density diagrams in X-ray structure analysis. The peaks in these diagrams naturally do not represent electron densities, but nuclear scattering densities; they indicate the positions of atomic nuclei in the unit cell. Since the nuclei have a diameter of the order of $10^{-13} - 10^{-12}$ cm and are thus about 10,000 times smaller than the diameter of the electron shells measured with X-rays, the observed diameter of the peaks (≈ 1 Å) is surprising. There are two reasons for this: (i) the thermal vibrations of the nuclei with a mean amplitude of about 0.1 Å and (ii) series-termination effects due to summation of the Fourier series over a finite number of terms. The size of the peaks in the Fourier diagrams is the resultant of these two effects.

Series-termination, which is much more pronounced in neutron diffraction diagrams than in X-ray diagrams, is known to result, in general, in small secondary peaks. In the X-ray diagram, each point in the electron cloud forms its own secondary peaks and these largely cancel out in the regions of low electron density between the atoms. In the neutron diagram on the other hand, the point nucleus is the only scattering center, and the only smearing is caused by thermal vibration. The region between the atoms in Fourier neutron diagrams is therefore very "disturbed" (cf. for example Fig. 8). The series-termination effects could be corrected by calculation, but the method is laborious [15], and this source of error is more easily eliminated by difference-Fourier synthesis, which is therefore more important in neutron diffraction than in X-ray diffraction. In a difference-Fourier calculation with only hydrogen left in the structure the only interference would then be from secondary peaks from the hydrogen atoms. It has been shown that the main effect of series termination lies not in secondary peaks but in the spread of these peaks. Thus, only difference-Fourier synthesis gives a reliable picture of structural details. In the ideal case, the Fourier space between the atoms should be zero between the peaks in neutron diffraction diagrams, and the peaks themselves should have circular symmetry. Deviations from spherical symmetry are thus interpreted as a direct indication of anisotropic thermal vibrations of the nuclei.

Since neutron diffraction analyses are generally a continuation of X-ray diffraction studies, the phases of the structure factors for calculating the Fourier series can be found from the models determined by X-ray methods. The problem of the phase determination is therefore less crucial than in X-ray structure analysis. Although there have been attempts to determine the phases directly from neutron diffraction data [16], these suggestions have not yet been applied in structure analysis. However, as in X-ray structure analysis, the neutron diffraction data are ultimately refined by least-squares methods to obtain the exact atomic thermal parameters.

4. Applications of Neutron Diffraction

The heavy expense involved in neutron diffraction experiments means that their use is justified only when other methods, particularly X-ray diffraction, fail to give satisfactory results. Neutron diffraction is important in:

1. Determination of the coordinates of light elements in the presence of heavy elements, particularly in locating hydrogen atoms: $Z_1 \gg Z_2$; $b_1 \approx b_2$.

2. Diffraction between isotopes or elements of neighboring atomic numbers: $Z_1 \approx Z_2$; $b_1 \neq b_2$.

3. Determination of the structure of crystals which absorb X-rays very strongly, for example lead and mercury compounds, or crystals which contain lanthanides or uranium:

$$\mu_{neutrons} \ll \mu_{X\text{-}rays}$$

4. Determination of the magnetic configuration, the moment distribution in the crystal, spin orientation, sublattice magnetization, and transition temperatures of crystals with magnetic ions.

5. Study of the thermal vibrations of atoms (nuclei).

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[15] *G. E. Bacon* and *R. S. Pease*, Proc. Roy. Soc. (London), Ser. A *220*, 397 (1953).

[16] *J. Karle*, Acta crystallogr. *20*, 881 (1966).

A number of examples will now be presented to give a brief review of some of the problems in which neutron diffraction has been used with particular success in recent years. Studies on glasses, liquids, and gases and the extensive field of inelastic neutron scattering will not be discussed in this review.

4.1. Location of Hydrogen Atoms, Studies on Hydrogen Bonds

By far the greatest number of neutron studies on crystals (more than 50 papers) have been concerned with the location of hydrogen atoms, an application for which neutron diffraction is much superior to X-ray diffraction. The X-ray scattering power of hydrogen is so small that the detection of hydrogen in X-ray diagrams presents considerable difficulties and the results are subject to relatively large errors. However, the neutron-scattering power of hydrogen (b = −3.78 f) is comparable to that of other elements, so that the atoms can be detected more easily and the parameters determined more accurately. Nearly all of these studies are on single crystals, but the crystals to

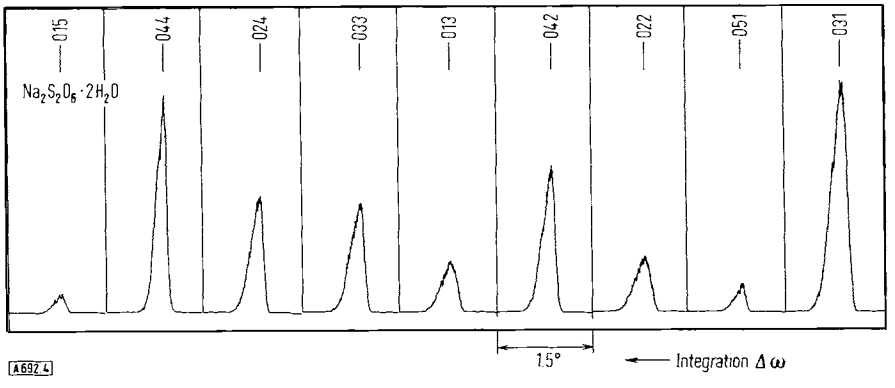


Fig. 4. Example of measurements on a single crystal of $Na_2S_2O_6 \cdot 2H_2O$. The time required for measurement is about 20 min per reflection, with an additional 5 min each for two measurements of the background intensity to the left and right of the reflection. (The crystal used weighed 0.58 g.)

be examined must be relatively large (several mm^3) because neutron fluxes are very low compared to the fluxes produced by X-ray tubes, and about 20–30 min is required to measure a single reflection, about ten times as long as in X-ray diffraction (see Fig. 4).

In the case of organic compounds with discrete molecules in the crystal, features of special interest are the molecular structure and the thermal behavior of the molecules or of molecular groups. Since the H atoms generally lie at the periphery of a molecule and are very light, their behavior provides information about the molecule as a whole. For example, in the oscillatory motion of a molecule the linear amplitudes of the H atoms are especially large because of the large distance of these atoms from the axis. Under certain circumstances, the relatively large thermal vibrations of the H atoms at room temperature can give rise to considerable errors in the apparent bond lengths; for instance, when the H atoms execute oscillations[17] or are to some extent coupled to the thermal vibrations of neighboring heavy atoms ("ride-on" motion[17]). A reliable knowledge of the temperature factors is required to allow for these effects in calculating the bond lengths, but since the effect of thermal vibrations is to reduce the intensity, at higher scattering angles, and in the case of X-ray diffraction this reduction is superimposed on the already rapidly decreasing form factor ($f(H) = 0.1$ when $\sin\Theta/\lambda = 0.45$ Å^{-1}), neutron studies are particularly valuable for detecting hydrogen atoms, and reliable studies on the thermal behavior of these atoms are possible only with the aid of neutrons. Moreover, it is relatively easy to make a fundamental change in the physical conditions under which the molecular vibrations are executed by replacing the hydrogen with deuterium (scattering length $b = 6.5f$), which is twice as heavy. Thermal vibrations can be further reduced by cooling. Because of the high penetration of neutrons, neutron measurements at low temperatures – *e.g.* 77 °K (liquid nitrogen) or 4.2 °K (liquid helium) – present no fundamental difficulties, although there is as yet no satisfactory means of programming the rotation of the crystal in three-dimensional space to the required angle settings φ and χ in a cryostat to satisfy the Bragg condition. Low-temperature studies are therefore at present mainly confined to projections on special crystallographic planes.

4.1.1. Benzene

Solid benzene was studied at −55 and −135 °C[18] (complementary to an X-ray structure determination at −3 °C[19]). It was found that benzene molecules execute angular oscillations in the ring plane about the sixfold axis which diminish rapidly with decreasing temperature; the RMS oscillations were 7.9, 4.9, and 2.5° at temperatures of −3, −55, and −135 °C. The C–H distance was found to be 1.077 Å at −55 °C and 1.09 Å at −135 °C. The mean C–C distance, corrected for thermal vibration, is 1.398 Å at both temperatures (Fig. 5).

[17] *D. W. J. Cruickshank*, Acta crystallogr. *9*, 754, 757 (1956); *14*, 896 (1961); *W. R. Busing* and *H. A. Levy*, *ibid. 17*, 142 (1964).

[18] *G. E. Bacon, N. A. Curry*, and *S. A. Wilson*, Proc. Roy. Soc. (London) Ser. A *279*, 98 (1964).

[19] *E. G. Cox, D. W. J. Cruickshank*, and *J. A. S. Smith*, Proc. Roy. Soc. (London), Ser. A *247*, 1 (1958).

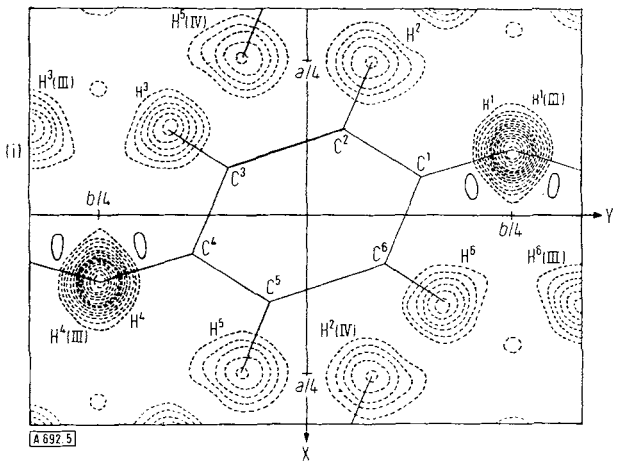


Fig. 5. Difference Fourier projection ($F_{obs}-F_{C_6}$) for benzene on the (001) plane at −135 °C. After subtraction of the C_6 skeleton, the diagram contains only the H atoms. These are indicated by dotted contours (negative regions) because of the negative nuclear scattering length of hydrogen.

4.1.2. Oxalic Acid Dihydrate

Although deuteration of a compound generally has no effect on the crystal structure, there are exceptions in the phenomenon described as the isotope effect. The best-known examples are potassium dihydrogen phosphate [20], resorcinol [21], and oxalic acid dihydrate [22]. Oxalic acid dihydrate was studied both by X-rays and neutrons in the form of $(COOH)_2 \cdot 2\ H_2O$ and $(COOD)_2 \cdot 2\ D_2O$, and thus provides a very good example for comparison. The crystal data for the two forms are given in Table 1.

Table 1. Crystallographic properties of oxalic acid dihydrate and [D_6]-oxalic acid dihydrate.

		$(COOH)_2 \cdot 2\ H_2O$ [23] (α form)	$(COOD)_2 \cdot 2\ D_2O$ [24] (β form)
a	(Å)	11.88	10.021
b	(Å)	3.60	5.052
c	(Å)	6.12	5.148
β	(°)	103.5	99.27
Space group		$P2_1/a$	$P2_1/a$
Z		2	2
V	(Å³)	254	257

The oxalic acid molecules are practically identical in the two structures: they are planar (distance of the D atoms from the plane through the carbon/oxygen atoms 0.02 Å) and have a center of symmetry. The only difference is in the hydroxyl groups, in which the O–D bond length (1.042 Å) is much shorter than the O–H bond length (1.057 Å). In contrast, the bond lengths in the water molecules are equal: O–D = 0.946 Å and 0.960 Å, O–H = 0.945 Å and 0.968 Å, although the angles are different: ∢ DOD = 110.5 °, ∢ HOH = 105.7 ° (∢ DOD in ice = 109.5 °). The hydrogen bonds O–H...O are not of the symmetric type, and in both structures the ^1H or ^2H atom is definitely associated with the carboxyl group. The hydrogen bonding appears to be weaker in the per-deuterated addition compound than in the un-deuterated form (O–H...O = 2.491, 2.518 Å; O–D... O = 2.540 Å). There is no direct relationship between the two structures, and for a long time no α ⇌ β phase change was observed. It is only recently that $(COOH)_2 \cdot 2\ H_2O$ has been prepared in the β form [25], and it remains to be seen whether the bond lengths in the two modifications are identical. The isotope effect in these crystals is possibly due to the considerable shortening of the hydrogen bonds in deuterium, for the major effect of the replacement of H by D is the difference in the zero-point energy, and the higher zero-point energy of the proton results in a reduction of bond length on the substitution O–H → O–D. There is also an effect on the strength of the hydrogen bonding. In the case of oxalic acid dihydrate this energy difference would appear to be so large that it cannot be compensated by merely stretching the hydrogen bond, and thus produces a phase change in the crystal structure.

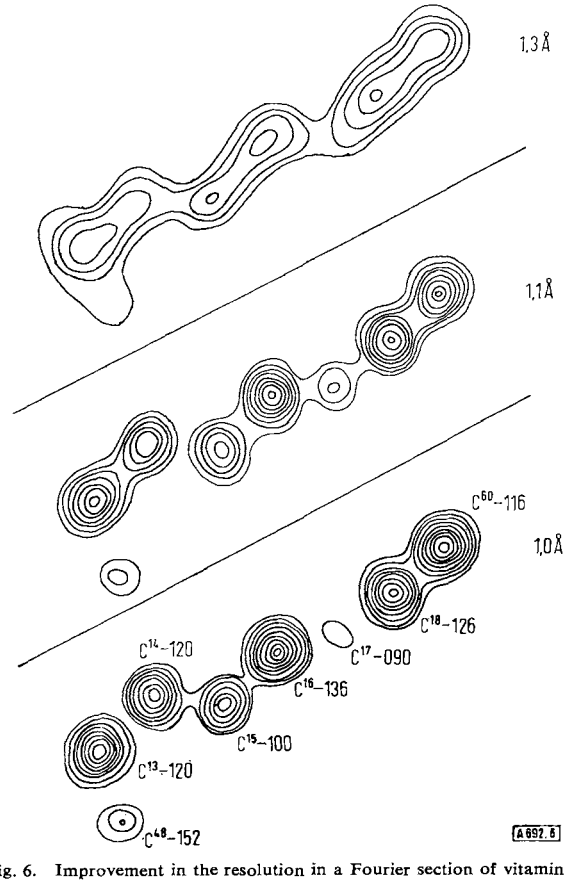


Fig. 6. Improvement in the resolution in a Fourier section of vitamin B_{12} at $y = 0.120b$ (part of diagram). It is not possible to distinguish individual atoms at a resolution of 1.3 Å; complete separation is achieved at 1.0 Å. The numbers next to the assignment of the atoms' identity give the y-coordinates in units of $10^3\ y/b$ [27].

[20] *A. R. Ubbelohde* and *I. Woodward*, Nature (London) *144*, 632 (1939).

[21] *J. M. Robertson*, Proc. Roy. Soc. (London), Ser. A *157*, 79 (1936); *167*, 122 (1938).

[22] *J. M. Robertson* and *A. R. Ubbelohde*, Proc. Roy. Soc. (London), Ser. A *170*, 222, 241 (1939).

[23] *F. R. Ahmed* and *D. W. J. Cruickshank*, Acta crystallogr. *6*, 385 (1953).

[24] *F. F. Iwasaki* and *Y. Saito*, Acta crystallogr. *23*, 56 (1967); *F. F. Iwasaki, H. Iwasaki*, and *Y. Saito*, *ibid. 23*, 64 (1967).

[25] *T. M. Sabine* and *P. Coppens*, private communication.

[26] *F. M. Moore, B. T. M. Willis*, and *D. C. Hodgkin*, Nature (London) *214*, 130 (1967).

[27] *D. C. Hodgkin, F. H. Moore*, and *B. H. O'Connor*, private communication.

4.1.3. Vitamin B_{12}

The most complicated molecule yet studied by neutron diffraction is a monocarboxylic acid derivative of cyanocobalamin with the empirical formula $C_{63}H_{87}O_{15}N_{13}PCo \cdot 16\ H_2O$ [26]. This compound forms monoclinic crystals with space group $P2_1$; the dimensions of the unit cell are $a = 14.915$ Å, $b = 17.486$ Å, $c = 16.409$ Å and $\beta = 104.11°$. As in X-ray structure analysis of proteins, measurements were first made on this vitamin B_{12} complex at a reduced resolution of 1.3 Å ($d > 1.3$ Å) and the results were subsequently refined at an increased resolution of 1.0 Å. The improvement achieved by the increased resolution is shown in Fig. 6 [27].

This example is also an impressive illustration of the work involved in such studies. For the 1.3 Å resolution 2000 independent reflections had to be measured, of which 1531 (*i.e.* three-quarters) were classed as observable ($I > \sigma(I)$, where $\sigma(I)$ is the standard deviation of the measured intensity I). However, since there are 820 parameters to be determined in the structure, identification of the atoms is difficult with 2000 reflections (Figures 7a and 7b). The resolution was therefore increased to 1.0 Å in the second stage of the experiment; 4400 reflections were measured, and 3000 of them had an intensity $I \geq \sigma(I)$. At approximately 30 min per reflection, the measurements took about 25 weeks. The crystal weighed 11 mg.

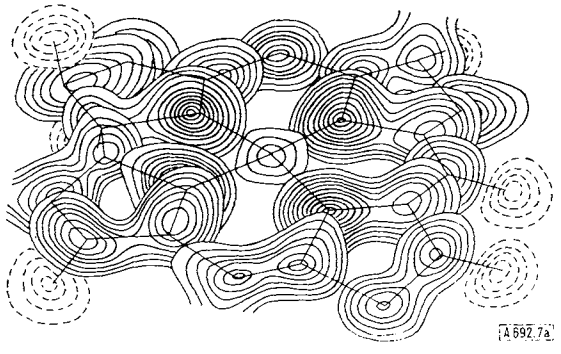


Fig. 7a. Three-dimensional superimposed neutron scattering density of the corrin unit in vitamin B_{12}. The central Co atom appears in the neutron Fourier diagram (resolution 1.3 Å) as a "light" atom because of its relatively low nuclear scattering length. H nuclei are negative (dotted contour lines).

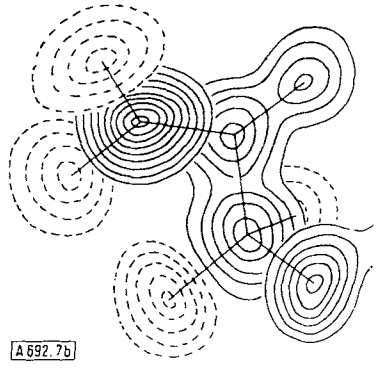


Fig. 7b. Neutron scattering density of the acetamide group at C^7 (cf. [26]). C and N can be distinguished unambiguously because of their different scattering lengths (b(C) = 6.61 f, b(N) = 9.40 f).

An X-ray structure analysis was carried out in parallel with the neutron diffraction measurements [28]. In these studies Bijvoet pairs of reflections [29] from the anomalous dispersions of cobalt were employed to determine the basic features of the crystal structure, and served to provide the preliminary model for analyzing the neutron data. The Patterson diagram of the neutron data was also calculated, but could not be interpreted for obvious reasons: with neutrons, hydrogen cannot be neglected in the vector diagram, and the neutron Patterson diagram for this complex thus contains about 52 000 peaks per formula unit, compared to 11 880 (neglecting H) in the X-ray Patterson diagram. Moreover, in the X-ray diagram the 108 interaction vectors of the Co atom with the C, N, O, and P atoms are about five times the magnitude of the vectors between the C, N, and O atoms, whereas with neutrons all nuclei have scattering powers of comparable orders of magnitude and produce similar Patterson peaks. In contrast, the cobalt nucleus is a "light" atom in the neutron Fourier diagram (Fig. 7a) because of the small scattering length of cobalt ($b = 2.5$ f).

The high incoherent background scattering from hydrogen poses particular difficulties in structure analyses on compounds containing hydrogen. This is essentially due to the nuclear-spin incoherence, resulting from the different possible orientations of the neutron spin ($I_n = 1/2$) to the nuclear spin ($I_{1_H} = 1/2$), and is particularly large in the case of hydrogen (about 34 barns). By comparison, the coherent scattering cross-section of hydrogen is only 1.79 barns. The situation is much more favorable with deuterium ($I_{2_H} = 1$), which has an incoherent scattering cross-section of about 2.2 barns. The signal-to-noise ratio in the measurements on the hydrogen-containing vitamin B_{12} complex thus averaged only 1.3:1, a relatively very low value.

4.1.4. Hydrogen Bonds in Inorganic Compounds

There have been a number of neutron diffraction studies on salts containing water of crystallization aimed at determining the position and nature of the hydrogen bonds in these crystals. Straight and bent O–H...O bonds have been found, as well as bifurcations and hydrogen atoms not involved in any bonding. A strict classification into different types is not, however, possible. A review of the results [30] shows that the position of the H_2O molecules is clearly determined by the electrostatic fields of the surrounding ions, so that there is no point in distinguishing between different types of hydrogen bonds. Other reviews [31, 32] contain correlation diagrams of the observed O–H and O–H...O distances.

The C–H distances determined by neutron diffraction are approximately an order of magnitude more accurate than the values found by X-ray diffraction. It is noteworthy that NMR and neutron diffraction meas-

[28] *C. K. Nockolds, T. N. M. Waters, S. Ramaseshan, J. M. Waters*, and *D. C. Hodgkin*, Nature (London) *214*, 129 (1967).
[29] *J. M. Bijvoet*, Nature (London) *173*, 888 (1964).
[30] *W. H. Baur*, Acta crystallogr. *19*, 909 (1965).
[31] *G. E. Bacon*: Application of Neutron Diffraction in Chemistry, Pergamon Press, London 1963, p. 30ff.
[32] *W. C. Hamilton*, Annu. Rev. physic. Chem. *13*, 19 (1962).

urements, which record the distances between atomic nuclei, generally give consistent values for C–H distances (1.06–1.10 Å), whereas X-ray diagrams, which define the centers of electron charge distribution, give values that are systematically about 0.2 Å shorter (the calculations already allow for the effects of thermal vibrations). Polarization of the H atoms and displacement of the H electron density toward the neighboring C atom is one possible explanation, although the shorter C–H distances could also be due to systematic errors in evaluating the X-ray data. This latter point has been frequently mentioned [32]. Possible sources of this kind of error include inaccurate form-factor curves for hydrogen or departures of the electron distribution of the C atoms from spherical symmetry.

4.2. Ferroelectricity

The advantages of neutron diffraction measurements are particularly important in structural studies on ferroelectric crystals, and in fact only neutron diffraction studies give meaningful results with such crystals. Ferroelectric crystals are known to exhibit spontaneous polarization below a characteristic temperature (the ferroelectric Curie point). This effect is associated with small displacements of individual atoms in the crystal structure. The ferroelectric transition is therefore always associated with a crystallographic phase transition to a crystal class with pyroelectric symmetry. A knowledge of the structural changes involved in this transition is required to understand ferroelectricity. The displacements are very small, and since the effect is essentially a change in the position of light atoms in the neighborhood of heavy atoms, it is necessary to detect small contributions to the scattered intensities. Since all elements have comparable neutron scattering powers, it is easier and more accurate to detect these small changes in parameters with neutrons than with X-rays. Neutron scattering power does not depend on the scattering angle, and neutron studies therefore have the additional advantage that sufficient intensity is observed at high scattering angles, at which the structure factors, and hence the intensities, are particularly sensitive to small changes in the parameters.

The most important ferroelectric crystals that have been studied with neutrons are $BaTiO_3$, KH_2PO_4, and $NaKC_4H_4O_6 \cdot 4\,H_2O$ (Rochelle salt). $BaTiO_3$ has three ferroelectric phases. Above the Curie point, it forms cubic crystals with the simple perovskite structure (Ti at the center of the cell, Ba at the corners of the cube, and O at the centers of the cube faces). On cooling there is a first transition at 120 °C to a tetragonal modification, with spontaneous polarization along the *c*-axis. At 5 °C a second phase change is observed to an orthorhombic form in which the dipoles are aligned parallel to the (cubic) [110] direction. Finally, at −90 °C there is a third transition to a rhombohedral form.

Highly accurate measurements on the tetragonal form were first made by *Evans* [33], using X-ray methods. These measurements were refined down to an *R* factor of 3.7%. However, in spite of this excellent agreement of the structure factors, the structure itself remained undetermined. It was later recognized that there were fundamental reasons why this should be so, for the thermal vibrations along the ferroelectric *z*-axis are correlated to the coordinate displacements along this axis. (The ions are displaced out of their special sites along the *c*-axis by 0.05 Å.) *Shirane* [34] discussed the reasons for this correlation in detail. It is due partly to the extremely high X-ray scattering power of barium and partly to the basic difficulty in distinguishing small changes in coordinates from the thermal vibration of atoms in a structure with pseudocentral symmetry because of the simultaneous and competing decreases in the scattering power with both the X-ray form factor, *f*, and the temperature factor, $\exp -2B(\sin\Theta/\lambda)^2$. The situation is much more favorable with neutron scattering, which is independent of the angle of scattering, and the structure of the tetragonal phase of $BaTiO_3$ was finally determined with neutrons [35].

The difficulties described can be illustrated by considering, for example, the pair of reflections (h0l) and (l0h). Such reflections are equivalent in the cubic structure: $I(h0l) = I(l0h)$, but not in the tetragonal phase: $I(h0l) \neq I(l0h)$. In X-ray diffraction, only very slight differences in intensity are observed because of the small differences in scattering power of the elements, whereas with neutrons the differences are large and very distinct; for example, for the pair of reflections (104) and (401) the differences are respectively 3 and 70%. A preliminary neutron diffraction study was limited to a projection with 50 reflections (h0l) measured in the zone (010). However, in spite of an excellent *R* factor there was again an initial high correlation between z_{Ti} and β_{33}(Ba), the anisotropic temperature factor for barium, which describes motion along the *z*-axis. The relationship between the parameters was practically linear. The measurements were then extended to the reflections (hhl), and the inclusion of this additional zone eliminated the correlation and led to an unambiguous determination of the structure. The final analysis used 84 reflections in the two zones (h0l) and (hhl). The crystal structure of the orthorhombic modification was then also determined at 1 °C by neutron diffraction [36].

The spontaneous electric polarization in $BaTiO_3$ is the result of a displacement of the Ti^{4+} ions by 0.13 Å along the polar axis inside the oxygen octahedra, which experience only slight distortion themselves. In the orthorhombic lattice the Ti–O distances along the polar axis are 1.90 and 2.11 Å, and perpendicular to the axis 2.00 Å. In the tetragonal phase the Ti–O

[33] *H. T. Evans*, Acta crystallogr. *4*, 377 (1951).

[34] *G. Shirane*, *F. Jona*, and *R. Pepinsky*, Proc. I. R. E. *43*, 1738 (1955).

[35] *B. C. Frazer*, *H. Danner*, and *R. Pepinsky*, Physic. Rev. *100*, 745 (1955).

[36] *G. Shirane*, *H. Danner*, and *R. Pepinsky*, Physic. Rev. *105*, 856 (1957).

distances along the polar axis are 1.86 and 2.17 Å; perpendicular to this axis there are four oxygen ions at a distance of 2.00 Å (displacement of the Ti^{4+} ions along [001] by 0.05 Å). The essential finding – for the orthorhombic phase as well – is that the oxygen octahedra remain practically undistorted and that the displacement of the Ti^{4+} ions inside the octahedra must be considered responsible for the ferroelectric properties.

Difficulties of an entirely different nature arose during X-ray studies on Rochelle salt when it was found during the measurements that there were changes in structure due to irradiation [37,38]. In this case too, a structure determination was possible only with the aid of neutrons. Above its Curie point (24 °C), Rochelle salt crystallizes to form orthorhombic crystals with the space group $P2_12_12$. On transition to the ferroelectric state, the axis of symmetry 2_1 parallel to the *b*-axis vanishes, and the crystal symmetry therefore becomes monoclinic with the space group $P2_1$. As a result of the change in symmetry, new reflections with the indices (0k0) are allowed, where k is an odd integer. However, these reflections are so weak that they cannot be observed with X-rays. The ferroelectric behavior of Rochelle salt was therefore assumed to be due to a slight displacement of the hydrogen atoms. This assumption was first confirmed by neutron diffraction studies in which the (0k0) reflections with $k = 2n + 1$ were measured at the phase change [39]. However, further neutron diffraction measurements on a deuterated crystal [37] showed that, although

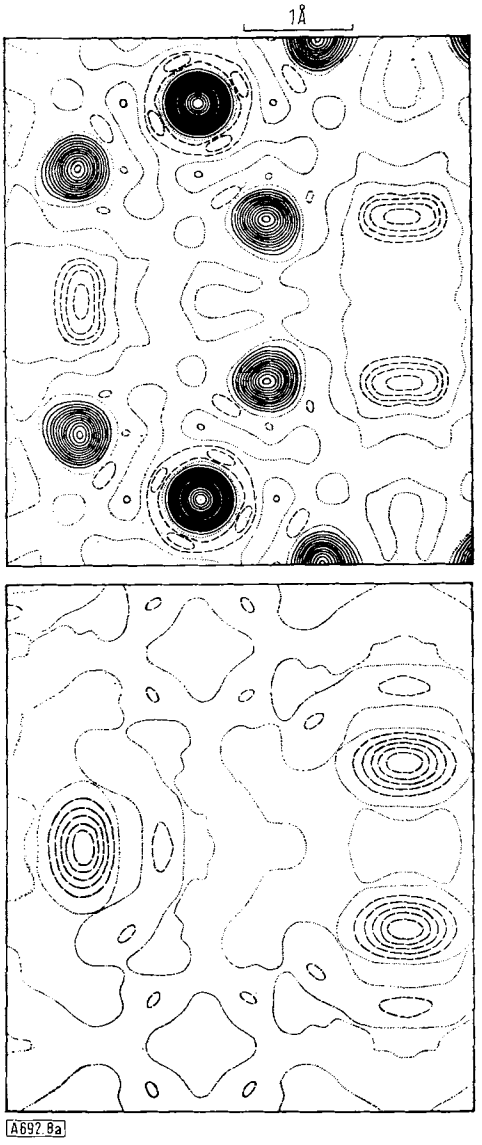


Fig. 8a. Neutron Fourier diagram (F_{obs}, top) and difference Fourier diagram.
($F_{obs}-F_{KPO_4}$, bottom) for KH_2PO_4 above the ferroelectric Curie temperature. Projection on the (001) plane, recorded at 20 °C; tetragonal symmetry. There is a distinct spread of the hydrogen nucleus density in the direction of the oxygen atoms.

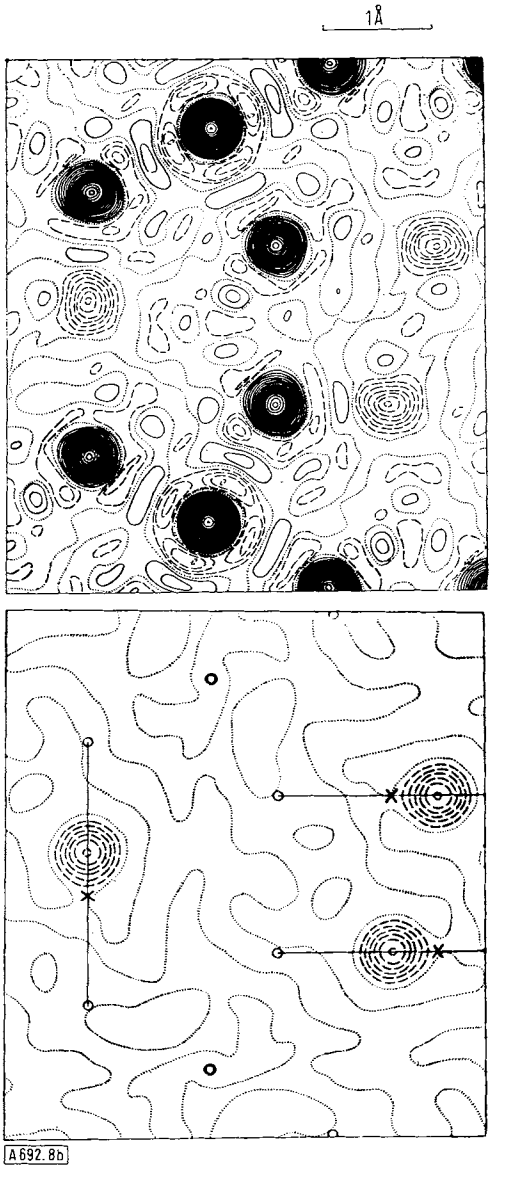


Fig. 8b. Fourier diagram (top) and difference Fourier diagram (bottom) for KH_2PO_4 in the ferroelectric state. Recorded at −180 °C, analogous to Fig. 8a; orthorhombic symmetry. There is a clear displacement of hydrogen nuclei in the direction of the applied external field toward neighboring oxygen ions. Reversal of the field produces displacement in the opposite direction.

[37] *B. C. Frazer*, J. physic. Soc. Japan *17*, Suppl. B-II, 376 (1962).

[38] *G. C. Moulton* and *W. G. Moulton*, J. chem. Physics *35*, 208 (1961); *K. Toyoda*, *A. Shimada*, and *T. Tanaka*, J. physic. Soc. Japan *15*, 536 (1960); *K. Okada*, *ibid. 16*, 414 (1961).

[39] *B. C. Frazer*, *M. McKeown*, and *R. Pepinsky*, Physic. Rev. *94*, 1435 (1954).

some hydrogen atoms are displaced, this is not by itself sufficient to explain the symmetry change and hence the ferroelectric properties.

The first compound to be analyzed by Fourier methods was potassium dihydrogen phosphate, KH_2PO_4, which has a ferroelectric Curie point at −123 °C. Neutron diffraction measurements were made on single crystals of KH_2PO_4 above (20 °C)[15] and below (−180 °C)[40] the transition temperature. From the observed changes in the reflections and the Fourier diagrams the ferroelectric properties of this salt can be attributed to the arrangement of the H atoms in the O−H...O hydrogen bonds perpendicular to the *c*-axis between the PO_4 tetrahedra (Fig. 8).

The arrangement of the H atoms depends on the direction of the external electric field. Reversal of the field causes reversal in the hydrogen bonds. This effect can be followed by direct observations of sensitive pairs of reflections. Above the transition temperature both equilibrium positions are occupied on the statistical average, and the hydrogen peaks therefore appear in the Fourier diagram as spread-out ellipsoids (Fig. 9).

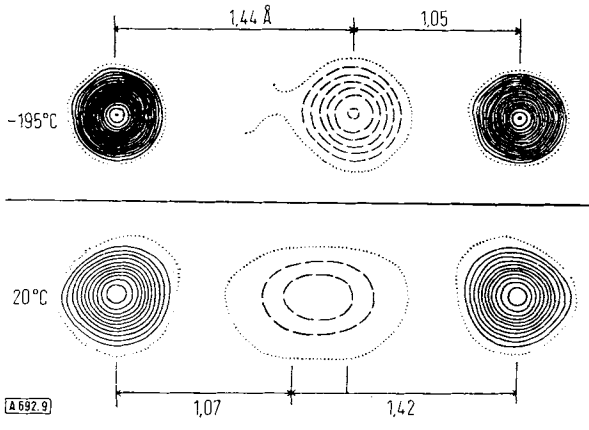


Fig. 9. Comparison of the hydrogen distribution in the hydrogen bonds of KH_2PO_4 above and below the ferroelectric Curie point.

4.3. Differentiation between Elements with Neighboring Atomic Numbers

The X-ray scattering powers of neighboring elements in the periodic table differ very little or not at all (*e.g.* $Mn^{2+} \triangleq Fe^{3+}$, $Mg^{2+} \triangleq Al^{3+}$), so that it is difficult or even impossible to determine their positions in the unit cell reliably from X-ray diffraction diagrams. The situation is quite different with neutron scattering. For example, V, Cr, Mn, Fe, and Co (Z = 23, 24, 25, 26, 27) have nuclear scattering lengths b = −0.5f, 3.5f, −3.6f, 9.6f, and 2.5f respectively. With few exceptions, all elements of similar atomic number can be distinguished without difficulty by neutron diffraction. Nickel (b = 10.3f) differs only slightly from iron (b = 9.6f) when the natural mixtures of isotopes are used. However, in unfavorable cases like this it is possible in principle to use pure or enriched isotopes (*e.g.* ^{57}Fe with b = 2.3f and ^{62}Ni with b = −8.7f); it is then always possible to locate the elements in the structure by appropriate selection. *Walker* and *Keating*[41] took advantage of this isotope specificity of nuclear scattering in studies on the short-range order in β-CuZn (β-brass) by using a crystal enriched with ^{65}Cu, which gave reflection differences seven times greater than with the natural crystal.

4.3.1. Ferrites

Ferrites are of technical interest because of their magnetic properties. They form cubic crystals with a spinel structure, space group Fd 3 m, with eight formula units XY_2O_4 in the unit cell. In the holes between the oxygen ions we distinguish between "A" or tetrahedral sites, which are surrounded by oxygen tetrahedra, and "B" or octahedral sites surrounded by oxygen octahedra. These tetrahedral and octahedral sites can be occupied by either 8 X^{2+} ions on the A sites and 16 Y^{3+} ions on the B sites (normal spinel) or 8 Y^{3+} on the A sites and 8 X^{2+} + 8 Y^{3+} on the B sites (inverted spinel). A continuous transition between these forms is possible. The distribution of the di- and trivalent cations is described by the degree of inversion x, which can be determined most reliably from neutron diffraction measurements. An additional parameter in ferrites is the oxygen coordinate u. The oxygen ions are displaced from their ideal positions u = 3/8, and once

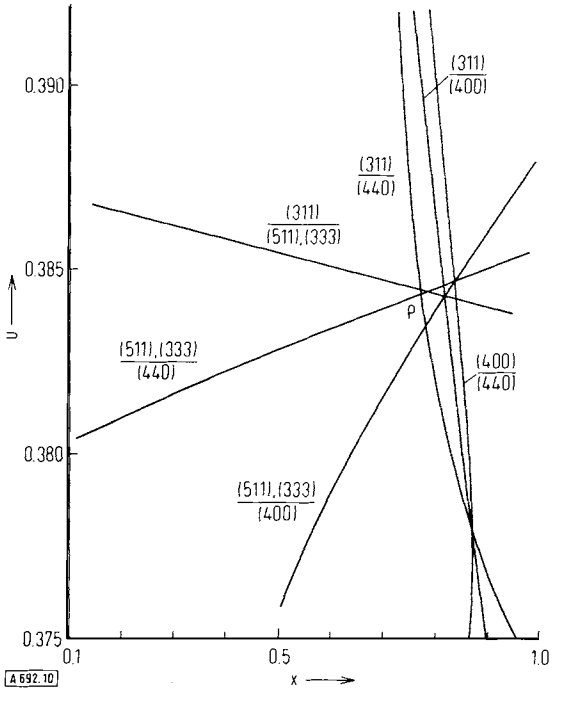


Fig. 10. Intensities of different pairs of reflections from $MnFe_2O_4$ as a function of the degree of inversion x and of the oxygen parameter u, for determining x and u by the method proposed by *Hastings* and *Corliss*[43].

[40] *G. E. Bacon* and *R. S. Pease*, Proc. Roy. Soc. (London), Ser. A *230*, 359 (1955); *S. W. Peterson, H. A. Levy*, and *S. H. Simensen*, J. Physique *21*, 2084 (1953); Physic. Rev. *93*, 1120 (1954).

[41] *C. B. Walker* and *D. T. Keating*, Physic. Rev. *130*, 1726 (1963).

[42] *L. M. Corliss, J. M. Hastings*, and *F. G. Brockman*, Physic. Rev. *90*, 1013 (1953).

[43] *J. M. Hastings* and *L. M. Corliss*, Physic Rev. *104*, 328 (1956).

again the exact oxygen parameters can be determined more accurately from neutron diffraction diagrams than from X-ray diffraction diagrams because of the relatively large scattering length of oxygen. The investigation of ferrites is therefore a two-parameter problem to determine x and u. A graphical method of solution has been proposed by *Hastings* and *Corliss* [42]. As example, Fig. 10 shows the results for $MnFe_2O_4$ [43], with $u = 0.3846 \pm 0.0003$ and $x = 0.81 \pm 0.03$ ($x = 1$ for normal spinel).

In this representation the intensity is calculated as a function of x and u for different pairs of reflections and compared with the observed values. The curves for the separate pairs all cut at or near a particular point which defines the parameters x and u. Other important ferrites studied by this method include $MnCr_2O_4$ [44], with $u = 0.3892 \pm 0.0005$ and $x = 1.00 \pm 0.01$ (normal spinel), Fe_2TiO_4 [45] with $u = 0.386 \pm 0.001$ and $x = 0.91 \pm 0.01$, and $MgFe_2O_4$ [42] with $u = 0.3817$ and $x = 0.87$.

Differentiation between Mg and Al in classical spinel, $MgAl_2O_4$, can also be accomplished only with neutrons, since Mg^{2+} and Al^{3+} (like Mn^{2+} and Fe^{3+} in $MnFe_2O_4$) have equal X-ray scattering powers and therefore cannot be distinguished by X-ray methods. Neutron diffraction studies [46] showed that $MgAl_2O_4$ is essentially a "normal" spinel ($u = 0.387 \pm 0.001$). All these measurements were made on polycrystalline samples.

4.3.2. Cyanides

Neutron diffraction measurements were carried out on cyanides in order to differentiate between the elements C and N and to determine the exact structure parameters in the presence of heavy elements. It was found that in $Hg(CN)_2$ it is the carbon and not the nitrogen atom that links the cyanide group to the metal [47]. The same was obtained for $K_3[Co(CN)_6]$ [48], in which the cobalt ion in the $[Co(CN)_6]^{3-}$ octahedron complex is surrounded by six cyanide ions in the order Co–C–N. An analysis on KCN, which forms cubic crystals with sodium chloride structure, was initially interpreted as indicating that the CN groups in the crystal rotate freely [49]. However, another study [50] showed that the data were more in accord with a model in which the CN groups are statistically oriented in [111] directions. Single-crystal neutron diffraction studies on $K_2[Zn(CN)_4]$, which also forms cubic crystals, conclusively disproved a model with freely rotating CN groups [51]. The sequence of the cyanide ion coordination in this compound is Zn–C–N–K–N–C–Zn. The Zn–C–N groups are linear with a C–N distance of 1.157 ± 0.009 Å.

4.3.3. Carbides

Location of the C atoms in the heavy metal carbides having the formulas MC_2 and M_2C_3 is very imprecise by X-ray diffraction in the presence of the heavy metal atoms. Typical examples are CaC_2, LaC_2 and UC_2 [52], which all form body-centered tetragonal crystals with space group I4/mmm; M = (000; $\frac{1}{2}\frac{1}{2}\frac{1}{2}$), C = (000; $\frac{1}{2}\frac{1}{2}\frac{1}{2}$) ± 00$z$ (C11a-type structure). In this structure (Fig. 11) pairs of C atoms lie parallel to the c-axis in a dumbbell arrangement between pairs of metal atoms. The free position parameter z can be determined very accurately from neutron diffraction diagrams, and from this the C–C distance can be found.

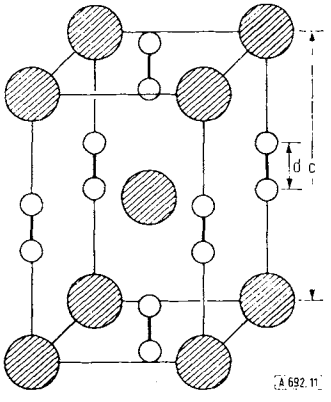


Fig. 11. Tetragonal structure of heavy metal carbides of the general formula MC_2 (with C–C groups along the C – axis between the metal atoms). ◎ = M, O = C.

For CaC_2, a C–C distance of 1.191 ± 0.009 Å was found in this way; this corresponds to the triple bond length in acetylene (the less precise X-ray structural analysis gave a value of 1.4 Å). In UC_2 on the other hand, the C–C distance is 1.340 ± 0.007 Å, corresponding to a C–C double bond. These values fit in well with the view that CaC_2 is an ionic crystal with discrete Ca_2^+ and C_2^{2-} ions, whereas UC_2 has metallic properties and U^{4+} ions in its crystal structure. LaC_2 and many lanthanide carbides such as CeC_2, TbC_2, YbC_2, LuC_2, and YC_2 have a mean C–C distance of 1.278 ± 0.002 Å and therefore occupy an intermediate position between the two extremes of CaC_2 and UC_2. This means that the C–C distance in carbides increases with increasing valence of the metal cation, and that carbides can be descibed generally as $M^{II}C_2$, $M^{III}C_2$, and $M^{IV}C_2$ (corresponding to CaC_2, LaC_2, and UC_2). It can be further shown by analysis of paramagnetic scattering that the metal ions in LaC_2 and the rare earth metal carbides are in the M^{3+} ground state.

[44] *J. M. Hastings* and *L. M. Corliss*, Physic. Rev. *126*, 556 (1962).

[45] *R. H. Forster* and *E. O. Hall*, Acta crystallogr. *18*, 857 (1965).

[46] *G. E. Bacon*, Acta crystallogr. *6*, 57 (1953).

[47] *J. Hvoslef*, Acta chem. scand. *12*, 1568 (1958).

[48] *N. A. Curry* and *W. A. Runciman*, Acta crystallogr. *12*, 674 (1959).

[49] *N. Elliott* and *J. M. Hastings*, Acta crystallogr. *14*, 1018 (1961).

[50] *A. Sequeira*, Acta crystallogr. *18*, 291 (1965).

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Therefore, one electron has been transferred to the conduction band (YbC_2, with $Yb^{2,8+}$, is an exception). In general, carbides of this type can therefore be represented as MC_2 with $M = M^{n+}$, $C_2 = C_2^{2-}$ and $n-2$ electrons in the conduction band.

Sesquicarbides form bcc crystals with space group $I\bar{4}3d$ (structure type $D5_c$), with free metal and carbon parameters. The C–C distance in La_2C_3, Pr_2C_3, and Tb_2C_3 [53] was found to be 1.238 Å, and in Ce_2C_3 1.276 Å. Taken with the results of an analysis of paramagnetic scattering, this leads to the conclusion that in Ce_2C_3 only 65% of the cerium ions are in a $^2F_{5/2}$ state as Ce^{3+}, with 35% as Ce^{4+} in the diamagnetic $^1S_0$ state. It follows that in both sesquicarbides and dicarbides the C–C distance increases with increasing valence of the metal.

UC_2 has also been studied with neutrons at 1700 and 1900 °C [54], and the results confirmed a transition from a tetragonal to a cubic phase at 1820 °C [55]. Above 1820 °C, UC_2 crystallizes in a NaCl type structure, with the C–C groups either rotating freely or randomly aligned in the [111] directions between the metal ions.

4.4. Investigation of Thermal Vibrations in Crystals

As with X-ray diffraction, the intensity in neutron diffraction diagrams decreases with increasing scattering angle 2 Θ owing to the thermal vibration of the atoms. This thermal vibration is described by the Debye-Waller factor B, and the observed intensity is given by the equation

$$I = I_0.K.L.A.F^2.e^{-2B\left(\frac{\sin\Theta}{\lambda}\right)^2} \quad (5)$$

where I_0 is the intensity of the incident primary beam, K is an apparatus constant, L the Lorentz factor, A the absorption factor, and F the structure factor from equation (3). It can be shown that the temperature factor B is related to the mean thermal amplitude of the atoms, u:

$$B = \frac{8}{3}\pi^2\langle u^2\rangle \quad (6)$$

so that a knowledge of B provides information about the thermal vibrations of the atoms.

Determination of the temperature factor B from X-ray diffraction diagrams is difficult and unreliable because in this case there is an additional drop in intensity due to the angle-dependent form factor f, so that the reflections in an X-ray diagram always become small at large values of 2Θ. A precise determination of B from X-ray diffraction data requires separation of these two effects, and this means that the electron distribution around an atom in the crystal should be known. (The form factor is the Fourier transform of the electron distribution of an atom.) In neutron diffraction diagrams, on the other hand, apart from the well-known effect of the Lorentz factor (for measurements on single crystals $L = 1/\sin 2\Theta$), the drop in intensity is due entirely to the thermal vibrations of the atoms and ions, and $2B(\sin\Theta/\lambda)^2$ varies linearly with $\ln|I|$.

Detailed studies were carried out on UO_2, ThO_2 [56], and CaF_2 [57], all of which crystallize with a fluorite structure. Between room temperature and 1100 °C the anions in single crystals of UO_2 and ThO_2 execute anisotropic thermal vibrations, preferentially in the [111] direction toward neighboring cations and increasing in amplitude with increasing temperature. This anisotropic thermal vibration in a crystal with cubic symmetry is surprising, for in a cubic system the ellipsoid of vibration, which generally describes the anisotropic temperature factors, reduces to a sphere. However, anisotropic effects are seen very clearly with neutrons when two or more reflections at the same scattering angle 2 Θ are studied, *e.g.* the reflections (755), (771), and (933). Such reflections show clear differences in intensity, increasing with increasing temperature, which can be interpreted only in terms of an anisotropic vibration of the anions along the cube diagonals. This behavior is described by introducing a "tetrahedral smearing function" which displaces the ions from their equilibrium positions by time-averaged small distances δ (about 0.08 Å at 1000 °C). The physical reason for this behavior is considered to be an anharmonic interaction between neighboring ions. (Similar intensity differences are seen with such reflections in X-ray diffraction diagrams, but in this case the differences are of different physical origin due to departures from spherical symmetry in the charge distribution of the electrons, particularly along the direction of the bonds [58]. The effect of the asymmetric charge distribution is much more pronounced than that of anisotropic thermal vibration.)

The measurements on UO_2 were recently repeated at 20 °C with higher accuracy [59]. It was possible to record reflections up to $\sin\Theta/\lambda = 1.08$ Å^{-1}; the resulting structure factors were accurate to 0.5% and the R factor was 0.32%. Neutron measurements of this accuracy are laborious, but they are quite possible and not particularly difficult. The fluorine ions in CaF_2, which was studied between room temperature and 500 °C, must also be assumed to execute anisotropic thermal vibrations in the [111] direction to accord with the experimental data. BaF_2, SrF_2, and Mg_2Si

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would be expected to behave analogously; Mg_2Si with a nuclear scattering length ratio (which determines the accuracy) of $b_{Si}:b_{Mg} = 0.693$ would be a particularly suitable experimental material ($b_u:b_0 = 1.440$).

A question of fundamental interest is whether the electron shells vibrate synchronously and with the same amplitude as the atomic nuclei. In a neutron diffraction study on fcc cobalt ($Co_{0.92}Fe_{0.08}$)[60], indications were found that the thermal behavior of the atomic nucleus possibly differs from that of the electron cloud. The measurements were made using polarized neutrons which enable very accurate determination of the ratio of the nuclear scattering amplitude $b.e^{-2W_n}$ to the magnetic scattering amplitude $p.e^{-2W_m}$ [$W = \frac{8}{3}\pi^2.\langle u^2\rangle(\sin\Theta/\lambda)^2$][61]. Differing results obtained at room temperature and 600 °C are due either to a change in the electron distribution (and hence in the form factors) of the 3d electrons at high temperature, or to differences in the behavior of W_n and W_m. Evaluation of the experimental data for the second case show that the mean square amplitude of the 3d electron shell at 600 °C is only 37% of the amplitude of the nucleus: $\langle u^2\rangle_m = 0.37\ \langle u^2\rangle_N$. This would mean that the "magnetic" electrons do not follow the thermal vibrations of the nucleus as if they were rigidly attached to it, but vibrate with a smaller amplitude.

4.5. Anomalous Dispersion

Brief mention should also be made of the phenomenon of anomalous dispersion. In X-ray diffraction this is known to result in violation of Friedel's law, with $I_{hkl} \neq I_{\bar{h}\bar{k}\bar{l}}$. Similar effects can be observed in neutron diffraction when a resonance line of the nucleus lies in the energy range of thermal neutrons. In such cases scattering is accompanied by a discontinuous phase change significantly different from 180° ($+b$) or 0° ($-b$), and the nuclear scattering amplitude assumes the complex form:

$$b = b_0 + \Delta b' + i\Delta b''$$

where $\Delta b'$ and $\Delta b''$ are correction terms for the real and imaginary components. The imaginary term $\Delta b''$ is directly proportional to the total scattering cross section. The effect is therefore particularly large for such elements as ^{113}Cd, ^{149}Sm, and ^{157}Gd. For these elements, $\Delta b''$ at resonance is greater than 47f[62]. Since $\Delta b'$ and $\Delta b''$ are strongly energy-dependent, the nuclear scattering lengths of these elements are generally wavelength-dependent. Anomalous dispersion of neutrons has been demonstrated experimentally in CdS, BP, and $^6Li_2SO_4 \cdot H_2O$[62]. These compounds crystallize with structures having no centers of symmetry, so that pairs of planes hkl and $\bar{h}\bar{k}\bar{l}$ scatter with different intensities.

For example, the nuclear scattering length of Cd at $\lambda = 1.075$Å was found to be $b = (3.8 + 1.2\,i)$f; the effect is even more pronounced at $\lambda = 0.68$ Å, corresponding to the ^{113}Cd resonance line: $b = (7.2 + 6.6\,i)$ f. (The resonance energy of ^{113}Cd is 0.178 eV ≙ 0.68 Å.) In a sample enriched with ^{113}Cd the imaginary part of the scattered amplitude ($\Delta b'' \approx 47$f) finally becomes larger than the real part.

As in X-ray diffraction, the method of anomalous dispersion is of principal importance in determinations of the absolute configuration of polar compounds by measurements of Bijvoet pairs of reflections[29]. However, the resonance lines of most nuclei are well below 1 Å, and practical application of this method will not be possible until neutron beams with wavelengths of the order of 0.1 Å and sufficiently high intensity are available. (The projected high-flux reactor at Grenoble has provision for a beam tube for neutrons of this short wavelength.)

5. Concluding Remarks

In addition to the applications of neutron diffraction selected for this review, there are others of equal importance, for example in studies on alloys, particularly of the transition metals, where again neighboring 3d elements make it difficult to determine the state of order by X-rays, or in studies on ammonium halides and on hydrides, particularly metal hydrides – *e.g.* those of Cu, Hf, Ti, Zr, and Pd, as well as ThH_2, ThD_2, ZrD_2 and UD_3. There is also no space for a detailed discussion of structure determinations on compounds of Pb, Hg, or the lanthanides. X-ray structure analysis on these compounds is difficult because of their strong absorption of X-rays.

Almost all these measurements are done on powder preparations. It has been found that the data obtained from neutron powder diffraction are much more informative than X-ray powder data, because the nuclear scattering lengths of the elements are comparable and the heavy elements which interfere with X-ray measurements are mostly confined to special sites. Powder analyses are naturally restricted to simpler structures with few parameters (up to ten), *e.g.* the perovskite-like structures of orthoferrites[63]. In recent years computer programs have been developed to utilize all the measurable peaks, which in powder diagrams generally result from the superposition of several planes. The programs enable the atomic parameters to be refined by least-squares methods from the observed intensities without it being necessary to resolve the peaks first into their components. This method is similar to the analysis of the structure of single crystals from structure factors. We have used it successfully in studies on $LaFeO_3$, $LaCrO_3$, $MnSO_4$, $MnSeO_4$, $NiSeO_4$, $CoSeO_4$, $ErPO_4$, and $ErVO_4$.

Received: March 15, 1968 [A 692 IE]
German version: Angew. Chem. *81*, 307 (1969)
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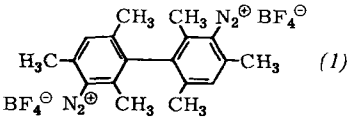
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Aryldiimine as an Intermediate during Reduction of Diazonium Salts with Tetrahydridoborate

By *M. Bloch, H. Musso,* and *U. I. Záhorszky*[*]

Dedicated to Professor H. Bredereck on the occasion of his 65th birthday

Aryldiazonium salts may be reduced to the corresponding hydrocarbons by complex hydrides in methanol at 0 °C[1]. The hydrogen introduced can be transferred from various sources as anion, radical, or proton. To discriminate between these possibilities, we treated bimesityl-3,3'-bis(diazonium) bis(tetrafluoroborate) *(1)* in methanol with sodium tetrahydridoborate; in each case the reducing agent or the solvent was deuterated in a different manner (98–99% D). The deuterium content of the resulting bimesityl, which could be isolated in approximately 22% yield by chromatography, was determined by mass spectrometry (± 1%).



(1)

Table 1. Dependence of the deuterium content of the bimesityl on the reaction conditions

	$NaBD_4$ CH_3OH	$NaBD_4$ CD_3OD	$NaBH_4$ CD_3OD	$NaBH_4$ CH_3OD	$4NaOCH_3$ CH_3OD	$4NaOCH_3$ CD_3OD
$[D_0]$-Bimesityl (%)	96	8	7	16	95	63
$[D_1]$-Bimesityl (%)	3	34	36	42	4	33
$[D_2]$-Bimesityl (%)	0	57	57	43	1	4.5
% D	2	74	75	64	3	21

As is evident from Table 1, it is not the hydrido hydrogen that appears in the product but the acidic proton of the methanol to the extent of about 85%.

Since the diazonium tetrafluoroborate *(1)* is stable for two hours in methanol at room temperature, the tetrahydridoborate must first reduce the diazonium salt to the aryldiimine. The latter compound then rapidly exchanges the N–H proton with the solvent and decomposes mainly *via* the diimine anion to give nitrogen and an aryl anion, which abstracts a proton or deuteron from the solvent, thus yielding the hydrocarbon[2,3].

$$Ar{-}N{\equiv}N^{\oplus} + NaBH_4 \rightarrow Ar{-}N{=}NH \overset{\pm H^{\oplus}}{\rightleftharpoons}$$

$$Ar{-}N{=}N^{\ominus} \rightarrow Ar^{\ominus} + N_2 \xrightarrow{+H^{\oplus}} Ar{-}H$$

In acetonitrile, the bimolecular decomposition of phenyldiimine was formulated as a free-radical process and an isotope effect $k_H/k_D = 4$–5 was observed[4]. The difference between the third and fourth columns of Table 1 shows that with hydride in methanol only about 15% of aryl radicals are formed that abstract hydrogen from the C–H bond. In the reaction with 4 mol. equiv. of non-deuterated sodium methoxide the percentage of radicals increases markedly (columns 5 and 6).

We attribute incomplete deuteration (75 and 21%) in $[D_4]$-methanol with $NaBD_4$ and with sodium methoxide, respectively, to the isotope effect[3,4] and to water present in compound *(1)*. If the salt is prepared in D_2O up to 85% deuteration is achieved.

About 10% of 3,3'-difluorobimesityl containing no deuterium and 8% of 3-fluorobimesityl (also deuterated) were obtained as by-products. Decomposition of *(1)* in boiling methanol affords 75% of 3,3'-difluorobimesityl and 13% of 3-fluoro-3'-methoxybimesityl (oil), but no bimesityl.

Experimental:

3,3'-Diaminobimesityl (270 mg) are diazotized in 20% hydrochloric acid (1.1 g) with $NaNO_2$ (138 mg) in water (1 ml) at 0 °C; the filtered solution is treated with $NaBF_4$ (330 mg) in water (0.8 ml) and the resulting precipitate is filtered off after 30 min. The salt (350 mg), which is washed with 5% $NaBF_4$ solution (0.2 ml), cold methanol (0.2 ml), and ether (1 ml) successively and dried over P_2O_5 for 5 h under vacuum, is suspended in methanol (2 ml) and treated at 0 °C, with stirring, with $NaBH_4$ (80 mg); heat is evolved during the reaction. After 2 h the reaction mixture is extracted with *n*-hexane and the residue obtained after evaporation of the solvent is separated by layer chromatography on silica gel (Merck PF 254) with light petroleum (60–70 °C) into three zones. After scraping the compounds off the plate they are eluted and finally sublimed under high vacuum: bimesityl (40 mg, 22% calc. w.r.t. *(1)*, $R_f = 0.57$, m.p. 101 °C); 3,3'-difluorobimesityl (20 mg, 10%, $R_f = 0.67$, m.p. 127 °C); 3-fluorobimesityl (15 mg, 8%, $R_f = 0.61$, m.p. 109 °C).

Received: February 12, 1969 [Z 950 IE]
German version: Angew. Chem. *81*, 392 (1969)
Publication delayed at the authors' request

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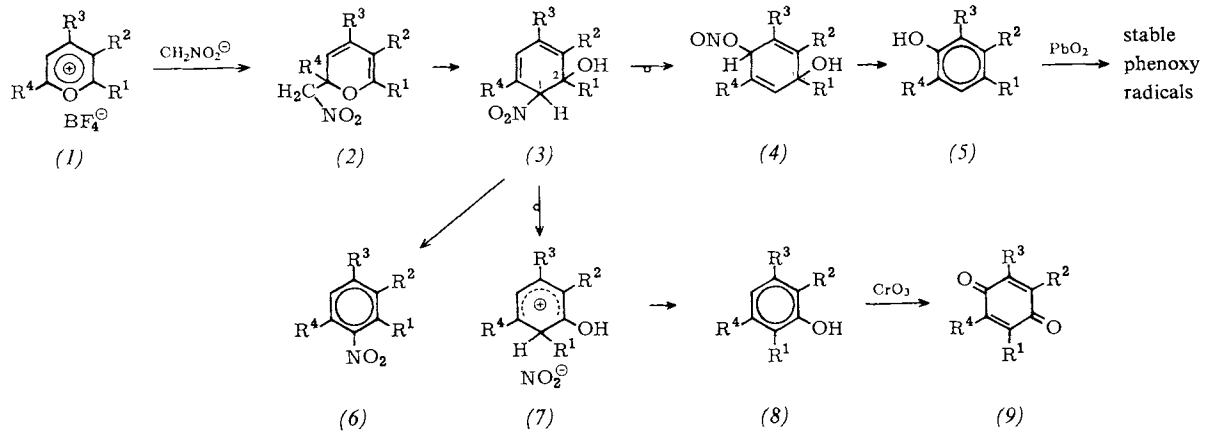
New Rearrangements during the Reaction of Pyrylium Salts with Nitromethane

By *K. Dimroth* and *G. Laubert*[*]

Dedicated to Professor H. Bredereck on the occasion of his 65th birthday

Whereas 2,4,6-trisubstituted pyrylium salts, and those carrying a greater number of substituents, are converted smoothly into nitrobenzene derivatives by nitromethane and an *excess* of base[1], reaction with only *one mol. equiv.* of base adopts a different course, especially in chlorobenzene, dichloroethane, or ethanol. Thus, 2,4,6-triphenylpyrylium tetrafluoroborate *(1a)* affords 2,4,6-triphenylphenol *(5a)*, 2,3,5-triphenylphenol *(8a)*, and 2,4,6-triphenylnitrobenzene *(6a)*. In a similar manner, 2,3,4,6-tetraphenylpyrylium tetrafluoroborate *(1b)* gives *(5b)*, *(8b)*, and *(6b)*.

If it is assumed that primary attack of the nitromethyl-anion on C-2 or C-6 to give *(2)* is followed by an intramolecular aldol condensation to yield the intermediate *(3)*, then the experimental findings may be interpreted as follows: Formation of the phenols *(5)* proceeds *via* 1,3-nitro-nitroso ester rearrangement to *(4)* and aromatization with subsequent hydrolysis of the phenol nitroso ester. The phenols *(8)* arise by a migration of the aryl group R^1 from C-2 to C-1 with



	R^1	R^2	R^3	R^4	(5) m.p. (°C)	(5) yield (%)	(6) m.p. (°)	(6) yield (%)	(8) m.p. (°C)	(8) yield (%)	(9) m.p. (°)	(9) yield (%)
(a)	C_6H_5	H	C_6H_5	C_6H_5	149–150 [2]	36	142–143 [1]	5	162–163	2	157	14
(b) [a]	C_6H_5	C_6H_5	C_6H_5	C_6H_5	244–245 [3]	7	216–217 [3]	19	272–273 [4]	5	309–310 [5, 6]	60
(c) [a]	$C_6H_4OCH_3$ [4]	C_6H_5	C_6H_5	C_6H_5	195–196	2	200–201	8	193–194	24	192–193	63

[a] Solvent: ethanol; base: triethylamine; 2 hours' reflux.

loss of $NO_2^{\ominus}$ and aromatization, whereas the normal formation of nitrobenzene to yield *(6)*, which proceeds without rearrangement, requires initial loss of the proton on C-1.

The intermediate *(3)* is not isolable. However, we have previously succeeded in isolating a similar, extremely labile intermediate having NO_2 and C_6H_5 attached to C-1 [3]. This compound undergoes not only a 1,3-nitro-nitroso ester rearrangement but also a 1,3-nitro rearrangement, which we were not able to observe in the present case.

The 1,2-aryl shift is favored by the presence of electron-donating substituents in the migrating aryl group. If the pyrylium salt *(1c)* is subjected to this reaction instead of the pyrylium salt *(1b)*, then the phenol *(8c)* is obtained in 24% yield instead of the phenol *(8b)* (5%). In the action of nitromethane on pyrylium salts the new rearrangements lead directly to phenols, which, depending on their substitution, are converted by oxidation into stable phenoxy radicals in the case of *(5)*, and into 1,4-quinones *(9)* in the case of *(8)*. In view of its simplicity and of the high overall yield, the new rearrangement process, which leads from *(1a)* to *(5a)* in *one step*, is certainly competitive with the multi-step process starting from *(6a)* [2].

Procedure

Ethyldiisopropylamine (1.9 g, 15 mmole) is added dropwise to a suspension of *(1a)* (5.9 g, 15 mmole) in chlorobenzene (60 ml) and nitromethane (3.7 g, 60 mmole) and the reaction mixture is refluxed for 15 h, during which nitrous fumes are evolved. The precipitated ammonium salt and unreacted pyrylium salt (2.21 g) are filtered off, and the filtrate is concentrated under vacuum and chromatographed on silica gel (benzene/cyclohexane 3:2). Crystallization from ethanol affords *(6a)* (0.30 g, 5%), *(5a)* (1.76 g, 36%), and *(8a)* (0.097 g, 2%), which is recrystallized from benzene/light petroleum.

Received: February 28, 1969 [Z 952 IE]
German version: Angew. Chem. *81*, 392 (1969)
Publication delayed at the authors' request

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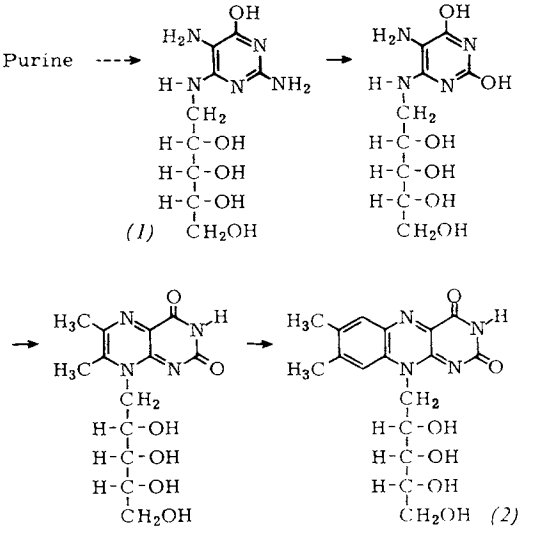
The Structure of the Purine Precursor in Riboflavin Biosynthesis [**]

By *A. Bacher* and *F. Lingens* [*]

Dedicated to Professor H. Bredereck on the occasion of his 65th birthday

Although the involvement of a purine in riboflavin (vitamin B_2) *(2)* biosynthesis has repeatedly been confirmed, the structure of the actual precursor compound has hitherto not been determined [1,2].

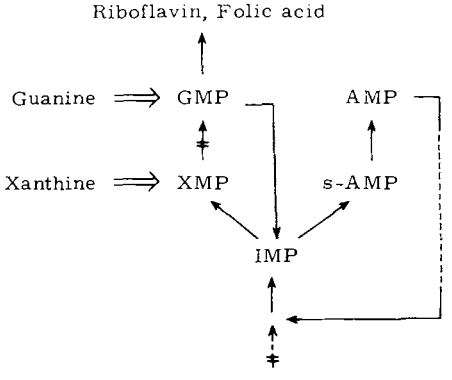
Studies on *Eremothecium ashbyii* [3] and riboflavin-less mutants of *Saccharomyces cerevisiae* [4,5] have suggested the



Scheme 1. Intermediates in the biosynthesis of riboflavin.

sequence of intermediates as shown in Fig. 1. The structural similarity of *(1)* and guanine seems to indicate that riboflavin is derived from a guanine compound. This assumption could be proved by experimental work on a purine-deficient mutant.

We started from a polyauxotrophic mutant exhibiting several genetic defects in the biosyntheses of the aromatic amino acids, namely *Aerobacter aerogenes* 62-1 [6]. Following treatment with 1-methyl-3-nitro-1-nitrosoguanidine (MNNG) we obtained a mutant 62-1 A showing a poorly defined genetic block in the common pathway of purine biosynthesis. Further exposure of this mutant to MNNG permitted isolation of a new mutant 62-1 AB exhibiting an additional block between xanthosine monophosphate (XMP) and guanosine monophosphate (GMP) (Fig. 2).



Scheme 2. Biosynthesis of purines in *Aerobacter aerogenes* according to *Magasanik* and *Karibian* [7] and genetic defects (=) of mutant 62-1 AB in purine metabolism. s-AMP = succinyladenosine monophosphate. => conversions of exogenic purines.

Feeding this mutant with purine bases results in the accumulation of riboflavin and xanthosine. After incubation of mutant 62-1 AB with ^{14}C-labeled purines according to Table 1, we found that [2-^{14}C]-xanthine is converted into xanthosine, but not into riboflavin. This means that riboflavin is not derived from a compound at the level of xanthine.

Table 1. Incorporation of radioactively labeled guanine or xanthine into xanthosine and riboflavin.

Added purines (mg/l)		Rel. activity (R. A.) [a] Xanthosine	Riboflavin
[2-^{14}C]-Guanine	5		
Adenine	5		
Hypoxanthine	10	1.6	89
Xanthine	8		
[2-^{14}C]-Xanthine	10·7		
Adenine	5	51	0.3
Guanine	5		

[a] R. A. = $\frac{\text{Sp. activity of isolated compound}}{\text{Sp. activity of proffered compound}} \times 100$

As expected, [2-^{14}C]-guanine is converted into riboflavin without significant dilution. Although adenosine monophosphate (AMP) and inosine monophosphate (IMP) may originate from guanine [7], these compounds can be excluded as precursors of riboflavin since in the presence of unlabeled adenine and hypoxanthine no significant isotope dilution takes place. This leads to the conclusion, confirmed by the results of accumulation studies [5], that riboflavin is derived from a compound at the level of guanine. It remains to be seen whether this substance is free guanine, a riboside, or ribotide.

Received: February 28, 1969; abbreviated: March 19, 1969 [Z 975 IE]
German version: Angew. Chem. *81*, 393 (1969)

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[**] This work was supported by the Fonds der Chemischen Industrie, the Deutsche Forschungsgemeinschaft, and Badische Anilin- und Soda-Fabrik.

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Tetracarbonyldiphosphanemolybdenum(0)

By *C. G. Barlow*, *E. A. V. Ebsworth*, and *G. C. Holywell* [*]

In view of the recent interest in complexes of transition metals with PH_3 [1,2], and of the preparation of tetracarbonylbisphosphinemolybdenum(0) from phosphine and tetracarbonylnorbornadienemolybdenum(0) [3], we have investigated the reaction between tetracarbonylnorbornadienemolybdenum(0) and P_2H_4 in pentane. At 0 °C a pale yellow microcrystalline solid separated over a period of an hour.

The infrared spectrum of this compound between 4000 and 200 cm^{-1} contains peaks in the regions associated with CO stretching, Mo–C–O bending, and Mo–C stretching; besides these, there were bands near 2200 cm^{-1}, near 1100 cm^{-1}, and at lower frequencies, which shifted to *ca.* 1600 cm^{-1} and 800 cm^{-1} in the spectrum of material prepared from P_2D_4 and which we assign to PH_2 stretching and bending modes. The C, H, and P analyses are in satisfactory agreement with the formulation of the compound as $P_2H_4Mo(CO)_4$. The compound is very slightly soluble in carbon disulfide, but we have been unable to obtain the proton resonance spectrum.

In the mass spectrum the fragments of the greatest mass appear to correspond to ions derived from $Mo(CO)_4(P_2H_4)_2$; there are groups of peaks at lower *m/e* ratios apparently corresponding to successive loss first of all four carbonyl groups and then of the four PH_2 groups. We therefore conclude that the compound should be represented as $[P_2H_4Mo(CO)_4]_x$, where x may be 2 or more.

Received: December 10, 1968 [Z 954 IE]
German version: Angew. Chem. *81*, 330 (1969)

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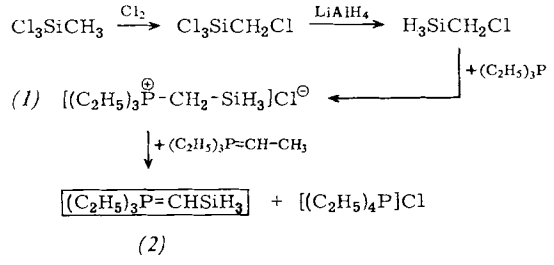
New Evidence for a (p→d)π Effect at Silicon [1]

By *H. Schmidbaur* and *W. Malisch* [*]

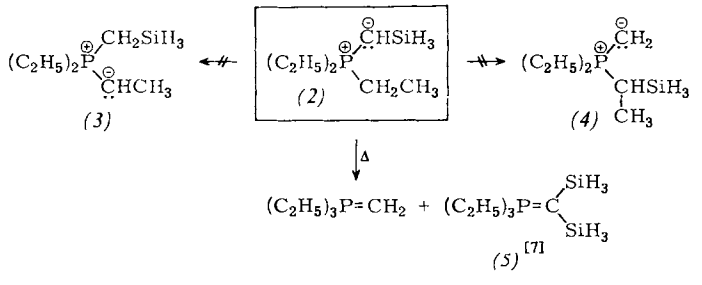
Recent investigations on model substances have clearly established that alkylsilyl substituents stabilize the carbanion function of phosphorus ylids to a surprisingly high extent [1–4].

This stabilizing effect is in contrast to the quite obvious destabilizing effect of simple alkyl groups on these anionic groups[5]. Only the *tert*-butyl group exerts an influence akin to that of trialkylsilyl groups. This led *Seyferth et al.*[2] to reject an interpretation that attributes the stabilizing properties of silyl substituents on ylidic carbanions to a ($2p_C \rightarrow 3d_{Si})\pi$ effect, although they and other authors[3,4] had originally preferred this explanation. The objection that the observed phenomena could be attributed solely to steric effects[2] could not initially be discounted.

In order to come to a decision we have now undertaken the synthesis of silyl-substituted ylids containing simple silyl (H_3Si-) instead of the extremely bulky trialkylsilyl groups. The following scheme shows a typical preparative procedure.



The critical last step is to be interpreted as a "transylidation" of triethyl(silylmethyl)phosphonium chloride *(1)* by triethylethylidenephosphorane. This reaction yields tetraethylphosphonium chloride and triethyl(silylmethylene)phosphorane *(2)* almost quantitatively, thus proving the thermodynamic preference of the latter over the possible alternative product diethyl(ethylidene)(silylmethyl)phosphorane *(3)*.



[7]

Earlier experiments with substituted and unsubstituted ylids have shown that the proton migration necessary for the conversion of *(2)* into *(3)* (particularly in the presence of the corresponding salt) is kinetically feasible[4]. Even a silyl migration *(2)* → *(4)* would be conceivable if it were thermodynamically advantageous[1,5]. However, isomerization of *(2)* to *(3)* or to *(4)* could be induced neither thermally nor catalytically.

There is no explanation for the preference of *(2)* over the other isomers on the basis of steric hindrance, nor of a simple inductive effect in the σ skeleton. In this and in many other cases the concept of a $(p \rightarrow d)\pi$ interaction currently represents the most promising theoretical model[6].

Procedure:

$ClCH_2SiH_3$ (2.7 g, 34 mmole) is added over a period of 1 h to $(C_2H_5)_3P$ (4.02 g, 34 mmole) with cooling (methanol/Dry Ice). At −30 °C quantitative formation of quaternary salt takes place spontaneously in an exothermic reaction to yield *(1)* (6.7 g) as a white crystalline powder, m.p. > 340 °C. IR: $\nu_{as}SiH_3$ 2180 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 60 MHz, TMS as external reference[8]): δSiH_3 −240, dt, J(HCSiH) 4, J(PCSiH) 8.2; δCH_2Si −151, dq, J(PCH) 16; δCH_3CH_2 −161, dq, J(PCH) 13, J(HCCH) 7.5; δCH_3 −88, dt, J(PCCH) 18.

$(C_2H_5)_3PCHCH_3$ (3.7 g, 25.4 mmole) is added to a suspension of *(1)* (5 g, 25.4 mmole) in ether (50 ml) and the mixture is stirred for 20 days at room temperature with exclusion of air. The solid reaction product $[(C_2H_5)_4P]Cl$ is filtered off and the ether removed from the filtrate under vacuum, whereupon compound *(2)* remains as a colorless, spontaneously inflammable liquid (78% yield): b.p. 36–38 °C/5 × 10^{-4} torr, mol. wt. (cryoscopic, benzene) 169 (calc. 162.3). IR: $\nu_{as}SiH_3$ 2090 cm^{-1}. ^{1}H-NMR (pure liquid, TMS as external reference[8]): δSiH_3 −239, dd, J(HCSiH) 4, J(PCSiH) 8.5; δCH +89, dq, J(PCH) 7; δCH_2 −92, dq, J(H_2CP), 10.5; δCH_3 −59, dt, J(HCCP) 16.5, J(HCCH) 7.7.

In a similar manner we obtained:

$(CH_3)_3P{=}CH{-}SiH_3$, m.p. −16 °C, mol. wt. 115.2 (calc. 120.2). IR: $\nu_{as}SiH_3$ 2100 cm^{-1}. ^{1}H-NMR (benzene, TMS as external reference): δSiH_3 −2.45, dd, J(HSiCP) 10.4 Hz, J(HSiCH) 3.8 Hz; δCH +77, dq, J(HCP) 6; δCH_3P −26, d, J(HCP) 12.5 Hz.

$(CH_3)_3P{=}C(SiH_3)_2$, m.p. 11–13 °C, b.p. 24–25 °C/4 × 10^{-2} torr, mol. wt. 143.5 (calc. 150.3). IR: $\nu_{as}SiH_3$ 2102. ^{1}H-NMR (see above): δSiH_3 −241.5, d, J(HSiCP) 10.2 Hz; δCH_3 −19.5, d, J(HCP) 12.5; $J(^1H^{13}C)$ 127.5 Hz, $J(^1H^{29}Si)$ 189 Hz.

Received: January 16, 1969 [Z 959 IE]
German version: Angew. Chem. *81*, 329 (1969)

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[8] All values in Hz; negative signs for lower field (60 MHz).

$FXeOTeF_5$: A Derivative of Xenon Difluoride

By *F. Sladky*[*]

Xenon difluoride reacts with oxyacids such as $HOSO_2F$, $HOClO_3$, and $HOPOF_2$ in the molar ratio 1:1 with elimination of HF.

The xenon-containing intermediate products are thermally unstable and decompose into the corresponding complex peroxides and oxides ($S_2O_6F_2$, Cl_2O_7, $P_2O_3F_4$)[1].

Pentafluoroorthotelluric acid[2], however, quantitatively yields a stable xenon-containing reaction product:

$$XeF_2 + HOTeF_5 \rightarrow FXeOTeF_5 + HF$$

Fluoroxenon pentafluoroorthotellurate is a pale yellow liquid (b.p. 53 °C/0.01 torr; m.p. −24 °C) which can be distilled without decomposition in a glass apparatus under vacuum. IR (liquid film between AgCl plates; 4000–400 cm^{-1}): 768 (s), 704 (vs), 623 (s), 520 (m), and 470 cm^{-1} (m). The ^{19}F-NMR spectrum indicates a value of 37 ppm for δ_{TeF} in the AB_4 part of the $OTeF_5$ grouping and a value of 66.3 ppm for δ_{XeF} (CF_3COOH as external standard).

$FXeOTeF_5$, like XeF_2 [3], can give up a fluoride ion to acceptors such as AsF_5:

$$FXeOTeF_5 + AsF_5 \rightarrow [F_5TeOXe]^+[AsF_6]^-$$

Reaction of $FXeOTeF_5$ with CsF proceeds *via* two routes in almost equal proportions:

$$FXeOTeF_5 + CsF \begin{cases} \nearrow TeF_6 + (FXeO^-Cs^+) \rightarrow CsF + Xe + {}^1/_2O_2 \\ \searrow XeF_2 + Cs[OTeF_5] \end{cases}$$

Experimental:

All reactions were followed gravimetrically and tensimetrically in easily weighable Kel–F reaction vessels fitted with Kel–F taps. Vacuum manipulations were carried out in a Monel system. The XeF_2 used in the experiments was prepared photolytically [4]. Reaction of 2.35 g (13.9 mmole) of XeF_2 with 3.33 g (13.9 mmole) of $HOTeF_5$ yields 5.20 g of $FXeOTeF_5$, yield 96%.

Received: January 10, 1969 [Z 960 IE]
German version: Angew. Chem. *81*, 330 (1969)

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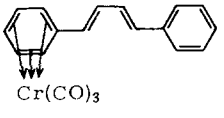
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Dibenzo[*a,e*]cyclooctene Complexes of Chromium and Molybdenum

By *J. Müller, P. Göser*, and *M. Elian* [*]

Most of the π-aromatic complexes of chromium are considerably more stable than its π-olefin complexes. For instance, reaction of $Cr(CO)_6$ with 1,4-diphenylbutadiene leads exclusively to tricarbonyl(1,4-diphenylbutadiene)chromium(0) *(1)* [1,2].



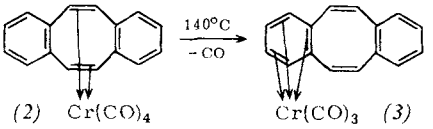
(1)

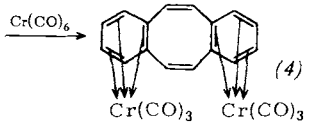
For steric reasons the olefinic π-electron system of dibenzo[*a,e*]cyclooctene [3] (= L) seems to be considerably better able to form complexes with chromium than is that of butadiene, and by its use we have been able to provide the first example of π-aromatic and π-olefin complexes from one ligand.

If the compound (L) is treated with tris(acetonitrile)tricarbonylchromium(0) [4] in 5–6-fold excess in di-*n*-butyl ether for 2 hours at 40 °C at water-pump vacuum and the ether is then removed and the residue eluted with warm hexane, the resulting solution affords crystals of the yellow tetracarbonyl(dibenzo[*a,e*]cyclooctene)chromium(0), $LCr(CO)_4$ *(2)*, m.p. 141–143 °C, in 90% yield (calculated on L). This can be sublimed almost without decomposition at 80–100 °C in a high vacuum and is thermally more stable than tetracarbonyl(1,5-cyclooctadiene)chromium(0) [5]. However, when heated in *n*-decane or di-*n*-butyl ether at 140 °C, *(2)* loses CO during 1.5 hours to form yellow tricarbonyl(dibenzo[*a,e*]cyclooctene)chromium(0), $LCr(CO)_3$ *(3)*, m.p. 168–170 °C, that is purified by chromatography on silicagel in benzene and recrystallization from methylene chloride/hexane.

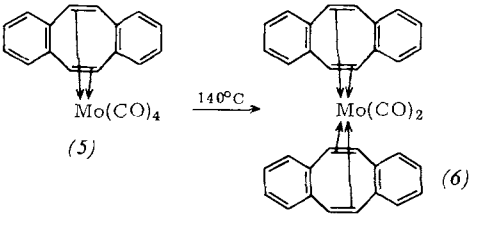
Complex *(3)* is apparently more stable than *(2)*. That the latter is formed first under mild conditions shows that less activation energy is required for complex formation of chromium with the olefinic π-electrons of ligand L (it is not necessary to compensate for the loss of resonance energy).

Heating this product *(3)* for 20 hours with a large excess of $Cr(CO)_6$ in di-*n*-butyl ether enables a further $Cr(CO)_3$ group to be introduced, thereby giving the orange, non-sublimable μ-dibenzo[*a,e*]cyclooctene-bis[tricarbonylchromium(0)], $LCr_2(CO)_6$ *(4)*, which can be purified in the same way as *(3)* (decomp. above 170 °C).

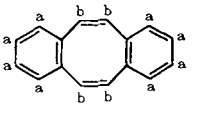
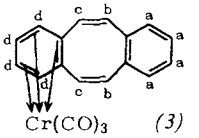




Treating an excess of tris(acetonitrile)tricarbonylmolybdenum(0) [4] with L in dioxane at 35 °C/15 torr for 2 hours gives a 65% yield (calculated on L) of tetracarbonyl(dibenzo[*a,e*]cyclooctene)molybdenum(0), $LMo(CO)_4$ *(5)*, which forms pale greenish-yellow crystals of m.p. 170 °C (decomp.). It has not yet proved possible to convert this into a complex analogous to *(3)*; instead, heating it in di-*n*-butyl ether for 6–8 hours leads to separation of decomposition products and formation of the lime-green *cis*-dicarbonylbis(dibenzo[*a,e*]-cyclooctene)molybdenum(0), *cis*-$L_2Mo(CO)_2$ *(6)*, m.p. 215 °C (decomp.). The contrasting behavior of chromium and molybdenum expresses clearly the differing tendencies of these metals to formation of π-aromatic and π-olefinic complexes.



The constitutions of the new complexes were proved by elemental analyses, mass spectra [6], the number and positions of the ν_{CO} vibrations, and the ^{1}H-NMR spectra (Table).

Compound	τ [a]	I_{rel}	Assignment
	2.73	2	a
	3.08	1	b
(2)	2.88	2	a
	4.70	1	b
 *(3)*	2.65	2	a
	3.12	1	b
	3.29	1	c
	4.35	2	d
(4)	4.26	2	a
	3.23	1	b
(5)	2.85	2	a
	4.23	1	b

[a] In deuterioacetone.

The following are among the characteristic ions appearing in the mass spectra: *(4)*: $LCr_2(CO)_6^+$ (I_{rel} = 12), $LCr_2(CO)_4^+$ (1.5), $LCr_2(CO)_3^+$ (21), $LCr_2(CO)_2^+$ (2.8), LCr_2CO^+ (3.2), LCr_2^+ (14), LCr^+ (85), Cr^+ (100); *(6)*: $L_2Mo(CO)_2^+$ (I_{rel} = 9.2), L_2MoCO^+ (28), L_2Mo^+ (28), LMo^+ (100), Mo^+ (2.3).

The IR spectra of the compounds in hexane solution included the following absorptions in the ν_{CO} region (in cm^{-1}): *(2)*: 2037, 1961, 1916; *(3)*: 1980, 1913; *(4)*: 1980, 1913; *(5)*: 2050, 1975, 1965, 1915; *(6)*: 1978, 1940.

Received: January 16, 1969 [Z 961 IE]
German version: Angew. Chem. *81*, 331 (1969)

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[6] Atlas-CH4; ion source T04; 50 eV.

A Tetrasulfide Chelate of Molybdenum[1]

By *H. Köpf*[*]

The few polychalcogenide chelates of platinum[2] and titanium[3] that have become known up to the present time all contain six-membered metal-chalcogen rings ("heterocyclohexachalcogens"). Thus, for example, attempts to prepare the four- and five-membered rings $(C_5H_5)_2TiS_3$ and $(C_5H_5)_2TiS_4$[4] always led to the stable six-membered ring $(C_5H_5)_2TiS_5$ *(1)*[5].

However, when we treated dichlorobis(cyclopentadienyl)-molybdenum(IV) *(2)* with ammonium pentasulfide we obtained, not the expected[6] pentasulfide, but the tetrasulfide chelate *(3)* and thus the first simple hetero derivative[7] of the still unknown cyclopentasulfur.

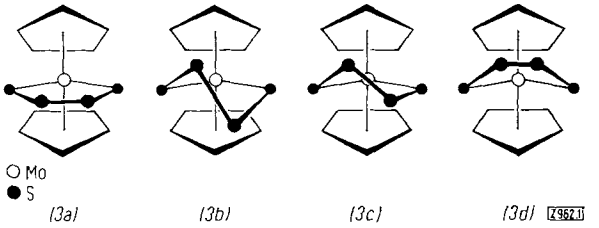
$$(C_5H_5)_2MoCl_2 + (NH_4)_2S_5 \rightarrow$$
(2)

$$(C_5H_5)_2Mo\begin{matrix}S\!-\!S\\ \|\\ S\!-\!S\end{matrix} + {}^1/_8\,S_8 + 2\,NH_4Cl$$
(3)

The composition $[(C_5H_5)_2MoS_4]_n$ of *(3)* follows from complete elemental analysis; according to ebullioscopic molecular-weight determinations in acetone $n = 1$. Compound *(3)* crystallizes from acetone as dark red, air-stable prisms that decompose slowly above 180 °C and rapidly at 250 °C. It is less soluble than *(1)* in organic solvents and the absorption of its orange to bright red solutions exhibits a hypsochromic shift (absorption shoulder at 400 nm).

The IR spectrum of *(3)* [KBr disk; cm^{-1}: 3100 s (ν_{CH}); 1430 vs, 1410 vs, 1350 w, 1120 vw, (ω_{CC}); 1075 w, 1063 w, 1012 m, 1000 s (δ_{CH}); 954 vw, 926 vw, 872 m, 832 vs, 822 vs (γ_{CH}); 482 w (ω_{SS}?)] shows the vibrations of the intact $(\pi\text{-}C_5H_5)_2Mo^{IV}$ system. The band at 482 cm^{-1} is tentatively assigned to a S_4 skeletal vibration.

Of the four ideal conformations *(3a–d)* that are conceivable for a MoS_4 five-membered ring, *(3a)* and *(3b)* have equivalent cyclopentadienyl rings, whereas in the case of *(3c)* and *(3d)* in the conformationally rigid state two separate ^{1}H-NMR signals for one axial and one equatorial cyclopentadienyl ligand – as have been observed[3], even at room temperature, for *(1)* – are to be expected.



(3a) *(3b)* *(3c)* *(3d)* [Z 962 I]

The ^{1}H-NMR spectrum of *(3)*, which was recorded for saturated solutions in acetone or dimethyl disulfide with TMS as external reference, contains only one sharp signal for the C_5H_5 protons at τ = 5.25 (in acetone) or 4.78 (in dimethyl disulfide) at room temperature, even with scale expansion, and this signal shows no splitting when the sample is cooled down to –95 °C (in acetone)[8].

Since the angle of twist $\sphericalangle$S–S–S–S of 75–100 °[9] necessary for stable sulfur rings can, moreover, only be realized in *(3b)* and *(3c)*, it is probably the conformer *(3b)* that is present in solution at sufficiently low temperatures.

Bis(cyclopentadienyl)tetrasulfidomolybdenum(IV) (3)

Bis(cyclopentadienyl)dihydridomolybdenum(IV) *(4)*[10] (2.3 g, 10 mmole) is refluxed for 3 h with chloroform (150 ml) in the absence of light and with exclusion of air and moisture to yield compound *(2)*[11]. After removal of the excess of chloroform under vacuum, the olive green residue is treated with 150 ml of a saturated solution of freshly prepared ammonium pentasulfide[12] in water/ethanol (1:5 v/v) and refluxed for 1 h with vigorous stirring. The reddish brown precipitate is filtered off, washed with ethanol, and recrystallized from acetone. Yield 3.1 g (88 % calculated with respect to *(4)*).

Received: January 22, 1969 [Z 962 IE]
German version: Angew. Chem. *81*, 332 (1969)

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Bis(sulfinylamido)mercury(II)

By *W. Verbeek* and *W. Sundermeyer* [*]

Not only many organic *N*-sulfinylamines [1] but also *N*-(trimethylsilyl)sulfinylamine [2] are known, the reactions of the latter being very similar to those of silyl pseudohalides.

We have obtained bis(sulfinylamido)mercury(II) *(1)* as the first sulfinylamide of a metal by reaction of mercury(II) fluoride with *N*-(trimethylsilyl)sulfinylamine. The reaction proceeds quantitatively.

$$HgF_2 + 2(CH_3)_3SiNSO \rightarrow Hg(NSO)_2 + 2(CH_3)_3SiF$$
(1)

Tetrahydrofuran is a particularly suitable solvent as *(1)* dissolves readily in it and can be recrystallized from it. 23 g of HgF_2 reacts with 27 g of $(CH_3)_3SiNSO$ in 40–60 ml of boiling, stirred, dry THF within 30 min in a strongly exothermic reaction.

The amide *(1)* crystallizes as colorless needles, m.p. 128 °C (decomp.), but, if heating is too slow, decomposition sets in below the melting point. In contrast to most organic sulfinylamines, it is surprisingly stable to hydrolysis and alcoholysis. Compound *(1)* was identified by analysis and its mass spectrum [3] [with reference to the isotope ^{202}Hg: m/e = 326, $Hg(NSO)_2$; 264, Hg(NSO); 202, Hg; 48, SO; 46, NS; 32, S]. The IR spectrum (Nujol) shows bands at 1250 s, 1217 s, 1078 s, 604 m, 590 m, 561 m, 313 s, and 280 w cm^{-1}.

Received: January 30, 1969 [Z 965a IE]
German version: Angew. Chem. *81*, 330 (1969)

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[3] We are very grateful to Dr. *Seidl*, Badische Anilin- und Soda-Fabrik, for measurement and discussion of the mass spectrum.

N-Halosulfinylamines

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In connection with our studies of the reaction of silyl pseudohalides with the halides of various elements we have treated *N*-(trimethylsilyl)sulfinylamine [1] with halogens. The reaction with chlorine led to an almost quantitative yield of *N*-chlorosulfinylamine *(1)*, in contrast to the reactions of organic *N*-sulfinylamines which afford thionyl chloride and the corresponding amine with scission of the N=S bond [2].

$$(CH_3)_3SiNSO + Cl_2 \rightarrow Cl{-}N{=}S{=}O + (CH_3)_3SiCl$$
(1)

Liquid chlorine (15.8 g) is added dropwise to $(CH_3)_3SiNSO$ (30 g) with stirring at −76 °C, a smooth reaction giving compound *(1)* which, however, can be obtained pure and free from the accompanying chlorotrimethylsilane only by preparative gas chromatography. Alternatively, the reaction mixture may be converted by partial fluorine exchange with HgF_2 into fluorotrimethylsilane and unchanged *(1)*, and the latter then separated by fractional distillation.

(1) is a clear liquid (b.p. 65.5 °C, m.p. −80 °C) with a suffocating odor; it can be distilled under an inert gas at atmospheric pressure without decomposition; the vapor-pressure curve is represented by $\log p = -1784/T + 8.15$. (Trouton constant 24.1 cal/deg). It was identified by analysis and its mass spectrum [3] which contains fragments at m/e = 49 (NCl), 48 (SO), 46 (NS), 35 (Cl), and 32 (S), as well as the molecular ion at m/e = 97 (referred to ^{35}Cl). The IR spectrum (gas) showed the six bands required for a linear tetraatomic molecule (with tentative assignments) at 1248 vs (νS=O), 995 w (νN=S), 676 s (νN−Cl), 532 s (δNSO), 359 s (γ), and 187 s cm^{-1} (δClNS).

Compound *(1)* reacts vigorously with mercury and explosively with water. When heated in air it deflagrates with a bluish-white flame.

The analogous reaction of *N*-(trimethylsilyl)sulfinylamine with bromine gives a difficultly separable mixture that contains *N*-bromosulfinylamine *(2)*. However, *(2)* is formed quantitatively on treatment of stoichiometric amounts of bis(sulfinylamido)mercury [4] with bromine in trichlorofluoromethane at room temperature.

$$Hg(NSO)_2 + 2\,Br_2 \rightarrow 2\,Br{-}N{=}S{=}O + HgBr_2$$
(2)

(2) is a colorless liquid (b.p. 12 °C/12 torr, m.p. −48 °C) which becomes yellow at room temperature owing to loss of bromine. It was identified by its IR spectrum and its mass spectrum [m/e = 141 (BrNSO), 93 (NBr), 79 (Br), 48 (SO), 46 (NS), and 32 (S), referred to ^{79}Br]. There are six IR bands also in this case (with tentative assignments) at 1245 vs (νS=O), 1003 w (νS=N), 621 s (νN−Br), 456 s (δNSO), 335 s (γ), and 161 s cm^{-1} (δBrNS).

Reaction of *N*-(trimethylsilyl)sulfinylamine with fluorine gives a poor yield of *N*-fluorosulfinylamine *(3)*.

$$(CH_3)_3SiNSO + F_2 \rightarrow F{-}N{=}S{=}O + (CH_3)_3SiF$$
(3)

Fluorine, diluted with nitrogen, is passed into a solution of $(CH_3)_3SiNSO$ in trichlorofluoromethane at −80 °C. *(3)* is obtained from the reaction mixture by preparative gas chromatography but tends to explode on crystallization (at −196 °C); it was characterized by its mass spectrum [m/e= 81 (FNSO), 48 (SO), 46 (NS), 33 (NF), and 32 (S)]. IR spectrum: 1246 vs (νS=O), 1007 vs (νN=S), 834 s (νN−F), 606 s (δNSO), 394 s (γ), and 228 s cm^{-1} (δFNS).

The ^{19}F–NMR spectrum [5] at room temperature shows a triplet (NF coupling), δ = −123.3 ppm, referred to $CFCl_3$ as internal standard, with J_{FN} = 112 Hz.

Received: February 5, 1969: revised: March 28, 1969 [Z 965b E]
German version: Angew. Chem. *81*, 331 (1969)

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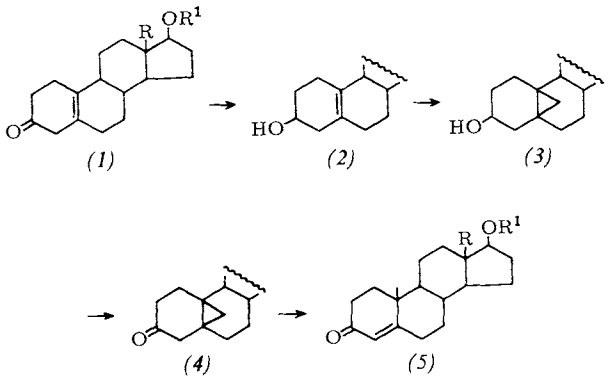
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Synthesis of Testosterones from Estrogens [1]

By *H. D. Berndt* and *R. Wiechert* [*]

The development of industrially applicable syntheses of estrones [2] aroused interest in effective methods for the introduction of an angular 10β-methyl group into 19-nor steroids.



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

(a), R = CH_3, R^1 = H
(b), R = CH_3, R^1 = $COCH_3$
(c), R = CH_3, R^1 = Tetrahydropyran-2-yl
(d), R = C_2H_5, R^1 = H
(e), R = C_2H_5, R^1 = $COCH_3$
(f), R = C_2H_5, R^1 = Tetrahydropyran-2-yl

Cpd.	M.p. (°C) [11]	$[\alpha]_D$ (°) [11]	Cpd.	M.p. (°C) [11]	$[\alpha]_D$ (°) [11]
(1a) [12]	190–193	+195	*(1d)*	105–106	+164
(2a) [5a]	144–146	+108	*(2d)*	162–163	+ 88
(3a) [13]	150–151	+ 21	*(3d)*	121–123	+ 19
(4a) [4a]	145–146	+ 25	*(4d)*	170–172	+ 21
(5a)	153–154	+113	*(5d)* [14]	175–176	+111
(1b) [15]	139–140	+153	*(1e)*	144–146	+142
(2b)	115–116	+ 85	*(2e)*	103–104	+ 77
(3b)	148–149	+ 19	*(3e)*	130–131	+ 23
(4b) [16]	142–144	+ 12	*(4e)*	140–141	+ 15
(5b)	138–139	+100	*(5e)*	114–115	+ 97
(1c)	132–135	+ 98	*(1f)*	146–147	+ 60
(2c)	135–137	+100	*(2f)*	113–114	+ 45
(3c)	132–135	+ 2	*(3f)*	102–105	− 38
(4c)	121–127	+ 89	*(4f)*	100–101	− 50

In spite of numerous experiments directed toward this aim[3], no simple and productive technique has hitherto been found.

For our investigations we chose the route *(1)*→*(5)* *via* the 5,10β-methylene steroids *(4)*[4]. For the success of this pathway it was essential to reduce 3-oxo-5(10)-estrenes *(1)* (which are readily obtainable by Birch reduction and subsequent enol-ether cleavage of steroids having an aromatic ring A) stereospecifically to 3β-hydroxy-5(10)-estrenes *(2)*. This reduction gives only 15–20% yields when carried out with complex metal hydrides, hydrogen in the presence of a platinum catalyst, or according to the Meerwein-Ponndorf method; the main products are 3α-hydroxy-5(10)-estrenes[4c,5]. A total yield of only about 30% is also obtained in the conversion of *(1)* into *(2)* by epimerization of 3α-hydroxy-5(10)-estrenes[5a] or *via* 5,10β-epoxysteroids[4c].

We have now found that 3-oxo-5(10)-estrenes *(1a)–(1f)* [IR: ν = 1710 cm^{-1} (C=O), NMR[6]: δ = 2.45 (intensity = 4, $W_{1/2}$ = 4 Hz) (H-1 and H-2), 2.75 (intensity = 2, $W_{1/2}$ = 5 Hz) (H-4)][7] can be converted into the corresponding 3β-hydroxy compounds *(2a)–(2f)* [NMR: δ = 3.90–4.20 (H-3); with *(2c)* and *(2f)* this signal partly overlaps with that of the OCH_2 group of the tetrahydropyranyl ether][7] in 65–90% yield by catalytic hydrogenation if highly active Raney nickel is used as catalyst and the reaction is performed under a hydrogen pressure as close to 200 atm as possible.

Compounds *(2b)*, *(2c)*, *(2e)*, and *(2f)* can, according to *Simmons-Smith*[8], be converted into the 5β,19-cycloandrostanes *(3b)*, *(3c)*, *(3e)*, and *(3f)*, respectively [IR: ν = 3050 cm^{-1} (cyclopropane), NMR: δ = 0.40 (cyclopropane)][7] in yields of up to 90% by refluxing with diiodomethane and zinc-copper couple[9] in ether/1,2-dimethoxyethane for 2 h. Jones oxidation[10] of the products with chromic acid in acetone smoothly affords the 3-ketones *(4b)*, *(4c)*, *(4e)*, and *(4f)* [IR: ν = 1705 cm^{-1} (C=O), 3050 cm^{-1} (cyclopropane), NMR: δ = 0.48 (cyclopropane), 2.52 (singlet, intensity = 2) (H-4)][7], which are isomerized on treatment with concentrated hydrochloric acid in glacial acetic acid (2:3) for 10 min at 70 °C[3b,3c,4c]. Mixtures of 17β-hydroxy and 17β-acetoxy steroids may then be isolated which can be hydrolyzed to the testosterones *(5a)* or *(5d)*, or acetylated to the testosterone acetates *(5b)* or *(5e)* [UV: ε_{240} = 16500; IR: ν = 1670 cm^{-1} (C=O), 1615 cm^{-1} (C=C); NMR: δ = 1.20 (CH_3-10), 5.70 (H-4)][7]. The yield of the reaction *(4)*→*(5)* again amounts to up to 90%.

Received: March 18, 1969 [Z 968 IE]
German version: Angew. Chem. *81*, 396 (1969)

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cis-Tricarbonyltris(phosphine)chromium(0)[1]

By *E. O. Fischer, E. Louis*, and *C. G. Kreiter*[*]

Stable mono- and bis-(phosphine) complexes of transition metals have already been reported by various authors[2–5]. We have now, for the first time, incorporated three PH_3 ligands into the molecule of an octahedral complex[**].

Reactions of the reactive tricarbonyl(hexamethylborazine)-chromium(0), $[B_3N_3(CH_3)_6]Cr(CO)_3$ [6] *(1)*, with tertiary phosphines and phosphites in suitable solvents lead rapidly to good yields of *cis*-tricarbonyl complexes, provided that steric factors do not introduce difficulties [7,8].

We have found that the analogous reaction with PH_3, namely:

$$(1) + 3\ PH_3 \xrightarrow{20\,^\circ C} \underset{(2)}{(PH_3)_3Cr(CO)_3} + B_3N_3(CH_3)_6$$

occurs in cyclohexane at room temperature almost quantitatively within a few minutes. Considering the low solubility of PH_3 in C_6H_{12} at atmospheric pressure, this shows once more the great tendency of PH_3 ligands for complex formation. The identity of the tricarbonyltris(phosphine)chromium(0) *(2)* produced was proved by total analysis and mass spectrometry and the IR and ^1H–NMR spectra show that it has exclusively the *cis*-configuration.

Thus the ν_{CO} region of the spectrum shows only two IR active fundamentals (A_1, E), as expected for a molecule of C_{3v} symmetry, and can be assigned on the basis of a series of known *cis*-$L_3Cr(CO)_3$ compounds (Table 1). The position of the A_1 band shows that for complex *(2)*, as in PH_3 complexes studied previously, the π-acceptor contribution to the metal-phosphorus bond is greater than in PR_3 compounds where R is alkyl or aryl.

Table 1. IR spectra (cm^{-1}) of *cis*-$L_3Cr(CO)_3$ complexes (Perkin-Elmer model 21, LiF optics).

Compound	ν_{CO} (A_1)	ν_{CO} (E)	Solvent
$(PH_3)_3Cr(CO)_3$	1972	1892	[a]
	1970	1887	[b]
$[P(n\text{-}C_4H_9)_3]_3Cr(CO)_3$ [7]	1920	1828	[b]
$[P(C_2H_5)_2C_6H_5]_3Cr(CO)_3$ [7]	1925	1835	[b]
$[P(OC_2H_5)_3]_3Cr(CO)_3$ [7]	1967	1874	[b]
$[B_3N_3(CH_3)_6]Cr(CO)_3$ [6, 8]	1963	1876	[b]

[a] *n*-Hexane. [b] Cyclohexane.

The IR spectrum of *(2)* (KBr pellet, NaCl optics) shows a band of moderate intensity at 2309 cm^{-1} in the ν_{PH} region and two strong to very strong bands at 1027 and 1004 cm^{-1} in the δ_{PH} region, and a further strong band at 917 cm^{-1}.

The ^1H-NMR spectrum (in CD_3COCD_3) shows two groups of signals, each containing three broadened bands, symmetrically around $\tau = 6.33$, which agrees with the *cis*-arrangement of the CO and PH_3 ligands [***]. In contrast, the *trans*-isomer would be expected to show two identical PH_3 groups and one unique PH_3 group differently shielded from the other two. The separations of the mutually symmetrical bands are 338, 308, and 282 Hz, and the intensities are in the ratio 1:0.98:0.46, respectively. The bands could not be resolved into single lines.

The rather complex structure of the proton resonance spectrum is caused by the nuclear-magnetic non-equivalence of the three PH_3 groups: We have here a $X_3X_3'X_3''$ partial spectrum of an $AA'A''X_3X_3'X_3''$ spin system. The almost identical chemical shifts of the PH protons in *(2)* and *cis*-$(PH_3)_2Cr(CO)_4$ ($\tau = 6.26$ in $CDCl_3$ [9]) suggest very similar electronic properties for the Cr–P–H_3 bonding. It seems reasonable to assume that the coupling constants between H and P in *(2)* are similar to those in *cis*-$(PH_3)_2Cr(CO)_4$.

Experimental:

Pure *(1)* (100 mg, 0.33 mole), obtained from $(CH_3CN)_3Cr(CO)_3$ according to ref. [6], is suspended in cyclohexane (30 ml) at room temperature and stirred vigorously under pure PH_3 (*ca.* 800 torr). A color change from orange-yellow to pale yellow is complete within 10 min. The product *(2)* is formed as a fine, pale-yellow precipitate. If larger amounts of *(1)* are used, the reaction requires a longer time since the solid *(1)* reacts slowly owing to its poor solubility.

For purification, *(2)* is collected on a G_4 fritted filter, washed several times with cold pentane, and finally dried at 0 °C *in vacuo*. The yield of crude product is 88% (70 mg).

Rapid working is required for complete purification of *(2)*. This is done by preparation of a saturated solution of the crude product in hexane at 25 °C [*ca.* 12 mg of *(2)* per 100 ml of hexane], filtration through filter wool, concentration of the filtrate to one-third of its volume under water-pump vacuum, and cooling to 0 °C. Decantation, washing with cold pentane, and drying *in vacuo* affords analytically pure *(2)*, which decomposes at 133–137 °C. Oxygen and moisture must be excluded during these operations.

Compound *(2)* dissolves only very slightly in aliphatic saturated hydrocarbons, moderately in ether, and readily in ethylene glycol dimethyl ether, tetrahydrofuran, or acetone. However, it decomposes rapidly in solution, especially if warmed or exposed to light. It sublimes slowly at 50–60 °C with slight decomposition. Mass spectrometry gave a molecular weight of 238.

Received: February 17, 1969 [Z 969 IE]
German version: Angew. Chem. *81*, 397 (1969)

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Association of Bis(trimethylsilyl)amidolithium and Methyl(trimethylsilanolato)beryllium in the Solid State

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Bis(trimethylsilyl)amidolithium, $[(CH_3)_3Si]_2NLi$, known since 1961 [1] and today a versatile reagent in preparative inorganic chemistry [2], is dimeric in solution, but, as we found by X-ray structure analysis, trimeric in the solid state.

Crystals obtained from petroleum ether [3] belong to space group $P2_1/c$ with twelve monomer units in the unit cell. The trimeric unit that is indicated thereby was confirmed by a complete X-ray structure analysis with more than 3000 photographic data: three crystallographically independent monomers are associated with formation of a planar six-membered ring with alternating nitrogen and lithium atoms. The bonding parameters given in Figure 1 are mean values

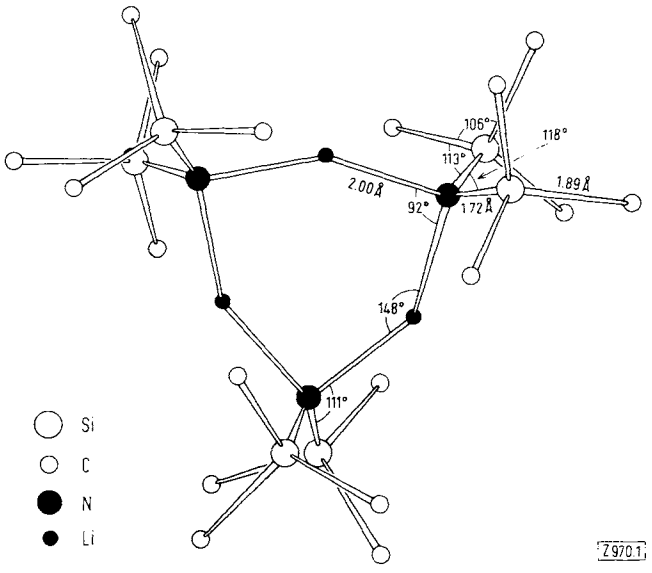


Fig. 1. *cyclo*-Tris[bis(trimethylsilyl)amidolithium] molecule, with bond lengths and bond angles. Estimated standard deviations are 0.02 to 0.05 Å and 1 to 2°.

of chemically equivalent individual distances and angles, deviations from the means being small and usually insignificant.

Comparison with the structures recently established for $\{[(CH_3)_3Si]_2N\}_3Fe$ (X-ray structure analysis[4]) and $[(CH_3)_3Si]_2NH$ (electron diffraction[5]) shows similar values for the Si–N atomic distances and a distinct minimum of the SiNSi bond angle for the structure now determined with the onium configuration of the nitrogen atom:

	$[(Me_3Si)_2NLi]_3$	$[(Me_3Si)_2N]_3Fe$	$(Me_3Si)_2NH$
Si–N	1.72 Å	1.731 Å	1.735 Å
∢ SiNSi	118°	121.2°	125.5°

Me = CH_3

On treatment of trimethylsilanol with dimethylberyllium a compound is formed[6] that crystallizes from petroleum ether in the space group C 2/c. The Patterson function with *ca.* 900 data measured on a single-crystal diffractometer permitted localization of two independent silicon atoms. An electron-density function phased therewith showed a tetrameric molecule of formula $[(CH_3)_3SiOBeCH_3]_4$ with a structure analogous to that of cubane, these facts being confirmed on refinement. The oxygen and beryllium atoms are situated at alternate vertices of an only slightly distorted cube (Figure 2); the O–Si and Be–C bonds lie on outward prolongations of the diagonals of the cube. A symmetry axis of the space group passes through the middle of the molecule, being parallel to the edges of the cube that are shown as approximately vertical in the Figure.

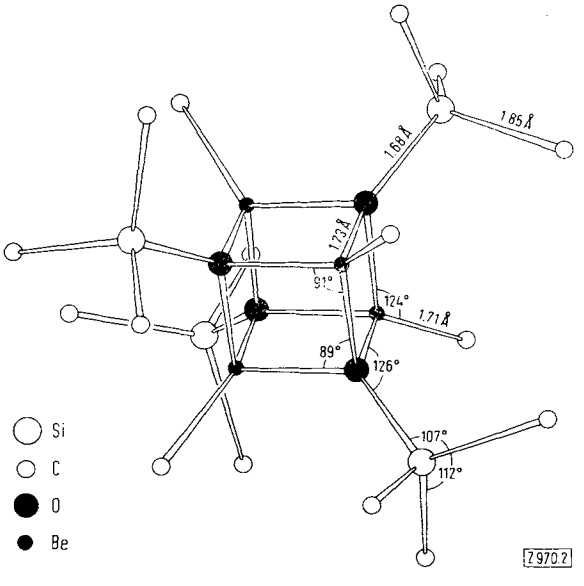


Fig. 2. *closo*-Tetrakis[methyl(trimethylsilanolato)beryllium] molecule, with bond lengths and bond angles. Estimated standard deviations are 0.01 to 0.02 Å and 1°.

None of the crystallographically independent but chemically equivalent bonding parameters differs significantly from the mean values given. The Be–O distance, 1.73 Å, is distinctly longer than in beryllium oxide[7] (1.65 Å). This results from repulsion between the large oxygen atoms, whose distance from one another in the cube is considerably smaller (2.47 Å) any way than in the more open BeO structure (2.70 Å).

The structure determined by us is the first certain oxaberyllia-cubane, although similar structures have been discussed for $[ROBeCH_3]_4$ where R = benzyl or phenyl[8].

Received: February 27, 1969 [Z 970 IE]
German version: Angew. Chem. *81*, 398 (1969)

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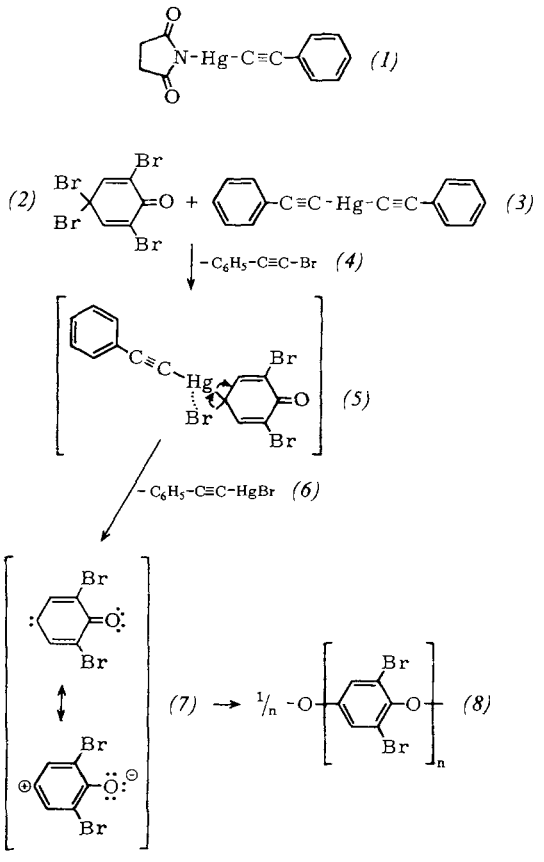
A New Synthesis of a Linear Poly(phenylene Oxide)

By *W. Ried* and *W. Merkel*[*]

N-Bromosuccinimide and mercury bis(phenylacetylide) in benzene afford compound *(1)* as well as 1-bromo-2-phenylacetylene *(4)*; and in THF the second phenylacetylene group is also replaced, affording mercury bis(succinimide). However, with 2,4,4,6-tetrabromo-2,5-cyclohexadienone *(2)*[1] we obtained poly(2,6-dibromo-1,4-phenylene oxide) *(8)*, 1-bromo-2-phenylacetylene *(4)*, and phenylethynylmercuric bromide *(6)* even at room temperature. Like *N*-bromosuccinimide, the ketone *(2)* contains a positively activated and thus very mobile bromine atom.

The polymer is a white amorphous powder, softening in the region 230–260 °C and with the formula $(C_6H_2OBr_2)_n$. An osmometric determination[2] in benzene at 36 °C leads to a mean molecular weight of 13000 ± 650, which corresponds to a mean chain length of 49–52 units. The IR spectrum (KBr disk) shows neither a C=O nor an O–H absorption, but there is a strong C–O–C band at about 1190 cm^{-1}.

Since the reaction under nitrogen proceeds in exactly the same way and here too no diphenoquinone can be detected, and in consideration of the by-products *(4)* and *(6)*, the reaction is postulated as occurring by way of *(5)* and *(7)*. Free



radicals are unlikely as intermediates because the pale yellow solution barely changes color during the reaction. If mercury diacetate or dichloride is used there is no formation of polymer. A formal consideration must thus include an acceptor for both bromine cations and bromide ions in order that polymerization may start. Up to the present a branched polymer of this type with a low molecular weight has been prepared only by oxidative coupling of 2,4,6-tribromophenol [3].

Poly(2,6-dibromo-1,4-phenylene oxide) (8):

Equivalent amounts of 2,4,4,6-tetrabromo-2,5-cyclohexadienone *(2)* and mercury bis(phenylacetylide) are dissolved in anhydrous THF and stirred for about 2 hours at room temperature. Addition of ether or methanol precipitates the polymer *(8)* together with *(6)*. The pure polymer is obtained by digestion of the crude product with benzene and subsequent precipitation by methanol. The reaction is quantitative.

Received: March 27, 1969 [Z 973 IE]
German version: Angew. Chem. *81*, 400 (1969)

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"Cyclosilane-d_{18}", a New ^{1}H–NMR Standard for Measurements up to 200 °C

By *L. Pohl* and *M. Eckle* [*]

During the past ten years numerous organosilicon compounds have been suggested as suitable stable internal standards for use in NMR measurements up to 200 °C – the upper limit of modern high-resolution NMR spectroscopy – in place of tetramethylsilane, which, on account of its low boiling point (27 °C), can be used only at temperatures up to 100 °C, even in sealed tubes. As can be seen from the table, however, not one of these compounds fulfills the requirements of a suitable standard, which should:

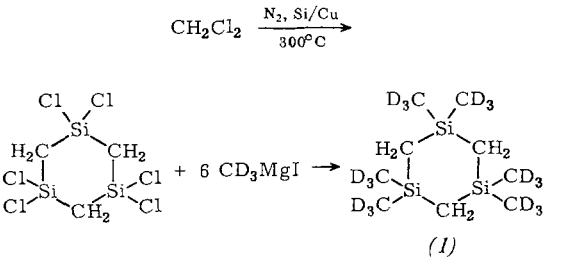
1. be chemically inactive and nonpolar,

2. be stable enough for measurements to be carried out at temperatures up to 200 °C,

3. have a chemical shift which permits measurements over the whole range downfield from δ = 0ppm.

Standard	B.p. (°C)	δ(ppm) in $CDCl_3$
Tetramethylsilane (TMS)	27	0.000
Hexamethyldisilane	113	0.037
Hexamethyldisilazane	126	0.042
Hexamethyldisiloxane	100	0.055
Octamethylcyclotetrasiloxane	134	0.085
Tris(trimethylsilyl)amine	m.p. 70	0.229
Tetrakis(trimethylsilyl)methane	m.p.307	0.236
"Cyclosilane-d_{18}" *(1)*	208	−0.327

We have now developed a standard, called "cyclosilane-d_{18}", which does satisfy the above requirements. It is 1,1,3,3,5,5-hexakis(trideuteriomethyl)-1,3,5-trisilacyclohexane *(1)*, which can be prepared according to the following reaction scheme [1]:



(1)

Compound *(1)* is a colorless liquid which boils without decomposition at 208 °C and has a ^{1}H-NMR singlet at δ = −0.327 ppm having a halfwidth of 0.5 Hz, thus permitting the recording of an unperturbed spectrum from δ = 0ppm downfield. It is very soluble in those solvents, such as [D_5]-pyridine (b.p. 116 °C), [D_2]-tetrachloroethane (148 °C), [D_7]-dimethylformamide (153 °C), [D_{12}]-tetramethylurea (176 °C), [D_8]-decalin (195 °C), hexachloroacetone (202 °C), hexachlorobutadiene (212 °C), and [D_{18}]-hexamethylphosphoric triamide (225 °C; HMPT), which come into consideration for measurements at increased temperatures. Compound *(1)* thus permits measurements with a stable internal standard to be carried out at 200 °C in unsealed sample tubes, *e.g.* in HMPT. Furthermore, it can also be used for internal field stabilization from temperatures of −100 °C upwards (with TMS as zero-point signal if necessary). "Cyclosilane-d_{18}" therefore represents a standard of unusual potential [2].

Received: January 23, 1969 [Z 963a IE]
German version: Angew. Chem. *81*, 394 (1969)

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[1] Analogous to the method used for the preparation of the non-deuterated compound: US-Pat. 2381002 (1942), General Electric; Brit. Pat. 667435 (1949), Dow Corning; *N. S. Nametkin*, Doklady Akad. Nauk SSSR (6) *43*, 1045 (1953); *W. A. Kriner*, J. org. Chemistry *29*, 1601 (1954); *J. Fritz*, Z. anorg. allg. Chem. *302*, 60 (1959).

[2] Product No. 3486: E. Merck AG, Darmstadt.

Sodium 3-Trimethylsilyltetradeuteriopropionate, a New Water-Soluble Standard for ^{1}H-NMR

By *L. Pohl* and *M. Eckle* [*]

Sodium 3-trimethylsilylpropanesulfonate $(CH_3)_3SiCH_2CH_2CH_2SO_3Na$, which was suggested by *Tiers* and *Kowalewsky* [1] as a water-soluble ^{1}H-NMR standard, suffers from the disadvantage that it gives rise not only to the desired trimethylsilyl signal at $\delta = 0.015$ ppm (in water), but also to three other absorption regions between $\delta = 0.5$ and 3.0 ppm which can cause interference, especially in the case of dilute solutions of samples, when the standard is used simultaneously as an internal "lock signal" because of the higher concentration required.

The sodium salt of 3-trimethylsilyltetradeuteriopropionic acid $(CH_3)_3SiCD_2CD_2COONa$ [2] *(1)*, m.p. 302–304 °C (uncorrected), which we have now synthesized, shows a single sharp resonance signal of half-width 0.5 Hz at $\delta = 0.00$ ppm exactly (in water, methanol) so that the conversion of observed chemical shifts to values measured against TMS is no longer necessary. The solubility in water and in a series of polar organic solvents, such as methanol, hexafluoroacetone · 3/2 H_2O, or HMPT, is higher than that of *Tiers'* salt *e.g.* by a factor of 10 in water and methanol. Owing to the lower molecular weight (172 instead of 218) and the consequently more favorable ratio trimethylsilyl/total molecule, less of the new standard is required (2 mg instead of 4–5 mg per 0.5 ml of sample solution), which largely obviates the salting out that sometimes occurs during the preparation of sample solutions. Aqueous solutions of *(1)* are weakly alkaline (0.05 N: pH = 7.92), while those of the sulfonate are acid (0.05 N: pH = 4.56). Compound *(1)* is stable toward acids and bases, and does not undergo deuterium/hydrogen exchange under normal conditions, even at elevated temperatures. Unlike *Tiers'* salt, which decomposes in solution above 120 °C, the new standard can be used up to at least 200 °C.

Preparation of (1):

Reaction of $(CH_3)_3SiCl$ with $NaC\equiv CH$ in propylene glycol ether affords $(CH_3)_3SiC\equiv CH$ in 70% yield. This compound is treated with C_2H_5MgBr in ether to yield $(CH_3)_3SiC\equiv CMgBr$, which is subsequently converted into $(CH_3)_3SiC\equiv CCOOD$ (yield 60%) by reaction with CO_2 and D_2O. The acid is deuterated with D_2 at 50 atm over a Pd/C catalyst and then neutralized with NaOH to give the sodium salt *(1)*. The degree of deuteration of the two methyl groups is at least 99%. Yield calculated with respect to $(CH_3)_3SiCl$ is 40%.

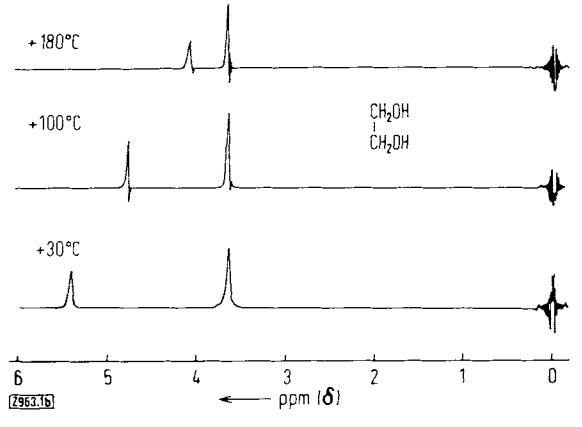


Fig. 1. Sodium 3-trimethylsilyltetradeuteriopropionate as lock and zero signal in ethylene glycol at various temperatures (Varian HA-100 D).

Received: February 19, 1969; revised: April 18, 1969 [Z 963b IE]
German version: Angew. Chemie *81*, 395 (1969)

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[2] Product No. 8652: E. Merck AG, Darmstadt.

Technetium(VII) Oxide: A Transition Metal Oxide with a Molecular Structure in the Solid State

By *B. Krebs* [*]

As previously reported, solid rhenium(VII) oxide forms a polymeric layer structure which contains a mixture of tetrahedrally and octahedrally coordinated rhenium and in which the molecular structure $O_3Re-O-ReO_3$ of the oxide in the gaseous phase is already latent [1]. The structure, bonding, and coordination in the corresponding (not isotypic) technetium oxide were hitherto unknown [2]. Comparison of its physical properties with those of the neighboring d^0 metal oxides indicates that the structure of Tc_2O_7 is more similar to that of the lower molecular oxides RuO_4 and OsO_4 than to the highly polymeric oxides MoO_3 and WO_3 [3].

Single crystals of Tc_2O_7 could be obtained as thin, pale-yellow, very hygroscopic plates (plate face (100)) by combustion of ^{99}Tc in a stream of oxygen at 400 °C [2] followed by slow sublimation of the oxide in a closed system.

Ditechnetium heptoxide crystallizes in the orthorhombic space group D_{2h}^{15}–Pbca with $a = 13.756 \pm 0.007$, $b = 7.439 \pm 0.004$, $c = 5.617 \pm 0.003$ Å, $V = 574.8$ Å^3. $Z = 4$; $d_{x\text{-ray}} = 3.582$, $d_{exp} = 3.5$ g/cm^3. The intensities of 625 independent reflections were recorded on a Hilger-Watts four circle diffractometer using Mo–K_α radiation. The structure was determined from the three-dimensional Patterson synthesis. The least squares refinement with anisotropic temperature factors converged to an R_1 factor of 4.9 %. As in Fig. 1 the structure consists of an arrangement of isolated Tc_2O_7 molecules with tetrahedral coordination of the technetium. Therefore, in addition to OsO_4 [8] and RuO_4 (and very probably Mn_2O_7), Tc_2O_7 is one of the few known transition metal oxides having a molecular structure in the solid state.

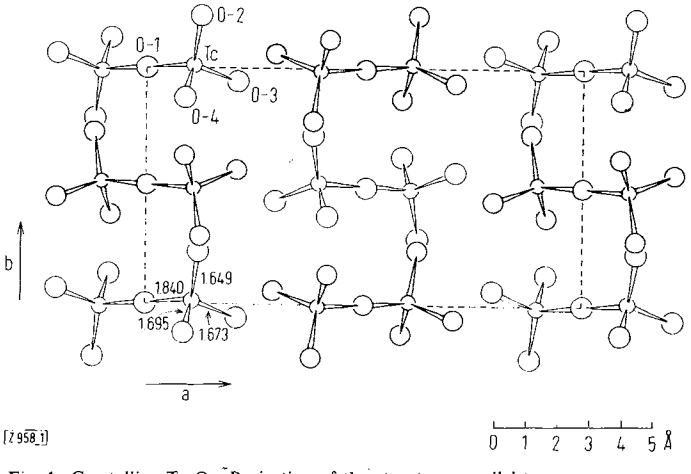


Fig. 1. Crystalline Tc_2O_7: Projection of the structure parallel to *c* (bond lengths in Å; uncorrected).

Tc_2O_7 differs from all previously investigated oxides and oxoanions having isolated $A_2O_7^{(n-)}$ structural units (*e.g.* Cl_2O_7, $S_2O_7^{2-}$, $P_2O_7^{4-}$, $Cr_2O_7^{2-}$) in that the configuration about the central O-atom is exactly linear as a result of the C_i symmetry of the molecule. The M_2O_7 units in the thortveitite type structure cannot be regarded as isolated anions. A statistical disorder of the bridge O-atom (potential maximum at 0,0,0, *etc.*), which would simulate a linear configuration, is most improbable. The experimentally determined principal vibration amplitudes of O-1 (with 0.25, 0.23, and 0.18 Å) are only slightly greater than those of O-2, O-3, and O-4.

Corresponding to the difference in the covalent radii, the bond lengths are about 0.02 – 0.03 Å shorter than those in similarly bonded rhenium compounds: the Tc–O bridge bonds (1.840 ± 0.001 Å) are comparable to the Re^{IV}–O and Ru^{IV}–O bonds in the symmetrical linear bridges of $[Cl_5Re-O-ReCl_5]^{4-}$ (1.86 Å)[4] and $[Cl_5Ru-O-RuCl_5]^{4-}$ (1.80 Å)[5]. The average value for the lengths of the terminal Tc–O bonds (1.673 Å; σ for a single value 0.006 Å) corresponds to the Re–O distances in the tetrahedra of ReO_3Cl (1.702 Å)[6], Re_2O_7 (1.70 Å)[1], and $Re_2O_7(OH_2)_2$ (1.73 Å)[7]. Angular distortion of the O–TcO_3 tetrahedra is only slight; the bond angles vary between 107.8 and 110.9°. It has not yet been possible to elucidate completely the nature of the crystalline red phase of probable composition $Tc_2O_7 \cdot H_2O$ in the system ditechnetium heptoxide–water.

Received: January 8, 1969 [Z 958 IE]
German version: Angew. Chem. 81, 328 (1969)

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[1] *B. Krebs, A. Müller,* and *H. Beyer,* Chem. Commun. *1968,* 263; Inorg. Chem. *8,* 436 (1969); *B. Krebs,* Habilitationsschrift, Universität Göttingen 1968.

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Preparation of Pure 2nd and 3rd Phase Graphite-Iron(III) Chloride Inclusion Compounds and of Graphite-Iron(III) Bromide Inclusion Compounds

By *D. Hohlwein, F. D. Grigutsch,* and *A. Knappwost*[*]

From the results of sorption measurements carried out by *Hooley* and *Bartlett*[1] we have developed a process for the preparation of graphite-$FeCl_3$ inclusion compounds in definite phases. Anhydrous $FeCl_3$ and graphite (in the ratio 5:1 by weight) are placed without mixing in opposite ends of a bomb tube. The tube is evacuated and, by using two ovens, each end is heated to a different but definite temperature. The graphite is heated to a higher temperature than that of the pure $FeCl_3$, so that a thermodynamic equilibrium can be set up between included and pure $FeCl_3$. On completion of reaction the equilibrium composition of the product is "frozen in" by quenching.

The disadvantage mentioned by us[2] regarding the methods of preparation previously adopted, *i.e.* formation of higher (metal-halide deficient) phases by subliming off metal halide without reaching thermodynamic equilibrium between inclusion compound and sublimate, does not occur in this process.

In accord with the 350 °C isotherm[1], a pure second phase with 48–51 wt-% $FeCl_3$ (after washing with 2 N HCl) occurs at T_1 (temperature of graphite) = 350 °C and T_2 (temperature of $FeCl_3$) = 300 °C. The Debyeogram shows the basal reflections of the second phase with $d = (9.38 + 3.35) = 12.73$ Å 002, 003, 004, 007, and 008 and, with lesser intensity, the graphite reflections 002 and 004. Because of the pronounced texture further reflections are not observable.

The third phase, with 34–40 % $FeCl_3$, is formed at T_1 = 410–420 °C, T_2 = 300 °C. In the Debyeogram the weak reflections 002 and 004 of the graphite occur in addition to the basal reflections 002, 003, 004, 005, 006, 007, 009, 0010, 0011 with $d = (9.38 + 2 \times 3.35) = 16.08$ Å.

Iron(II) bromide, bromine, and graphite undergo reaction in a bomb tube to give graphite-$FeBr_3$ inclusion compounds. At a reaction temperature of 100 °C the included $FeBr_3$ can amount to 55 wt-% (after washing). If the lattice dimensions of the $FeBr_3$ in the layer planes, like those of the $FeCl_3$, do not alter during the inclusion reaction this $FeBr_3$ content corresponds analytically to a compound of the second phase. The observed X-ray reflections, however, have not as yet been interpreted.

Received: January 27, 1969 [Z 964 IE]
German version: Angew. Chem. 81, 333 (1969)

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[1] *J. G. Hooley* and *M. Bartlett,* Carbon *5,* 417 (1967).

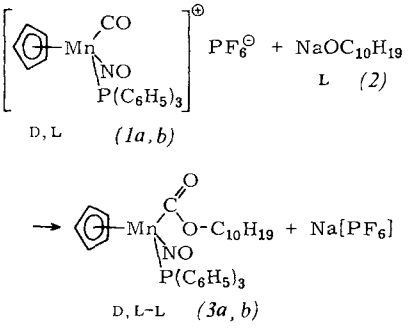
[2] *A. Knappwost* and *F. D. Grigutsch,* unpublished.

Optical Activity at an Asymmetrical Manganese Atom

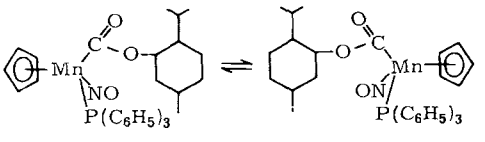
By *H. Brunner*[*]

The compounds $[C_5H_5Mn(CO)(NO)P(C_6H_5)_3]^+[PF_6]^-$[1] *(1)* and $[C_5H_5Mn(COOCH_3)(NO)P(C_6H_5)_3]$[1], which is prepared from *(1)* by methoxide addition, contain four different substituents attached to a central manganese atom. Since these complexes have pseudotetrahedral structures enantiomeric pairs must exist. The diastereomers occurring on introduction of an optically active agent into the molecule ought to be separable from each other, provided that the configurations are sufficiently stable.

Addition of the optically active L-mentholate anion *(2)* to the carbonyl group of the D,L mixture *(1a,b)* leads to the formation of the D, L-L derivative *(3a,b)*. The IR spectrum (KBr) of the red crystalline product contains, in addition to the bands of cyclopentadienyl-, triphenylphosphine-, and menthyl residues, the NO stretching vibration at 1724 cm^{-1} and the absorption of the CO double bond at 1616 cm^{-1}.



The difference in solubility between the two diastereomers *(3a)* and *(3b)* is so great that they can easily be separated from each other; the dextrorotatory isomer *(3a)* dissolves in pentane, whereas the levorotatory isomer *(3b)* is sparingly soluble in aliphatic hydrocarbons.



The high specific rotations of both forms slowly decrease in benzene solution and reach an equilibrium value of $[\alpha]_{578}^{25} = +105°$ which is to be ascribed to the remaining optical activity of the menthyl group after racemization at the manganese atom. The diastereomers *(3a)* and *(3b)* are configurationally stable in the solid state. On prolonged heating in pentane *(3a)* is converted into the difficultly soluble *(3b)*; conversion of *(3b)* into the more easily soluble diastereomer *(3a)* is possible by extraction from the equilibrium mixture with pentane.

Experimental:

To 3.75 g (6.4 mmoles) of compound *(1)* [1] at 0 °C is added a solution of Na-mentholate *(2)* [prepared from lg (6.4 mmoles) (−)-menthol and excess of sodium] in 30 ml of tetrahydrofuran saturated with N_2. The deep-red reaction mixture is evaporated and the residue is dissolved in 50 ml of benzene. The red benzene solution is filtered over anhydrous Na_2SO_4 and concentrated. Pentane is added to the concentrated benzene solution and the precipitate thus obtained is isolated and extracted with pentane until the eluate is colorless. The extract contains 1.5 g (40 %) of the dextrorotatory diastereomer *(3a)* which separates out partially racemized. The residue from the extraction contains 1.3 g (35 %) of the levorotatory diastereomer *(3b)*, $[\alpha]_{578}^{25} = -450°$ (c = 0.1 g/100 ml; benzene). If pentane is added to the extracted product – which, depending on the conditions, is more or less dextrorotatory – and the mixture is filtered so that the filtrate drops into a receiver cooled to −50 °C, pure *(3a)*, $[\alpha]_{578}^{25} = +460°$ C (c = 0.1 g/100 ml benzene) separates out.

Received: February 4, 1969 [Z 966 IE]
German version: Angew. Chem. *81*, 395 (1969)

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[1] *H. Brunner*, Z. anorg. allg. Chem., in press.

Stable Salts Containing the Unusual Anions $[Fe(CN)_5NO]^{3-}$ and $[Fe(CN)_5NOH]^{2-}$

By *R. Nast* and *J. Schmidt* [*]

The previously postulated anions $[Fe(CN)_5NO]^{3-}$ and $[Fe(CN)_5NOH]^{2-}$ [1] can be prepared by reduction of $Na_2[Fe(CN)_5NO]$ *(1)* with sodium in liquid ammonia. We have succeeded in preparing for the first time the ocher-yellow compound trisodium pentacyanonitrosylferrate-2-ammonia, $Na_3[Fe(CN)_5NO] \cdot 2NH_3$ *(2)*, which is sparingly soluble at −70 °C and is sensitive to air. At temperatures above −30 °C, compound *(2)* disproportionates – as can be followed IR spectroscopically – according to the following scheme:

$$2\,[Fe(CN)_5NO]^{3-} \rightarrow [Fe(CN)_5NO]^{2-} + [Fe(CN)_4NO]^{3-} + CN^-$$

On addition of $[Et_4N]Cl$ (Et = C_2H_5) to the brown solution of this compound in liquid ammonia at − 40 °C, gold-brown crystals of $[Et_4N]_3[Fe(CN)_5NO]$ *(3)* precipitate which are stable at room temperature. With $[Ph_4X]Cl$ (Ph = C_6H_5), however, we obtained blue stable compounds of the composition $[Ph_4X]_2[Fe(CN)_5NOH]$ (*(5)*: X = P; *(6)*: X = As). In proton active organic solvents such as acetonitrile, *(3)* is also present in the temperature-dependent equilibrium.

$$[Et_4N]_3[Fe(CN)_5NO] + H^+ \rightleftharpoons [Et_4N]_2[Fe(CN)_5NOH] + [Et_4N]^+$$
$$(3) \qquad\qquad (4)$$

After addition of acetic acid, the blue stable salt *(4)* can be precipitated with ether.

All the stable complexes are paramagnetic with $\mu \approx 1.75$ BM. The UV-absorptions of *ca.* 4000 and 6050 Å for the brown anions and the blue anions agree with the values given in the literature [1].

Table 1. Stretching vibrations (cm^{-1}) of the complexes *(1)*–*(6)*.

	νNO	νCN	F_{NO} [a]	N_{NO} [b]	
(1)·2 H_2O	1935	2142–2170	16.5	2.2	(KBr)
(2)	1608	2095; 2110 sh	11.4	1.6	(nujol
(3)	1568	2075	10.9	1.6	(nujol)
(4)	1746	2100; 2110 sh	13.4	1.8	(nujol)
(5)	1741	2110; 2120 sh	13.4	1.8	(H_3CCN)
(6)	1742	2103; 2110 sh	13.4	1.8	(nujol)

[a] F_{NO} (mdynes/Å): VFF force constants in −NOH without consideration of the proton.

[b] N_{NO}: bond order according to *H. Siebert*.

The decrease of about 0.6 in the NO bond order on going from $[Fe(CN)_5NO]^{2-}$ to $[Fe(CN)_5NO]^{3-}$ supports the concept of *Manoharan* and *Gray* [2], according to which an e* orbital having predominant π^*_{NO} character is occupied in the reduction. It seems to us that the increase in bond order of *ca.* 0.2 on protonation is understandable only if a strong contribution of the H1s orbital to the unpaired e* (π^*_{NO}) electron of the complex is assumed. This view is further supported by the difference (observed by us and by *van Voorst* and *Hemmerich* [1]) between the ESR spectra of the blue and the brown anions. Accordingly, the proton must be bound to the NO group with participation of the unpaired electron in a type of bonding which has yet to be elucidated. The existence of a FeCNH grouping can be excluded on the basis of the IR spectra and chemical reactions.

To regard $[Fe(CN)_5NOH]^{2-}$ as a Brønsted acid having a pK_a value of 6.5 [1] appears to us to be unjustified since the precipitation of $[Ph_4X]_2[Fe(CN)_5NOH]$ from liquid ammonia at the high basicity of the solvent cannot then be explained. Participation of the unpaired electron in the protonation is plausible since no protonation at the NO has hitherto been observed in any NO^+ complex.

Further reduction of $[Fe(CN)_5NO]^{3-}$ yields $[Fe(CN)_4NO]^{3-}$ and $[Fe(CN)_3NO]^{4-}$ [3].

Received: February 28, 1969 [Z 971 IE]
German version: Angew. Chem. *81*, 399 (1969)
Publication delayed at authors' request

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[1] *J. D. W. van Voorst* and *P. Hemmerich*, J. chem. Physics *45*, 3914 (1966); see also *R. G. Hayes*, *ibid. 48*, 4806 (1968).

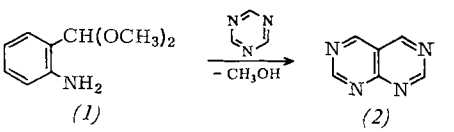
[2] *P. T. Manoharan* and *H. B. Gray*, J. Amer. chem. Soc. *87*, 3340 (1965).

[3] *R. Nast* and *J. Schmidt*, unpublished.

Synthesis of Pyrimido[4,5-*d*]pyrimidine

By *H. Bredereck*, *G. Simchen*, and *M. Krämer* [*]

Pyrimido[4,5-*d*]pyrimidine *(2)* is a theoretically interesting compound because of the anellation of two π-electron deficient systems; however, attempts to prepare it or its derivatives bearing substituents in position 2 from 4-aminopyrimidine-5-carbaldehyde [1,2] by condensation with formamidine, acetamidine [3], and benzamidine [3], and with formamidinium acetate, have failed since the water formed during



(1) *(2)*

the reaction leads to ring opening. We have succeeded in preparing *(2)* by direct reaction of 4-amino-5-dimethoxymethylpyrimidine *(1)* [2] with *s*-triazine.

Compound *(2)* is very sensitive toward water. Its structure has been proved by elemental analysis and by IR and NMR spectroscopy. The NMR signals [δ = 9.91 (H^2 and H^7), δ = 9.76 (H^4 and H^7)] are shifted to lower field strengths than those of pyrimidine.

Pyrimido[4,5,-d]pyrimidine (2)

2.5 g (15 mmoles) of 3-amino-5-dimethoxymethylpyrimidine and 1.2 g (15 mmoles) of *s*-triazine are intimately mixed by grinding in a dish-shaped mortar in the absence of moisture. The mixture is then heated to 130 °C (oil bath temperature) in an atmosphere of highly pure nitrogen over a period of 90 minutes. The product is immediately sublimed from the reaction mixture at 110 °C (oil bath temperature) and 0.05 torr. 0.8 g of crude product, m.p. 90–135 °C (decomp.), is obtained, which, after recrystallization from anhydrous benzene or anhydrous tetrahydrofuran, affords 0.3 g of pure *(2)* [m.p. 193 °C (decomp.); yield 15 %].

Received: March 7, 1969 [Z 967 IE]
German version: Angew. Chem. *81*, 396 (1969)

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[1] *H. Bredereck, G. Simchen,* and *H. Traut,* Chem. Ber. *100,* 3664 (1967).

[2] *M. Krämer,* Dissertation, Universität Stuttgart, in preparation.

[3] *H. Traut,* Dissertation, Universität Stuttgart 1966.

CONFERENCE REPORTS

Macromolecular Colloquium

The Macromolecular Colloquium was held at Freiburg/Br. (Germany) from February 27 to March 1, 1969.

From the lectures:

Determination of the Compatibility of Polymers in Solution

By *D. Berek* [*]

The compatibility of two chemically different polymers in solution can be determined by investigation of the viscosities and the phase relations (phase equilibria, critical concentrations, and limiting miscible concentrations) of the mixtures. These parameters were determined for three binary polymer combinations of polystyrene, polypropylene, and polymethyl methacrylate in toluene and for the system polystyrene + polypropylene in various solvents. It was found that the critical concentration of the ternary system can be readily found by measurement of the limiting concentration of the mixture at a given, calculated (theoretical) relative concentration of the polymers in the system. The critical concentration c_c depends on the molecular weight of the polymer as follows:

$$c_c = A\overline{M}^{-2/3} + c_\infty \qquad (1)$$

where $\overline{M}$ is the weighted average of the molecular weights of the two polymers in the system and A and c_∞ are constants for the given system.

Eq. (1) can be used for the approximate determination of the molecular weight of one of the polymers if the molecular weight of the other is known. This method also allows the estimation of the molecular weights of polymers that would have been blended without solvents.

The observed dependence of the critical concentrations on the chemical nature of the solvent can be eliminated by the introduction of the Staudinger indices of both polymers in the solvent used.

The polymer-polymer interaction parameters b_{23} obtained from the viscosity measurements permit the quantitative characterization of the compatibility of the given polymer pair in solution. There is a simple relation between the b_{23} values and the corresponding Flory-Huggins polymer-polymer interaction parameters χ_{23} calculated from the critical concentrations.

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Structure of Cellulose Fibrils

By *R. Muggli, K. Mühlethaler,* and *H.-G. Elias* (Lecturer) [*]

The smallest structural elements in cellulose fibers are the elementary fibrils having a diameter of about 35 Å. To establish whether the chain molecules are present in the extended or the folded state, molecular weight determinations were carried out on thin transverse sections of ramie fibers and the results were compared with those obtained for whole fibers. Gel permeation chromatograms of the carbanilates of the uncut and the cut cellulose samples showed that the molecular weights of the fractions having the highest molecular weights decrease very appreciably on cutting. Theoretical calculations showed that the degree of breakdown for molecules in the extended state agrees closely with the experimental findings [1].

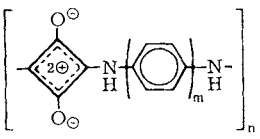
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[1] *R. Muggli,* Dissertation, ETH Zürich, 1968.

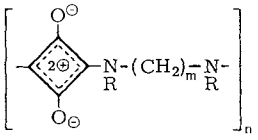
Polar Superpolyamides

By *J. Gauger* (Lecturer) and *G. Manecke* [*]

1,3-Polyamides of squaric acid [*(1)* and *(2)*] have been synthesized by polycondensation of 1,2-dihydroxycyclobutenedione (squaric acid) with bifunctional primary or secondary

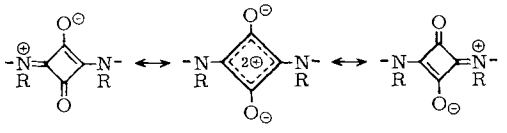


(1), m = 1 or 2



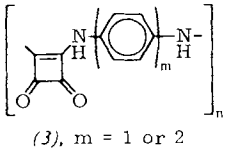
(2), m = 6,8 or 10; R = H, alkyl or aryl

amines. These products are the first members of a new group of polyamides containing the mesomeric cyclobutenediyliumdiolate system.

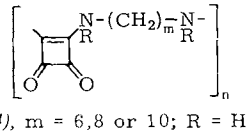


This system contains strongly polar CO groups, which could explain the high mechanical stability of the polycondensates. The polyamides with R=H are thermally very stable and do not melt below 350 °C (hydrogen bonds and dipole-dipole interactions), whereas those with R = alkyl or aryl are fusible thermoplastics. Copolyamides have been prepared by co-polycondensation of salts of squaric acid with diamines (squarates) and nylon salts.

If esters of squaric acid are used as the starting materials, the 1,2-polyamide isomers [*(3)* and *(4)*] of *(1)* and *(2)* are obtained.



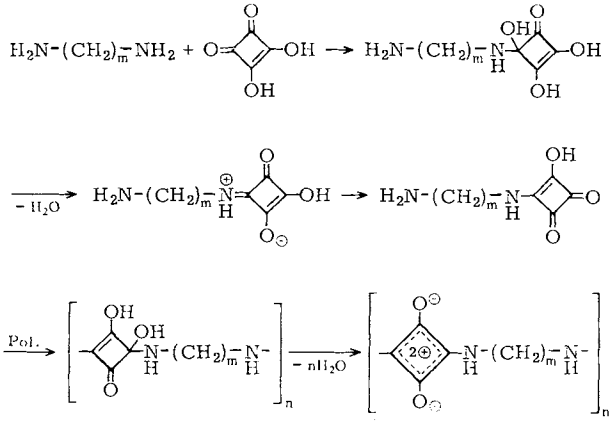
(3), m = 1 or 2



(4), m = 6,8 or 10; R = H, alkyl or aryl

The properties of both groups of polyamides have been characterized by thermogravimetric measurements and determination of the Staudinger indices.

The formation of *(2)*, R = H, was followed by IR spectroscopy and by isolation of intermediates. The reaction scheme



indicated has been confirmed by investigations on the mode of formation of monomeric model compounds and by isolation of the monomeric intermediates.

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Preparation of Block and Craft Copolymers by an Anionic Method

By *G. Greber* (Lecturer) and *W. Behr* [*]

Using an anionic method, we synthesized a series of pure block and graft copolymers in which stereospecific poly-1,4-*cis*-isoprene blocks or side chains are combined with corresponding blocks or chains of atactic vinyl polymers.

We also tested the ability of terminal or lateral vinylsilyl and α-substituted *p*-vinylphenyl groups in the polymer molecule to form radical-anions and their suitability for use in graft and block reactions.

A simple method was also developed for the preparation of interesting block and graft copolymers in which organic polymer molecules (possibly having a stereospecific structure) are covalently linked to methylpolysiloxane blocks or side chains by hydrolysis-resistant Si–C bonds. Organic polymer molecules with terminal or lateral sodium or potassium silanolate groups were used as macromolecular initiators for the polymerization of hexamethylcyclotrisiloxane. Organic polymer molecules with lateral silanol groups were obtained by copolymerization of *p*-vinylphenyldimethylsilanol with vinyl monomers. Polystyrene or poly-1,4-*cis*-isoprene molecules were obtained by termination of the corresponding "living" polymers with *n*-butoxydimethylchlorosilane followed by hydrolysis to remove the protective *n*-butoxy groups.

In the synthesis of graft copolymers by the method described here, it can be decided in advance, by choice of the backbone copolymer, whether the arrangement of the grafting sites in the product will be random or regular.

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Temperature Dependence of the Thermal Conductivity of Amorphous High Polymers

By *G. Hirsch* (Lecturer) and *G. Rehage* [*]

The thermal conductivities of high polymers above and below their glass transition temperatures were determined in a continuous series of measurements with an apparatus operating on the stationary measuring principle. The investigations on polymers differing in the intensity of their polar character led to conclusions regarding the heat conduction mechanism in high polymers and its temperature dependence. Further investigations on the corresponding metal-containing or cross-linked products yielded information on the extent to which these modifications affect the thermal conductivity.

The measurements showed that heat transport in amorphous high polymers is strongly influenced not only by the increase in mobility of the polymer chains (glass transition temperature) but also by the increase in mobility of the side groups which occurs at lower temperature. These results lead to a heat conduction model in which the heat is transported by intermolecular interactions. In addition to the thermal expansion, the possibility of exchange of position of the side groups must also be considered. The intensity of the heat flow is determined by the number and intensity of the intermolecular interactions. These are increasingly intensified when exchange of position occurs as a result of increase in mobility of the side groups. The increase in mobility of the main chains allows further interactions, but this does not lead to increased intensification of the heat transport, since the competing effect of thermal expansion, which weakens the interactions and hence also the effects of exchange of position, becomes more pronounced. The intensity of the heat transport is also influenced by the difference in the polar character of the various polymers because there are differences in the distance laws for the interaction forces. By combination of

all these effects it is possible to deduce a temperature dependence for the thermal conductivity of amorphous polymers that is in good agreement with the experimental results.

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Stimulation of Crystallization of Polymers by Nucleating Agents of High Molecular Weight

By *M. Hoffmann* [*]

Some polymers which do not crystallize easily can be induced to do so more rapidly and extensively by intimately mixing them with a low percentage of a chemically almost identical yet readily crystallizing polymer. Hence the dilatometrically measured crystallization rate of the slow-crystallizing polychloroprene Neoprene W is increased 20 times and the maximum degree of crystallization increased 4.5 times by the addition of 6% of the fast-crystallizing polychloroprene Neoprene HC at 20 °C. Experiments at various temperatures show, moreover, that the melting point of the mixture is 13 °C higher than that of the slow-crystallizing polychloroprene, and that the dependence of the rate of crystallization on temperature is lower than in non-mixed polychloroprenes. The crystallization rate at 22 °C is proportional to the square of the concentration of the added nucleating agent, whereas the increase in the degree of crystallization is proportional to the root of this concentration. It follows from these observations and the rise in the melting point that mixed crystals are formed. Similar stimulation of crystallization is found with polyvinyl chloride and similar polymers and with *cis*-polyisoprene and *cis*-polybutadiene. Such findings are contrary, however, to those made with mixtures of polyethylene and ethylene copolymers and with some other polymers and copolymers. Here there is no stimulation of crystallization, apparently because chain-folding prevents mixed crystallization.

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Formation of Macro-Zwitterions in Ionic Polymerizations

By *K. Boehlke, M. J. Han, V. Jaacks* (Lecturer), *N. Mathes*, and *K. Zimmerschied* [*]

Several ionic polymerizations involve the formation of macro-zwitterions (polymer chains having a positive charge at one end and a negative charge at the other). Lewis acids such as SO_3 or BF_3 and bases such as R_3N or R_3P are suitable initiators and heterocyclic or carbonyl compounds are the preferred monomers. The charge separation during initiation and during the first propagation steps does not present an insuperable energy barrier. The formation of macro-zwitterions has been proven by investigation of the end groups and, in the case of dissolved polymers, by measurement of their (very high) dipole moment. In many cases the zwitterion structure is at least partly destroyed by transfer reactions in the further course of the polymerization. The following systems have been studied:

1. Anionic polymerization of β-propiolactone and of pivalolactone with tertiary amines or with preformed low molecular weight betaines. Since these polymerizations (and only these) proceeded homogeneously, the dielectric constants of the solutions could be measured. From the results a value of 40 Debye was calculated for the dipole moment of an oligomeric macro-zwitterion

$$(CH_3)_3N^{\oplus}-CH_2-CO-(OCH_2CH_2CO)_n-O^{\ominus}$$

with $n \approx 7$ in chloroform at 0 °C. Model calculations show that the chain ends are at about the same distance as in random coils of non-ionic polymer.

2. Anionic polymerization of anhydrous formaldehyde with tertiary amines and phosphines. Triphenylphosphine is incorporated into the polyoxymethylene, indicating zwitterion initiation with formation of

$$(C_6H_5)_3\overset{\oplus}{P}-(CH_2O)_n-CH_2-O^{\ominus}$$

With triethylamine, on the other hand, water or methylene glycol appears to act as a cocatalyst with formation of the low molecular weight cation $Et_3\overset{\oplus}{N}H$.

3. Anionic and simultaneous cationic polymerization of anhydrous formaldehyde initiated by diazomethane. The primary reaction product $^{\oplus}CH_2-CH_2-O^{\ominus}$ grows at both ends by addition of formaldehyde. Termination by combination of the ions is largely prevented by the heterogeneity of the polymerization medium.

4. Polymerization of crystalline trioxane on sublimation or on irradiation with γ rays. As in case 3, both anionic and cationic chain ends have been detected in the polyoxymethylene.

5. Cationic polymerization of dissolved trioxane with $TiCl_4$. In this case chain propagation *via* zwitterions of the structure $Cl_4\overset{\ominus}{Ti}-(OCH_2)_n-\overset{\oplus}{O}CH_2$ seems to be prevented by side reactions.

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ORD and CD Measurements on Substituted Polysaccharides

By *H. Bittiger* and *G. Keilich* (Lecturer) [*]

Optical rotatory dispersion (ORD) and circular dichroism (CD) have been measured in substituted polysaccharides between 600 and 215 nm, in oder to investigate the influence of the substituents on the behavior of these polymers and to find relations between configuration and conformation on the one hand and these spectra on the other.

1. 2,3,6-Tris(*O*-trimethylsilyl)cellulose and -amylose in *n*-hexane (600–215 nm) and 2,3,6-tri-*O*-methylcellulose and -amylose and 2,3,6-tri-*O*-acetylcellulose and -amylose in chloroform (600–235 nm) exhibit no Cotton effects in the spectral ranges indicated, but give normal ORD curves that can be described by one-term Drude equations (λ_0 between

$$[M] = K/(\lambda^2 - \lambda_0^2)$$

200 and 130 nm). The direction of rotation corresponds to that of the unsubstituted polysaccharides (cellulose in cuprammonium [1] and amylose in water or dimethyl sulfoxide).

2. Tribenzoylpolyglycans (2,3,6-tribenzoylcellulose, -amylose, and -mannan, 2,3,4-tribenzoyldextran, and tribenzoylpullulan) exhibit Cotton effects in dioxane between 280 and 220 nm. The CD spectra of the tribenzoylpolysaccharides differ in the number, position, and sign of the extrema; they

can be interpreted on the basis of the positions of the substituents and the configuration of the monosaccharide units.

3. Carbanilyl derivatives behave quite differently. All trisubstituted and disubstituted β-polyglycans have only a single negative Cotton effect at 238–240 nm. The CD spectra of the corresponding α-polyglycans have a minimum at 240–242 nm and a maximum at 223–225 nm; the ORD curves are asymmetric and cross the abscissa in two places, at 241–243 nm and 220–222 nm. The derivatives of disaccharides with β- and α-glycosidic linkages behave similarly, whereas pentacarbanilylglucose has a single positive Cotton effect. The striking difference between the CD and ORD curves of tricarbanilyl-β-polyglycans and tricarbanilyl-α-polyglycans can be explained with the aid of the excition theory, which has been applied to helical polymers by *Moffit et al.*[2]. The effects suggest a planar arrangement of the chains in the case of β-polyglycans and a helical arrangement in α-polyglycans.

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[1] Cuprammonium consists of 12 g of $Cu(OH)_2$, 2 g of CuCl, and 1 l of 25% NH_3.

[2] *W. Moffit*, Proc. nat. Acad. Sci. USA *42*, 736 (1956); J. chem. Physics *25*, 467 (1956); *W. Moffit, D. D. Fitts*, and *J. G. Kirkwood*, Proc. nat. Acad. Sci. USA *43*, 723 (1957); *W. Moffit* and *A. Moscowitz*, J. chem. Physics *30*, 648 (1959).

Synthesis of Coding Polynucleotides with Repeating Base Sequences

By *H. Kössel* (Lecturer), *H. Büchi, T. M. Jacob, A. R. Morgan, S. A. Narang, E. Ohtsuka, R. D. Wells*, and *H. G. Khorana*[*]

The following types of reactions are used for the chemical synthesis of deoxypolynucleotides with repeating base sequences.

(A) polycondensation of mononucleotides,

(B) polycondensation of preformed dinucleotide or trinucleotide blocks,

(C) stepwise condensation of mononucleotides with preformed oligonucleotide blocks,

(D) condensation of preformed oligonucleotide blocks.

Type A leads to a mixture of homopolymers of various chain lengths. Type B gives mixtures of polydeoxydinucleotides or polydeoxytrinucleotides of various chain lengths. The strictly repeating base sequences of the polycondensation products are dictated by the base sequences of the preformed di- or trinucleotide blocks. Reaction types C and D lead to polydeoxynucleotides of any (*i.e.* repeating or non-repeating) base sequence.

Dicyclohexylcarbodiimide or aromatic sulfonyl chlorides are used as condensing agents. Specific protective groups are necessary for the nucleotide components to ensure that the condensations lead to 3′ → 5′-phosphoric acid diester linkages. Chains of up to 20 nucleotide units are obtained (molecular weight ≈ 7000).

To obtain high molecular weight, DNA-like polynucleotides, pairs of deoxypolynucleotides with complementary base sequences and containing at least 8–12 nucleotide units must be elongated with DNA polymerase in the presence of the four deoxynucleoside triphosphates. The resulting products consist of 1.5×10^2 to 6×10^3 nucleotide units per single strand. The strictly repeating base sequences are retained in this reaction.

The individual strands of the DNA-like polynucleotides are selectively transcribed with DNA-dependent RNA polymerase in the presence of the corresponding ribonucleoside triphosphates to give messenger-RNA-like ribopolynucleotides with repeating base sequences. When used as a messenger in the cell-free protein biosynthesis system of *E. coli*, these products stimulate the formation of polypeptides with defined repeating amino-acid sequences, and so allow the assignment of trinucleotide sequences to individual amino acids.

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Polymerization of Ethylene with Methyltitanium Trichloride and Methyltitanium Dichloride

By *K. Kühlein* (Lecturer) and *K. Clauss*[*]

Polymerization experiments were carried out with CH_3TiCl_3 and CH_3TiCl_2 to clarify the question whether the active species in the polymerization of olefins with Ziegler catalysts is a two-component system or a one-component system.

In the polymerization of ethylene with CH_3TiCl_3 under the conditions of Ziegler polymerization (20–100 °C)[1], partial decomposition of the CH_3TiCl_3 yields the two-component system $TiCl_3/CH_3TiCl_3$, which, like a Ti^{III}/Al system, gives a high molecular weight polyethylene with little branching. In order to suppress the conversion of the CH_3TiCl_3 into the two-component system and so determine its specific activity, the reaction with ethylene was investigated below −50 °C. Depending on the solvent, a slow growth reaction on the Ti–C bond was observed, and this was accompanied by displacement by the monomer.

Under the same conditions, CH_3TiCl_2, which was obtained without complexing agents for the first time, exhibited a very high polymerization activity for ethylene. High molecular weight polyethylene having a reduced viscosity of 4 to 6 is obtained rapidly even at −70 °C. The experiments appear to confirm the views developed by *Cossee*[2].

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Cation Radicals in Vinyl Polymerization

By *A. Ledwith*[*]

One-electron oxidation of olefins leads to cation radicals which may dimerize to give propagating di-cationic species. Olefins that react readily with one-electron oxidants have powerful electron releasing substituents, *e.g. N*-vinylcarbazole, *p*-methoxystyrene. Polymerization of these monomers is readily effected using stable cation radicals as initiators *e.g.* $(BrC_6H_4)_3N^+ClO_4^-$. Cation radicals also play a vital role in the catalytic cyclodimerization of electron rich olefins.

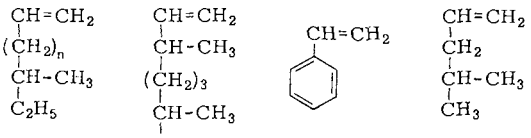
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Optical Activity and Conformation in Solution of Copolymers of Optically Active α-Olefins with Styrene and 4-Methyl-1-pentene

By *P. Pino* (Lecturer), *F. Ciardelli*, and *C. Carlini*[*]

Optically active poly-α-olefins derived from *(1)* and *(2)* were investigated[1] in order to obtain a better insight into the relationships between stereoregularity and conformation of

isotactic polymers in solution. On the basis of the data obtained it was proposed that the macromolecular main chains of poly-*(1)* and poly-*(2)* in solution were in a helical conformation, both screw senses being present. However, when the asymmetric carbon atom is in the α or β position with respect to the main chain (as in poly-*(1a)*, poly-*(1b)*, or poly-*(2)*) one of the screw senses is largely favored, the prevailing one being determined by the chirality of the monomer.



(1a), n = 0
(1b), n = 1
(1c), n = 2

(2)

(3)

(4)

To confirm this hypothesis, optically active stereoregular copolymers of styrene *(3)* with *(R)*-3,7-dimethyl-1-octene *(2)*[2], *(S)*-4-methyl-1-hexene *(1b)*, and *(S)*-5-methyl-1-heptene *(1c)* as well as of 4-methyl-1-pentene *(4)* with *(1b)*[3] were prepared with Ziegler-Natta type catalysts. In these cases, the units derived from *(3)* and *(4)* do not contain asymmetric carbon atoms in the side chain and any contributions they may make to the optical rotation of the copolymer should be attributed to a displacement of the conformational equilibrium of the above units towards dissymmetric conformations of one predominant chirality. In fact also in "isotactic" copolymers of vinyl monomers the optical activity connected with the tertiary carbon atoms in the main chain should be vanishingly small.

ORD and CD measurements of the styrene copolymers in chloroform solution showed a Cotton effect between 275 and 245 nm connected with a $\pi \rightarrow \pi^*$ transition of the aromatic chromophore[2]. The sign of the above Cotton effect is positive or negative when the chirality of the optically active comonomer is *(S)* or *(R)*, respectively. These results show that the units derived from styrene, which *per se* should be optically inactive, contribute to the optical rotation of the copolymer, and that the sign of this contribution depends on the chirality of the optically active comonomer and hence on the prevailing screw sense of the helical conformation of the copolymer macromolecules.

In the case of the copolymer from *(4)* and *(1b)* the optical rotation at 589 nm in hydrocarbon solution is higher, at each composition, than that of the corresponding homopolymer mixtures and increases with increasing stereoregularity. The optical rotation per mole of *(4)* in the copolymer, $[\Phi]_{(4)}$, was found to increase with increasing the content of *(1b)* reaching a limiting value at 50% of *(1b)*.

Taking in account the value calculated according to *Brewster*[4] for the molar optical rotation of units from *(4)* included in right- or left-handed helical sections, the highest value found for $[\Phi]_{(4)} = +160°$ is in excellent agreement with our model, according to which most of the units derived from *(4)* should be included in left-handed helical sections, which largely prevail when the optically active comonomer has *(S)* chirality[1].

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Semisynthetic and Synthetic Macromolecules in Immunochemical Research

By *E. Rüde* (Lecturer), *K. Himmelspach,* and *C. Sorg*[*]

The investigation of the chemical principles of immunological processes has been greatly aided by the use of semisynthetic antigens ("artificial antigens") prepared by the attachment of low molecular weight compounds to natural antigens, which are mostly proteins. *K. Landsteiner* showed that immunization of test animals with antigens of this type leads *inter alia* to the formation of antibodies that react specifically with the groups introduced. Thus antibodies are directed not against the macromolecular antigen as a whole, but against definite structural subunits, the determinant groups.

The first artificial antigen capable of producing protective antibodies was synthesized in 1939 by coupling cellobiuronic acid to protein. This antigen contained a determinant group of a bacterial surface antigen, and when used for the immunization of test animals, it protected them against infection by the corresponding bacterial strain. Methods have now been developed that allow the conversion of higher oligosaccharides of bacterial origin into full antigens by coupling with proteins without loss of their serological specificity.

In addition to semisynthetic antigens of this type, fully synthetic polypeptide antigens are finding increasing use in the clarification of immunological problems. These synthetic antigens, which are mostly prepared by polymerization of *N*-carboxy-α-amino acid anhydrides, have well defined structures. Because of their great variability, they allow a systematic study of the chemical and physical parameters that are important to immunogenicity, *i.e.* to the ability of a substance to initiate the formation of antibodies in higher organisms. By incorporation of monosaccharides and disaccharides into a very weakly immunogenic synthetic polypeptide, for example, the effects of sugars on the immunogenicity of this model antigen were studied. It has recently been shown that branched polymers in which peptide side chains are bound to a polyvinyl alcohol backbone initiate antibody formation upon injection, and even pure vinyl polymers have been found to be immunogenic under certain conditions.

Synthetic polymers and chemically modified natural antigens play an important part in the detection and isolation of antibodies. Thus it has been shown that macromolecules esterified with fatty acids are readily fixed to the surface of erythrocytes by adsorption. This considerably widened the scope of the important passive hemagglutination method for the detection of antibodies. Methods that permit the labeling of polysaccharides with radioactive iodine are also important, since the binding to antibodies can be measured directly and very sensitively with the aid of these labeled derivatives.

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Investigations on the Structure of Fibroin

By *W. Schade*[*]

Whereas the amino-acid sequences of many globular proteins and even the complete three-dimensional structures of some are known, even the molecular weights of the fibrous proteins wool and silk are not known accurately. The difficulties in the determination of the structures of fibrous proteins are due to the fact that they are probably built up from several different protein chains, which cannot be directly separated from one another because of their poor solubility.

A considerable advance in the investigation of silk has resulted from the realization that the crystalline and amorphous components of fibroin, which were detected some time ago

by X-ray analysis, have different chemical compositions and can be separated by enzymatic degradation. The amino-acid sequences of the degradation products obtained in this way have been largely established.

To establish the arrangement of the peptide fragments of the crystalline and amorphous regions in the fibroin molecules, it would be necessary to determine the sequences of larger peptides or of the fibroin molecules themselves.

Larger peptide fragments can be obtained by mild acid or alkaline partial hydrolysis followed by chromatographic separation of the fragments on a column. This method has the advantage that the original fiber structure is partly retained and can be examined microscopically. Intact fibroin has also been resolved into several components by disk electrophoresis.

This confirms the hypothesis frequently advanced in the literature that fibroin consists of several different protein chains. The results of the investigations also indicate that the crystalline and amorphous regions do not alternate in the same chain but are contained in separate chains.

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Recent Results on the Kinetics of Anionic Polymerizations

By *L. L. Böhm, B. J. Schmitt,* and *G. V. Schulz* (Lecturer) [*]

The active end group of polystyrylsodium exists in three forms in polar solvents (*e.g.* tetrahydrofuran and tetrahydropyran): the free anion, the solvent-separated ion pair, and the contact ion pair. The equilibria between the three forms are shifted by temperature changes; addition of a sodium salt (*e.g.* sodium tetraphenylborate) changes the degree of dissociation. The following parameters can be determined for any solvent by measurement of the conductivity of the living ends and the polymerization rate as functions of the temperature, the concentration of the living ends, and the sodium ion concentration:

1. enthalpy and entropy differences between the two types of ion pairs;
2. enthalpy and entropy of the electrolytic dissociation;
3. activation energy and activation entropy of the monomer addition for all three forms of the active end group.

The extremely strong dependence of the polymerization rate on the solvent and its anomalous temperature dependence can be easily and quantitatively explained with the aid of these parameters.

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Microseparation of Phases in Swollen Gels and its Investigation by Light Scattering

By *K. Dušek* and *B. Sedláček* (Lecturer) [*]

The interaction of *n*-butanol and poly(ethylene glycol monomethacrylate) crosslinked with ethylene glycol dimethacrylate has been studied by light-scattering measurements. The swollen and homogeneous gels contain small concentrations of heterogeneous zones having diameters $> 3\,\mu m$. Phase separation (microsyneresis) occurs in the interior of the swollen gel with falling temperature, and droplets having a diameter of about $0.15\,\mu m$ are formed.

This order of magnitude confirms the view that the size of the particles formed is determined by the retractive force of the deformed network and by the interfacial energy between the swollen gel and the *n*-butanol.

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The Combination Reaction During the Thermal Decomposition of Aliphatic Azo Compounds in the Presence of Oxygen. Cage Reaction and Cross-Termination

By *W. Vogt* [*]

On thermal decomposition of azoisobutyronitrile (AIBN), a certain amount of tetramethylsuccinonitrile is always formed by combination of the initially formed 2-cyanoisopropyl radicals. Depending on whether the two combining radicals come from the same molecule or from two different molecules of AIBN, we speak of primary combination or cross-combination (or termination). The theory of the cage effect enables us to predict that the primary combination will be much less influenced than the cross-combination by the presence of a free-radical scavenger.

We were interested in whether any cross-combination occurs at all in the presence of oxygen, which is a particularly effective free-radical scavenger.

To clarify this question, we decomposed a mixture of tetramethylazoacetonitrile (=AIBN) and tetraethylazoacetonitrile in the presence of oxygen and determined the resulting 2,2-dimethyl-3,3-diethylsuccinonitrile (which can only be formed by cross-combination) by quantitative gas chromatography. 2,2-Dimethyl-2′-2′-diethylazoacetonitrile was treated in the same way and the products were examined for tetramethyl- and tetraethylsuccinonitriles.

The experiments were carried out at 90 °C and an oxygen pressure of about 1 atm with a total concentration of azo compounds of about 0.1 mole/l. The figures given for the following solvents are the maximum values found for the cross-combination in mole-%, based on the total quantity of azo compound decomposed: benzene (<1 %); toluene (<0.6 %); *n*-propyl acetate (<0.5 %), dioxane (<0.3 %); cyclohexane (<0.1 %); methyl methacrylate (<0.1 %).

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Interpretation of Coils and Structure in the Aggregated Polymer State

By *B. Vollmert* (Lecturer) and *H. Stutz* [*]

Polymers (A) containing free OH groups were prepared by copolymerization of butyl acrylate with small quantities of hydroxybutyl acrylate, and polymers (B) containing free NCO groups were prepared by copolymerization of butyl acrylate with small quantities of isocyanatoethyl acrylate. When the polymers were mixed in solution (at various polymer concentrations and with various concentrations of OH and NCO groups along the chains) in ratios such that the functional groups were present in the stoichiometric ratio of 1:1, they gave conversions of up to 16%. It was therefore concluded that the polymer coils in concentrated solutions and gels interpenetrate only in relatively thin zones on their surfaces.

The application of these results makes it necessary to revise our views on the rubbery-elastic state and the glass state.

It is concluded from the classical theory *(P. Flory)* that intramolecular cross-linkages ("loops") have no influence on the degree of swelling and the mechanical modulus of gels,

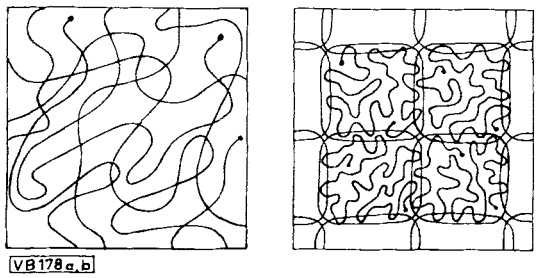


Fig. 1. Left: Classical model of aggregated polymer state. Right: Individual coil-structure model of aggregated polymer state.

whereas our *Individual coil structure* model of cross-linked polymer systems suggests that the degree of swelling (= swelling ratio) decreases and the modulus increases by additional intramolecular crosslinking.

Experiments with our A-B-polymer system, however, showed that intramolecular cross-linkages have a strong influence on the mechanical properties of gels. The modulus of intermolecular crosslinking gels without any intramolecular crosslinking is lower and the modulus of the same gels with additional intramolecular crosslinkages is higher than is predicted by the classical theory.

According to the ICS-model, the proportion of intramolecular crosslinkages in ordinarily mixed crosslinked system is much higher than assumed until now (70–80%).

Contrary to the classical theory, chain entanglements (physical crosslinkages) are not to be expected in the aggregated polymer state.

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Investigations on the Epitactic and Topotactic Polymerization of Trioxane and Tetroxane[**]

By *A. Munoz-Escalona, E. W. Fischer,* and *G. Wegner* (Lecturer)[*]

Though the formation of polyoxymethylene [POM] from crystalline trioxane was one of the first examples of polymerization in the solid state, the mechanism of the polymerization and the morphology of the resulting polymers are still largely unknown. The same is true of the polymerization of tetroxane, which can also be converted into polyoxymethylene in the solid state.

We have polymerized single crystals of both monomers by the action of γ radiation, by the addition of boron trifluoride-ether, and by slow sublimation of monomer. The resulting polymers were investigated by large-angle and small-angle-X-ray scattering and by electron microscopy.

Large-angle X-ray photographs of the polymers from trioxane always exhibit well oriented fiber diagrams with pronounced twinning, irrespective of the polymerization method. The small-angle scattering for these samples shows no long period, indicating a texture with extended polymer chains parallel to the fiber axis. Examination in the electron microscope shows well-ordered fibrils, but the twinning structure cannot be observed. A different morphological structure is obtained on polymerization of crystalline tetroxane. Large-angle X-ray diagrams of samples polymerized by γ radiation between 60 and 100 °C showed that very few twins are formed at 60 °C, and none between 80 and 100 °C. Small-angle diagrams reveal a long period which increases with the reaction temperature. It is found on examination in the electron microscope that the fibrils of POM formed by this method show ripples perpendicular to the fiber axis. It follows from this and from the results of molecular weight measurements that the structure in this case involves folded chains.

When tetroxane is polymerized by the action of boron trifluoride-ether or by slow sublimation, regularly shaped hexagonal lamellae with distinct growth spirals are formed. Some signs indicate that epitactic polymerization occurs in this case. The reasons for the differences in structure and morphology of POM from trioxane and from tetroxane are probably mainly concerned with the different lattice structures of the two monomers.

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Solution Properties of Random Copolymers of Methyl Methacrylate and *n*-Butyl Acrylate

By *W. Wunderlich*[*]

Viscosity measurements and light-scattering measurements have been carried out on chemically homogeneous random copolymers of methyl methacrylate (MMA) and *n*-butyl acrylate (BA). In the good solvent chloroform, the copolymers in the composition range $79.5 \geqslant [\text{MMA}] \geqslant 20.5$ wt-% show a uniform relation between the viscosity $[\eta]$ and the molecular weight *(M)*, which lies between that of PMMA and that of PBA: $[\eta] = 4.2 \times 10^{-3} M^{0.8}$ ($\text{cm}^3\,\text{g}^{-1}$), $T = 20\,^\circ\text{C}$. In the fair solvent acetone the $[\eta]$ $-M$ function for MMA/BA = 56/44 wt-% is above those of PMMA and PBA. The values of the second osmotic virial coefficient A_2 behave in the same way. Using equations given by *Stockmayer-Fixman, Burchard,* and *Kurata et al.*, the effects of the short-range and the long-range interactions on the composition dependence of $[\eta]$ and A_2 were estimated from the molecular weight dependence of A_2 and $[\eta]$. It was found that the short-range interactions correspond to the mean of the values for the two comonomers, while the long-range interactions are considerably greater than those of the corresponding homopolymers. The increase in the viscosity and in A_2 in the random copolymers can be explained as a result of intramolecular incompatibility.

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Structural Investigations on Semicrystalline Polyethylene and Ethylene-Propylene Copolymers

By *P. Zugenmaier* (Lecturer) and *H.-J. Cantow*[*]

The crystal structures of polyethylene crystallized from the melt and from solution, as well as of ethylene-propylene copolymers, were investigated by X-ray diffraction. With linear polyethylene that had been crystallized extremely slowly from the melt, reflections were observed over the entire range of angles. The previously unknown reflections were indexed by a new procedure, which also permits the extremely accurate determination of the lattice parameters.

The reflection intensities were calculated for a simple polyethylene model. Comparison of the calculated and measured intensities for various samples of homopolymer and copolymer that had been crystallized and treated with fuming nitric acid gave the following results.

1. The angle between the plane containing the carbon backbone of the polymer chain and the lattice vector α is $\delta = 45 \pm 1\,^\circ$ for highly annealed linear polyethylene. The angle δ is smaller near the folds, *i.e.* at the crystallite surface, than in the interior of the crystalline zone. This decrease is due to the strain where the chain is folded.

2. No methyl side groups were found inside the crystalline zones in homopolymers or copolymers.

3. The disorder function, which describes the deviations of the atoms from their ideal position, is anisotropic. The magnitude of the anisotropy depends on the crystallization conditions. The influence of strain on the disorder function could be detected in the case of copolymers.

German version: Angew. Chem. *81*, 334 (1969) [VB 178 IE]

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X-Ray Spectroscopic Studies of the Chemical Bond in Oxides

By *H.-U. Chun* [*]

The contribution of the valence electrons of an atom toward the screening of the nuclear charge is so low in the case of elements having large nuclear charges and for electron transitions between the innermost shells that no measurable shift of an X-ray line occurs when the valence electrons take part in chemical bonding. In the case of the lighter elements, however, the bonding is observed to exert a definite effect on the energy and form of X-ray spectral lines, as has been demonstrated in particular by *Faessler* [1] for the K lines of Si, P, and S compounds, and by *Meisel* [2] for the K_α lines of Ti, V, Cr, Mn, Fe, Co, and Ni in their compounds. The effect is greatest in the X-ray K spectra of compounds of the elements Li to F since the L shell involved in the K → L transition ($K_{\alpha 1,2}$ line) actually contains the valence electrons. The X-ray spectra of the series Li to F can provide a great deal of information about changes in the bonding of one of these elements in various compounds, *e.g.* about the nature of the metal-oxygen bond in oxides.

The O–K spectra of BeO, MgO, CaO, SrO, BaO, Sc_2O_3, Y_2O_3, La_2O_3, Sm_2O_3, Yb_2O_3, NiO, ZnO [4], α-Al_2O_3, and γ-Al_2O_3 [5] were recorded at high resolution by means of a spectrograph constructed for X-ray spectroscopic investigation of light elements [3]. The spectra were produced by direct electronic excitation (2–4 kV, 1–10 mA) of a thin layer of powdered sample applied to the anode of an X-ray tube. Evaluation of the spectra showed that characteristic relationships exist between the type of spectrum (number and intensity ratios of the lines) and the energy of the individual lines in the O–K spectrum on the one hand, and the nature of the metal-oxygen bond in these oxides on the other.

Of the alkaline earth oxides, only CaO, SrO, and BaO give the O–K spectrum typical of the O^{2-} ion, while the O–K spectrum of MgO and also of the oxides of the lanthanides evidence a transition state between ionic and covalent bonding. For NiO, ZnO, BeO, α-Al_2O_3, and γ-Al_2O_3 the metal-oxygen bond is deduced to be largely covalent from the spectra. As the metal-oxygen distance and the ionic character increase within a series of oxides having the same crystal structure, all the lines of the O–K spectrum are seen to shift toward shorter wavelengths (Table 1).

Table 1. Wavelengths (Å) of the O–K lines $\alpha_{1,2}$, α_3, and α_4 of metal oxides.

Oxide	Crystal structure	M–O-distance (Å)	$\alpha_{1,2}$ [a]	α_3 [a]	α_4 [a]
NiO	[c]	2.097	23.622	—	—
MgO	[c]	2.104	23.599	23.560	23.521
CaO	[c]	2.401	23.609	23.525	23.481
SrO	[c]	2.573	23.605	23.519	23.475
BaO	[c]	2.762	23.595	23.501	23.460
BeO	[d]	1.64	23.596	—	—
ZnO	[d]	1.98	23.564	—	—
Sc_2O_3	[e]	2.11 [b]	23.597	—	23.515
Yb_2O_3	[e]	2.25 [b]	23.585	32.538	23.501
Y_2O_3	[e]	2.28 [b]	23.578	23.535	23.478

[a] Standard deviation ± 0.008 Å. [b] Mean M–O distance.
[c] NaCl type. [d] Wurtzite type. [e] C type of the lanthanide oxides.

The O–K band of γ-Al_2O_3 (maximum: 23.591 Å) is shifted to lower energies compared to that of α-Al_2O_3 (maximum: 23.562 Å) and the bands of both oxides exhibit a fine structure that is due to the short-range order in their lattices.

The results of these investigations show that conclusions concerning the relative ionic character of the metal-oxygen bond in oxides and concerning the structure of regions of short-range order can be reached with the aid of the X-ray spectroscopic technique. Moreover, the use of this method can contribute to our knowledge of the structure of oxidic surface layers.

Lecture at Mainz (Germany) on November 7, 1968 [VB 193 IE]
German version: Angew. Chem. *81*, 400 (1969)

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The Boundary between Fluid Phases as a Barrier for the Passage of Molecules

By *W. Nitsch* [*]

The phase change of molecules at the boundary between fluid phases is to be regarded as a kinetic consequence of transport processes and boundary layer reactions; during the reaction step, solvations of the exchanging molecules can occur, the rates of which determine the barriers for the passage through the boundary layer. Since this process is generally transport-controlled, or is regarded as such, little is known about this type of heterogeneous reaction, which can be of significance for mass transfer. It may be deduced from the laws of diffusion that the boundary reactions in stationary phases or under conditions of laminar flow can only be found for very short phase contact times. Owing to the inadequate knowledge of the hydrodynamics applying to turbulent motion of phases the corresponding transport processes under such conditions are not known. A description of the boundary layer processes on turbulent flow depends on the realization of a flow state in which the mass transfer is independent of the flow, *i.e.* proceeds at a maximum rate and is thus reaction-controlled.

A number of examples of the description of reactions in stationary phases and in phases in turbulent flow, as carried out in our laboratory, will now be considered. The boundary layer reactions occurring on physical absorption of a gas could first be delineated for the transport of oxygen and nitrogen in a film of water that was continuously being reformed on a horizontal roller that was partly immersed in an absorption bath [1]. As a result of the contact times that could be realized by means of this method (down to 10^{-4} s), the relevant boundary layer reactions could be investigated. The collision yield factors for the reaction of nitrogen and oxygen with water are of the order of $\alpha = 10^{-4}$. The boundary layer reaction between carbon dioxide and water, on the other hand, is too fast to be investigated by the above technique.

The realization of mass transfer independent of the flow state, and therefore reaction-controlled, could be accom-

plished with the system propionic acid/water/carbon tetrachloride in a flow apparatus specially developed for this purpose[2]. The resulting kinetic data are plausible if the boundary layer reaction occurring on transfer of a caroxylic acid is formulated as a series of three individual reaction steps[3]. For the passage through the boundary layer from water to carbon tetrachloride, these steps are:

1) Adsorption of the carboxylic acid molecule, which exists as the monomer in water;

2) dimerization of the adsorbed molecules; and

3) desorption of the dimer into the CCl_4 phase.

The same processes occur in the reverse order on passage in the opposite direction. The dependence of the rate constants on the length of the fatty acid residues lends support to the above interpretation. This dependence corresponds quantitatively to established adsorption phenomena.

Lecture at Stuttgart (Germany) on January 9, 1969 [VB 194 IE]
German version: Angew. Chem. *81*, 401 (1969)

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Cyclization of Unsaturated Fatty Acids

By *V. Wolf*[*]

The cyclization of 9,12,15-*c,c,c*- (linolenic acid), of 9,12,15-*t,t,t*- (linolenelaidic acid), of 9,11,13-*c,t,t*- (α-eleostearic acid), and of 9,11,13-*t,t,t*-octadecatrienecarboxylic acid (β-eleostearic acid) has been studied in alkaline diethylene glycol solutions at 180–220 °C. An alkali-induced ionic reaction occurs in which the non-conjugated acids undergo allylic rearrangement, whereas *cis-trans* rearrangement and double-bond shifts are observed in systems already containing two or three conjugated double bonds or in cases in which such conjugated systems are formed.

The α,γ,ε-*t,c,t*-triene formed in this manner is cyclized in a thermal multi-center process to give 5,6-disubstituted 1,3-cyclohexadiene. Compounds of this kind occur in equilibrium with all conceivable cyclohexadienes and cyclohexenes having conjugated semi-cyclic double bonds. About 10% of the cyclic dienes form *o*-substituted aromatic carboxylic acids. The aromatization proceeds by loss of either two hydrogen atoms, or one hydrogen atom and one side chain, or two side chains. Interpretation of the mechanism is greatly facilitated by the diverse but highly characteristic distribution of the lengths of the alkyl and ester side chains for each of the acids investigated.

Lecture at Freiburg (Germany) on January 24, 1969 [VB 195 IE]
German version: Angew. Chem. *8*, 402 (1969)

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New Investigations of the Biosynthesis of Flavonoids

By *H. Grisebach*[*]

trans-Cinnamic acid which is formed from L-phenylalanine by the enzyme phenylalanine-ammoniumlyase is an important precursor for the formation of flavonoids. Its hydroxylation to 4-hydroxycinnamic acid (*p*-coumaric acid) is catalyzed by a microsome fraction from peas[1]. This enzyme belongs to the mixed-function hydroxylyases; it could be shown that the H atom originally in the *para*-position migrates into the *ortho*-position to the hydroxyl group ("NIH shift"). A similar reaction occurs in the biosynthesis of several flavonoids.

Further hydroxylation of *p*-coumaric acid, giving caffeic acid, can be catalyzed by an enzyme (or several enzymes) of phenolase type[2]. This enzyme, purified from spinach beet, can also hydroxylate several flavonoids at the 3′-position of the B-ring.

According to our results, chalcones are the central intermediates in the biosynthesis of flavonoids. The enzyme chalcone-flavanone-isomerase, first enriched by *E. Wong*, has been found to be present in all plants so far studied. The substrate specificity of several isoenzymes, which are found in plants, were investigated. It remains unsolved whether the further changes start from the chalcone or the flavanone precursors. Kinetic experiments with the pair [^{14}C]chalcone-[^{3}H]flavanone have been carried out in this connection.

Coumestanes and related natural products are biogenetically to be counted among the isoflavones since, like isoflavanones, the latter can be converted into coumestanes. Coumestrol and a new coumestane have been isolated from Mung bean *(Phaseolus aureus)*.

Dihydrodaidzein can be converted into daidzein in seedlings of the Mung bean. Dihydroisoflavones are, however, probably not intermediates in the biosynthesis of isoflavones. The fate of the hydrogen was studied in the conversion of 7,4′-dihydroxy[2-^{14}C-3-$^{3}H_2$]flavanone and 5,7,4′-trihydroxy-[2-^{14}C-2-^{3}H]flavanone; the H atom on C-2 is retained but a H atom is lost from C-3.

Work by *W. Barz* in our Institute indicates that some isoflavones and coumestrols in *Cicer arietinum* and *Phaseolus aureus* undergo a turnover whose biological half-life is of the order of 50 hours. Thus synthetic and degradative reactions will have to be considered in future studies of the metabolism of these compounds.

Lecture at Berlin on February 24, 1969 [VB 197 IE]
German version: Angew. Chem. *81*, 403 (1969)

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[1] *D. W. Russel* and *E. E. Conn*, Arch. Biochem. Biophys., No. *122*, p. 256 (1967).

[2] *P. F. T. Vaughan* and *V. S. Butt*, Biochem. J., in press.

Investigation of Binding of Inhibitors to Ribonuclease by NMR Spectroscopy

By *H. Rüterjans*[*]

Hitherto, high-resolution nuclear resonance spectra have been little used for the structural analysis of such macromolecules. The signals are broad and overlap because of the small mobility of the individual molecular groups. Only a limited number of the signals in the NMR spectra can be unequivocally assigned to particular protons of the protein. As example can be cited the signals of the C-2 protons of the histidine-imidazole rings, which are shifted beyond the spectral region of the remaining protons to lower field. Furthermore, the signals of these protons shift about 1.0 ppm to higher field during the deprotonation to the uncharged imidazole ring; if the chemical shift of the imidazole C-2 protons is plotted against the pH value, "titration curves" and p*K* values of the histidines are obtained.

In the case of bovine pancreatic ribonuclease A, different p*K* values are obtained for the four histidines present in the enzyme. From NMR investigations on carboxyalkyl derivatives of RNase A and on the subtilisin-cleaved enzyme (RNase S), these p*K* values can be assigned to the histidines 12, 48, 105, and 119 of the polypeptide chain[1]. The p*K* values of the histidines 12 and 119 of the active site are unusually low; they increase by about 1.0 and 0.7 respectively if the NaCl concen-

tration is increased from 0.1 M to 0.4 M, whereas the pK value of His 105 increases by only 0.2 on changing the ionic strength by this amount. This finding indicates that a positively charged group, probably the ε-amino group of the lysine 41, is immediately adjacent to the two imidazole rings of His 12 and His 119. Furthermore, from an accurate analysis of the titration curves of His 12 and His 119 it can be shown that the imidazole rings of these two histidines are coupled by a hydrogen bond in a specific conformation of the enzyme. There are many indications that this specific conformation of the RNase A is the catalytic form of the enzyme.

If competitive inhibitors, such as cytosine 3′-monophosphate or cytosine 2′-monophosphate, are added to a solution of RNase A, the C-2 NMR-signals of His 12 and His 119 shift to lower field, indicating protonation of the imidazole rings. On addition of inhibitors both histidines remain protonated until decomposition of the RNase-inhibitor complex at pH values of about 7–9. The chemical shift and line width of the two signals are different. The fact that this shift of the C-2 NMR-signals to lower field is also observed on addition of sodium phosphate and sodium pyrophosphate, lends further support to the conclusion that the ε-amino groups of Lys 41 and of the positively charged imidazole rings of His 119 probably fix the doubly negatively charged phosphate group of the inhibitor [2].

Lecture at Münster on January 27, 1969 [VB 196 IE]
German version: Angew. Chem. *81*, 402 (1969)

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[1] *D. H. Meadows, O. Jardetzky, R. M. Epand, H. H. Rüterjans,* and *H. A. Scheraga*, Proc. nat. Acad. Sci. USA *60*, 766 (1968).

[2] *H. H. Rüterjans* and *H. Witzel*, European J. Biochem. *9*, 118 (1969).

Molecular Structure from Rotational Spectra

By *H. D. Rudolph* [*]

Rotation spectroscopy, in addition to electron-, X-ray-, and neutron diffraction, furnishes data concerning the geometry of a molecule. For known atomic masses, the bond lengths and angles determine the three principal moments of inertia, upon which the rotational energy terms of the freely rotating molecule (gas phase) alone depend. Once the spectrum has been assigned then the principal moments of inertia are known.

Molecules containing isotopes have different moments of inertia because of the different masses; consequently, they have different spectra despite the fact that they have the same geometry. If the spectra of a large enough number of isotopically substituted molecules have been analyzed a sufficiently large set of principal moments of inertia can be accumulated to derive from it the structural parameters.

Rotation-vibration interactions give rise to difficulties. Whenever possible one attempts the determination of an "r_s-structure" (s = substitution): For the location of an atom only the *differences* of the principal moments of inertia before and after the isotopic substitution of that particular atom are used. Thus the greater part of the vibration-rotation interaction which is independent of isotopic substitution is eliminated. Only one atom at a time may be substituted. At least partial r_s-structures have been given for some 500 smaller or moderately sized molecules. The accuracy of the bond lengths lies between 0.001 and 0.01 Å. For the determination of the physically defined "equilibrium structure" (minimum of the potential surface), explicit consideration of vibration-rotation interaction is necessary, *i.e.* the analysis of the rotational spectra also in the excited states of each vibration of all molecular isotopes is required. The effort for such an investigation to be carried out is justified only in the case of the smallest molecules. It is believed, however, that the above r_s-structure comes very near the equilibrium structure.

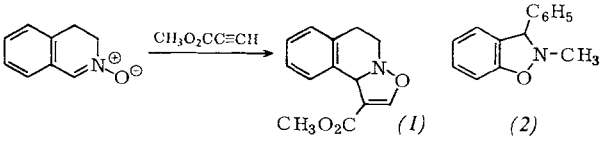
In addition to providing data about geometry, rotation spectroscopy also furnishes a great deal of further data concerning structure: definite dipole moment components, internal mobility, *etc.* The instrumentation is characterized by high resolution but low intensity of the spectra recorded, and by the use of waveguide techniques, as well as monochromatic, tunable radiation sources.

Lecture at Kiel on November 14, 1968 [VB 192 IE]
German version: Angew. Chem. *81*, 401 (1969)

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SELECTED ABSTRACTS

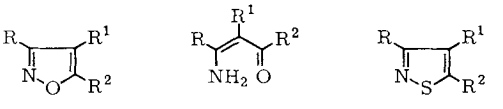
Isoxazol-4-ine derivatives such as *(1)* have been prepared for the first time by *M. Seidl, R. Huisgen,* and *R. Knorr* by 1,3-dipolar cycloaddition of nitrones to alkynecarboxylic esters, *e.g.* methyl propiolate, ethyl phenylpropiolate, and dimethyl acetylenedicarboxylate. The five-membered heterocycle produced can be stabilized in different ways. Thus the thermolabile compound *(1)*, m.p. 53–55 °C, is converted into a betaine by cleavage of the five-membered ring in boiling glacial acetic acid. On the assumption that the isoxazol-4-ine ring could be stabilized by incorporation of the double bond



(1) *(2)*

of a benzene ring, the previously unknown benz[*d*]isoxazolines were synthesized from nitrones and arynes *e.g.* dehydrobenzene. Compound *(2)*, yield 100%, melts at 59–59.5 °C. / Chem. Ber. *102*, 904 (1969) / –Ma. [Rd 999 IE]

The synthesis of substituted isothiazoles from isoxazoles has been reported by *D. N. McGregor, U. Corbin, J. E. Swigor,* and *L. C. Cheney*. The isoxazole ring *(1)* is first opened up by reduction with Raney Ni–H_2 (in CH_3OH, C_2H_5OH; at *ca.*

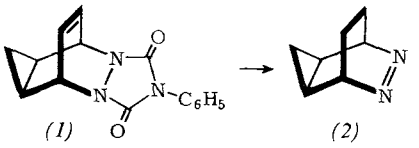


(1) *(2)* *(3)*

3 atm) and the enamine ketone *(2)* thus formed is converted into the isothiazole *(3)* by treatment with P_2S_5 followed by oxidation with *e.g.* chloranil. The yields are between 38 and 90%. / Tetrahedron *25*, 389 (1969) / –Ma. [Rd 1000 IE]

The synthesis and pyrolysis of 6,7-diazatricyclo[3.2.2.0^{2,4}]-non-6-ene *(2)* has been investigated by *M. Martin* and *W. R. Roth*. The synthesis is accomplished by Diels-Alder addition of 1,3,5-cycloheptatriene and 4-phenyl-1,2,4-triazoline-

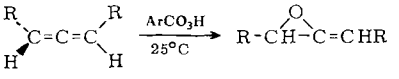
3,5-dione to form the adduct *(1)* which after catalytic hydrogenation, alkaline hydrolysis, decarboxylation, and oxidation with $CuCl_2$ affords a stable Cu complex from which the compound *(2)* can be isolated by treatment with aqueous NH_3 at 0 °C (yield 45%). Solutions of *(2)* gradually decompose at room temperature into 1,4-cycloheptadiene and N_2;



(1) *(2)*

similar decomposition takes place on photochemical excitation in ether at −60 °C. / Chem. Ber. *102*, 811 (1969) / −Ma.
[Rd 1 IE]

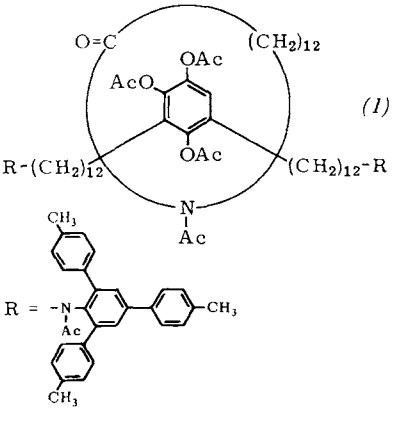
An allene oxide, 2-*tert*-butyl-3-(2,2-dimethylpropylidene)-oxirane *(2)* has been synthesized by *R. L. Camp* and *F. D. Greene*; it is the first representative of a molecular species that has been assumed to occur as an intermediate but has never been isolated. Reaction of an excess of 2,2,4,4-tetramethyl-2,3-pentadiene *(1)* with *m*-chloroperbenzoic acid in hexane followed by distillation and gas-chromatographic separation affords, as main fraction, a liquid which on the



(1) R = $C(CH_3)_3$ *(2)*

basis of its mass- and NMR-spectra proves to have the structure *(2)*. On heating to 100 °C isomerization to 2,3-di-*tert*-butylcyclopropanone takes place. / J. Amer. chem. Soc. *90*, 7349 (1969) / −Ma.
[Rd 2 IE]

Rotaxanes, novel aggregates of a macrocycle and an elongated molecule with bulky end groups, have been obtained by *G. Schill* and *H. Zollenkopf* by specific synthesis from a diansa compound containing two paraffin chains with reactive end groups. One bulky residue is attached to each chain and the precursor, in which the "ring" is still joined to the "dumb-bell" by a bond on the nitrogen, is split to give the rotaxane. Compound *(1)*, the rotaxane from 1,2,4-triacetoxy-

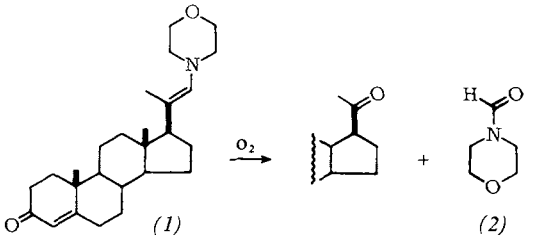


(1)

3,5-bis[12-(*N*-acetyl-2,4,6-tri-*p*-tolylanilino)dodecyl]benzene and 1-acetyl-1-aza-14-cyclohexacosanone, melts at 65–67 °C. Its IR spectrum contains one weak band more than an equimolar mixture of the components; *(1)* is uniform in the thin layer chromatogram, and its R_f value is different from those of its components. / Liebigs Ann. Chem. *721*, 53 (1969) / −Kr.
[Rd 3 IE]

The catalytic reduction of nitrous oxide by dinitridohydrido-tris(triphenylphosphine)cobalt has been studied by *L. S. Pu, A. Yamamoto*, and *S. Ikeda*. N_2O, which acts as a competitive inhibitor of the fixation of nitrogen in biological systems, was allowed to react with $H(N_2)Co[P(C_6H_5)_3]_3$ in benzene. The red solution effervesced and turned first yellowish green and then pale blue. Free $P(C_6H_5)_3$ present during the reaction was oxidized to $OP(C_6H_5)_3$. When $H_3Co[P(C_6H_5)_3]_3$, $P(C_6H_5)_3$, and N_2O were allowed to react, the $\nu(N_2)$ band at 2088 cm^{-1} and the ν(PO) band at 1200 cm^{-1} were observed after a short time. The escaping gas consisted of H_2 and N_2. / Chem. Commun. *1969*, 189 / −Kr.
[Rd 4 IE]

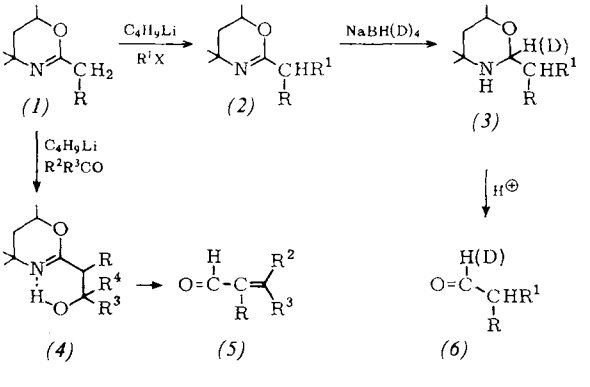
The Cu-catalyzed oxidation of enamines, according to *V. Van Rheenen*, leads under mild conditions to good yields of ketone and amide. The enamine *(1)*, for example, is quantitatively split into progesterone and *N*-formylmorpholine *(2)* by O_2 in the presence of CuCl in $CHCl_3$ at 0 °C. *N*-(2-Methylethylidene)morpholine (the morpholine enamine of isobutyraldehyde) gives acetone and *(2)*. Suitable catalysts are CuCN



(1) *(2)*

and the chlorides and bromides of Cu^{I} and Cu^{II}. Pyridine and trimethyl phosphite completely inhibit the reaction. / Chem. Commun. *1969*, 314 / −Ma.
[Rd 7 IE]

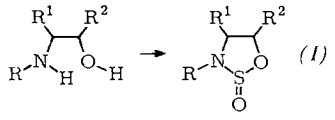
A new aldehyde synthesis from dihydro-1,3-oxazines *(1)* has been described by *A. I. Meyers et al.* Compounds *(1)* react with phenyllithium, *n*-butyllithium, or *tert*-butyllithium in THF at −78 °C to form the lithium salts, and then with alkyl halides to give compounds *(2)* in high yields. Reduction of *(2)* with $NaBH_4$ (or $NaBD_4$) gives tetrahydro-1,3-oxazines *(3)*, hydrolysis of which with dilute oxalic acid



(1) *(2)* *(3)* *(4)* *(5)* *(6)*

leads to aldehydes *(6)* (overall yield 47–70%). Addition of an aldehyde or ketone to the Li salt formed from *(1)* gives an oxazinyl alcohol *(4)*, from which an α,β-unsaturated aldehyde *(5)* is obtained (48–69%) by reduction and hydrolysis. Alicyclic and α,α-disubstituted aldehydes can be prepared with the aid of α,ω-dibromoalkanes. / J. Amer. chem. Soc. *91*, 763, 764, 765 (1969) / −Ma.
[Rd 8 IE]

1,2,3-Oxathiazolidines, members of a new heterocyclic system, have been synthesized by *J. A. Deyrup* and *C. L. Moyer.* 1,2,3-Oxathiazolidine *S*-oxides *(1)* are obtained by reaction of β-amino alcohols with $SOCl_2$ in the presence of bases such as triethylamine or pyridine as proton acceptors in hexane or benzene. The yields were between 15 and 99%. *cis-trans*

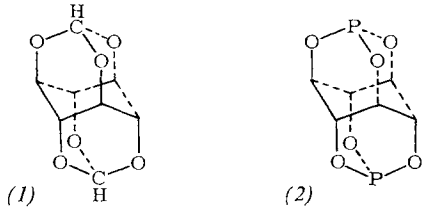


(1)

Isomers were observed in several cases, and these are ascribed to asymmetry at the S atom. The cyclization can also be applied to larger rings, as is shown by the conversion of 3-*tert*-butylamino-1-propanol into 3-*tert*-butyltetrahydro-1,2,3-oxathiazine *S*-oxide. / J. org. Chemistry *34*, 175 (1969) / –Ma.

[Rd 9 IE]

Hexaoxadiamantanes have been synthesized by *O. Vogl, B. C. Anderson,* and *D. M. Simons.* The reaction of scyllite (all-*trans*-hexahydroxycyclohexane) with triethyl orthoformate in DMSO, succinodinitrile, tetramethylene sulfone, acetic anhydride, *etc.* at 150–200 °C gives a polymeric product, which forms hexaoxadiamantane *(1)*, m.p. 302–304 °C, on



(1) *(2)*

pyrolysis at 250–350 °C. The rather low yield of about 15% is due to many side reactions. Reaction of scyllite with trimethyl phosphite in DMSO similarly gave hexaoxadiphosphadiamantane *(2)*, m.p. 276–280 °C. / J. org. Chemistry *34*, 204 (1969) / –Ma.

[Rd 10 IE]

The dissociation constants of some phosphoric acid derivatives have been determined by *C. J. Peacock* and *G. Nickless* by potentiometric titration, theoretical titration curves with the dissociation constants as parameters being matched to the experimental curves by means of a computer. Reliable values were obtained for ortho-, monothio-, monoamido-, and diamidophosphoric acids, whereas the values found for diamidothio- and tetrathiophosphoric acids are less certain.

The results were used as the basis for a discussion of the position at which the ions are protonated. The most acid proton

Anion	pK_1	pK_2	pK_3
PO_4^{3-}	1.85	6.69	12.3
PO_3S^{3-}	1.67	5.40	10.14
PS_4^{3-}	1.8	3.5	6.6
$PO_3NH_2^{2-}$	2.74	8.17	
$PO_2(NH_2)_2^-$	1.18	5.00	
$POS(NH_2)_2^-$	2.0	4.3	

in monothiophosphoric acid is that bound to the sulfur; the dianion of monoamidophosphoric acid is evidently protonated first on the nitrogen. It is interesting to note that the monoanions of diamidophosphoric and diamidothiophosphoric acids take up two protons each, *i.e.* first one on the nitrogen and then one on the oxygen. The cationic two-proton adducts could not be isolated. / Z. Naturforsch. *24a*, 245 (1969) / –Hz.

[Rd 11 IE]

The spectroscopic and photochemical properties of benzene-chloroform mixtures at low temperatures ($T \geqslant 77$ °K) in saturated hydrocarbons have been studied by *N. C. Perrins* and *J. P. Simons.* Displacements of the benzene band at 250 nm indicate hydrogen bonding of the proton of chloroform (and other incompletely halogenated alkanes and alkenes) with the aromatic ring. The C–H axis of $CHCl_3$ in the associates should be perpendicular to the plane of the benzene ring. It is possible to distinguish two association steps, in which one and then two molecules of the halogen compound associate with benzene. The thermodynamic data for the first association step at 77 °K are $\Delta G = -(354 \pm 70)$ cal/mole; $\Delta H = -(1170 \pm 120)$ cal/mole; $\Delta S = -(9.3 \pm 2.5)$ cal deg^{-1} $mole^{-1}$. On irradiation of the benzene-chloroform solutions, instead of the usual addition of solvent, only chloroform adds on to the benzene. / Trans. Faraday Soc. *65*, 390 (1969) / –Hz.

[Rd 12 IE]

The increase in the catalytic activity of magnesium oxide powder for hydrogen-deuterium exchange in the presence of 3–7 eV (180–400 nm) UV radiation has been studied by *C. G. Harkins, W. W. Shang,* and *T. W. Leland.* The relative increase in the first order rate constant, when plotted against the energy of the light used, shows distinct maxima at 5.7, 4.9, and 4.0 eV. To interpret these photocatalytic maxima, the band structure of MgO is discussed, taking into account internal impurities and adsorbed water. The authors conclude that a catalytically active surface state is reached from various initial states. The catalytic activity is thought to be due to hydroxide groups on the surface with localized defect electrons, *i.e.* to OH radicals bound to the surface. "Reaction rate spectroscopy" should also be of use in the investigation of other catalytic effects on the surfaces of semiconductors or insulators. / J. physic. Chem. *73*, 130 (1969) / –Hz.

[Rd 13 IE]

BOOK REVIEWS

Hochauflösende ESR-Spektroskopie, dargestellt anhand aromatischer Radikal-Ionen (High-Resolution ESR Spectroscopy, with Special Reference to Aromatic Radical Ions). By *F. Gerson.* Vol. 1 of "Chemische Taschenbücher", edited by *W. Foerst* and *H. Grünewald.* Verlag Chemie GmbH., Weinheim/Bergstrasse 1967. 1st Edit., 210 pp., 42 illustrations, 14 tables, DM 16.–.

This volume is the first of a new series of monographs being published by Verlag Chemie under the title "Chemische Taschenbücher". These pocket books are aimed at providing both advanced students and qualified chemists with a reasonably priced introduction to specialist fields of chemistry. The choice of High Resolution Electron Spin Resonance as the subject of the opening volume is particularly fortunate, since this is an important physical method by which surprisingly accurate predictions can be made about the residence time of an unpaired electron on the individual atoms.

The author uses a general section to introduce the reader to the fundamentals of ESR spectroscopy, starting with the quantum nature of the electron and the interaction of its spin with a magnetic field. He then shows how, in organic radicals, the interaction of the unpaired electron with atoms that have

nuclear spin leads to the hyperfine structure of ESR spectra. The chemical production of radicals and their measurement in the ESR spectrometer are described only briefly, and the main emphasis is laid on understanding the theoretical interpretation of spectra with hyperfine structure and of their relation to concepts of the electronic structure of organic radicals that can be derived from HMO theory and its refinements.

For this purpose the author confines his attention almost wholly to radicals anions and cations of aromatic hydrocarbons and their aza derivatives, ions that have been particularly thoroughly studied. The book thus gains much in clarity and immediacy, especially as the author himself is a recognized master of the field. Several of the inherent problems are given a first, very clear interpretation without making too great mathematical demands; examples are the formation, by π-σ spin polarization, of a finite spin density at the H atoms of benzene situated at the nodal plane of the unpaired π-electron; the formation of negative spin densities by π-π spin polarization; and the occurrence of relatively large coupling constants on β-hydrogen atoms owing to hyperconjugation.

A relatively short Appendix 1 follows, describing methods of quantitative calculation used in estimating π-σ and π-π spin polarization; here, however, considerable knowledge of the techniques of quantum-mechanical calculation is assumed, and this the ordinary chemist may often not possess.

In that section devoted to nitrogen-free and nitrogen-containing aromatic radical ions, it is shown how far predictions from ESR spectroscopy can be extended, and to what extent the results of quantum-mechanical calculations agree with experimental results. The examples are excellently chosen to demonstrate, by concrete cases, the extraordinary power of prediction inherent in ESR spectroscopy.

The writing is concise and there is no unecessary repetition The book requires concentrated reading, but it makes no demand beyond the capacity of a student who is reasonably familiar with HMO theory. This is an excellent book and it is also an aesthetic pleasure owing to the splendid illustrations of typical ESR spectra (most of them from the author's Zürich school), very clear schematic drawings, and the clean and pleasant photomechanical reproduction of typescript. References covering the literature up to the end of 1965 are an aid to deeper study.

It is to be hoped that the book has a wide circulation and that the later volumes in the series will be equally successful.

K. Dimroth [NB 809 IE]

Theorie der Molekülspektren (Theory of Molecular Spectra). By *W. A. Bingel.* From the series "Chemische Taschenbücher", Vol. 2, edited by *W. Först* and *H. Grünewald.* Verlag Chemie GmbH, Weinheim/Bergstr. 1967. 1st Edit., 206 pp., 62 figures, 21 tables, bound DM 16.—.

This volume of the series "Chemische Taschenbücher" fills a gap among German-language monographs on molecular spectroscopy, since apart from a few specialized works with very narrowly limited subject matter, recent German literature has nothing to offer as an introduction to the theory of spectra. The author of the present book has therefore concentrated on the fundamental theoretical relations. A short introduction is followed by a discussion of rotation and rotation-vibration spectra; the vibrational and rotational structure of electronic transitions is then also discussed. Special attention is given to intensities and selection rules, which are hardly mentioned in other, more experimentally oriented books. The relation between the theory of the chemical bond and UV spectroscopy is presented in a clear manner. The author's own special interests are reflected in a very comprehensive discussion of the classification of the electronic states of diatomic and triatomic molecules.

Since the book is intended primarily as an introduction for beginners, the treatment of infrared and Raman spectra has had to be kept relatively brief. The author has tried to explain the essential relations with the minimum use of formal mathematics. The success of the treatment will depend on the reader's background knowledge. The book is well worth the price, and it is to be hoped that it will be widely read, particularly by the younger chemistry students.

Th. Ackermann [NB 792 IE]

Gruppentheorie für Chemiker, Physiko-Chemiker, Mineralogen ab 5. Semester (Group Theory for Chemists, Physical Chemists, and Mineralogists in their 5th Semester and Beyond). By *K. Mathiak* and *P. Stingl.* From the Series: Hochschul-Studienbuch. Friedr. Vieweg und Sohn, Braunschweig, Akademische Verlagsgesellschaft, Frankfurt/M. 1968, paperback DM 9.80.

The modern chemist is making ever-increasing use of numerical methods (particularly quantum mechanical approximation methods) and sooner or later he is bound to have to come to terms with the mathematical fundamentals of these techniques. The present book by *Mathiak* and *Stingl* provides an opportunity for him to get acquainted with the important subject of group theory. Since the inclusion of numerous examples and problems imparts the necessary "substance" to the highly abstract subject matter, the reader can profit considerably from a study of the sections entitled "Abstract Group Theory", "Symmetry Groups of Molecules", and "Representation Theory". An additional section on "Vector Spaces" has been included to furnish the necessary background. However, the section on the application of group theory to Hückel theory and molecular vibrations will do little to stimulate the faith of the reader in this book, since it not only contains many obscurities, inaccuracies, and mistakes, but unfortunately also makes no mention of the most important applications of group theory: Selection rules and polarization of electronic transitions, band forms and polarization for IR bands, degree of depolarization of Raman bands, as well as considerations of the symmetry types of overtones and combination frequencies in vibration spectra.

The apparently unavoidable mistakes in the character tables are found in this book, *e.g.*, in the groups C_4, C_{4h}, C_{6v}, and D_{4h}.

K. Wilhelm [NB 787 IE]

Grundzüge der Radio- und Reaktorchemie (Fundamentals of Radiochemistry and Reactor Chemistry). By *F. Hecht.* Akademische Verlagsgesellschaft, Frankfurt/M. 1958. 1st Edit., x, 426 pp., 130 figures, 39 tables, paperback DM 25.-.

Though radiochemistry or nuclear chemistry forms part of the curriculum of a number of universities where German is spoken, there has until now been no satisfactory German-language textbook in this field, and the standard work for radiochemists is therefore the excellent "Nuclear and Radiochemistry" (2nd Edit., 1966) by *Friedländer, Kennedy,* and *Miller.* Because of its strong physical orientation, however, this cannot really be recommended as an introduction. The book by *Hecht* is intended to fill this gap, and can be said to have succeeded in this object.

The book is divided into the following sections:

1. Nuclear-physical data, 2. Nuclear reactions, 3. Radiation measurements, 4. Radiochemical procedures, 5. Artificial radioactivity, 6. Nuclear reactors, 7. The effects of radiation and radiation loading, 8. Use of radionuclides in industry and medicine, and 9. Chemistry of hot atoms. The chapter size ranges from 6 pages (Chapter 9) to more than 100 (Chapter 4). This very lucidly written book is of particular value for students choosing radiochemistry as a subsidiary subject as well as for practical chemists seeking an introduction to experimental radiochemical techniques. However, these are not the only readers to whom the extensive Chapters 3 and 4, which are outstanding for the expert knowledge shown by the author, will appeal. Special mention should be

made of the numerous figures and graphs. The various types of reactors are discussed in Chapter 6, though the reviewer would have expected a more detailed discussion of nuclear-physical principles (*e.g.* four-factor formula); however, this is a shortcoming of all (even English-language) books on radiochemistry and nuclear chemistry. Even physical principles are sometimes unfortunately not discussed at length; there was no need to avoid mathematical formulations almost completely. What the Friedländer-Kennedy-Miller book lacks in chemistry, the Hecht book lacks in physics. One would also have expected that in 1968 (the year of publication), the new position regarding the No isotope (dating from 1963–1965) could have been presented; moreover, the symbol Mv for element 101 (p. 241) was changed by the IUPAC into Md almost ten years ago. These and other minor points can, however, be corrected in a later edition.

The presentation and print are well below average, even if allowance is made for the relatively low price. At least two types of paper had been used in the reviewer's copy, several pages showed variation in print thickness or unsharp print, and the paper binding delaminated after use for a short time, so that the life of the book will probably be limited.

C. Keller [NB 799 IE]

Synthesen mit Kohlenmonoxid (Syntheses with Carbon Monoxide). By *J. Falbe*. Vol. 10 in the Series "Organische Chemie in Einzeldarstellungen". Springer Verlag, Berlin, Heidelberg, New York, 1967. 1st Edit., vii + 212 pp., 20 tables, DM 48.–.

Except for a few omissions, the author has succeeded in writing a comprehensive monograph on syntheses involving CO, and even experts in this field can find something new in it. Hydroformylation, carbonylation, the Gattermann-Koch synthesis, and carbonylation with Pd catalysts are described in detail, irrespective of their technical importance. It is obviously impossible in such a comprehensive book to consider singly the entire literature quoted and to specify in each case the importance of the individual works.

It is mentioned in the Preface that, prior to their detailed investigation, Reppe syntheses and Roelen reactions were described after World War II in FIAT, BIOS, and CIOS Reports. Despite this, workers engaged in the subsequent intensive research in this field outside Germany hardly took into account the previous investigations, with the result that many aspects have been discovered twice. This could have been brought to light still better by modifying the structure of the book.

In connection with the reaction mechanisms, mention is made again of the three-membered ring and ketene theory, which was rejected years ago. On the other hand, only footnotes are devoted to the important hypotheses proposed a long time ago about the intermediates of hydroformylation and carbonylation (FIAT, Houben-Weyl). At the same time, a detailed account is found on the mechanisms which were proposed much later, and which closely resemble these hypotheses.

This does not alter the fact that this is a very good book, which can be recommended to those who work in this field.

H. Kröper [NB 791 IE]

Comprehensive Biochemistry, Vol. 20: Metabolism of Cyclic Compounds. By *M. Florkin* and *E. H. Stotz*. Elsevier Publishing Co., Amsterdam, London, New York, 1968. 1st Edit., xiii + 533 pp., 135 figs., 34 tables; Dfl. 75.–.

This volume[1] deals with the biosynthesis and the degradation of complicated organic molecules arising in the metabolism of carbohydrates and amino acids. It bears witness to the great progress made in the last 15 years in the elucidation of structural relationships by new methods and improved techniques. Not only is the literature well documented up to 1967, but also a great number of quotations are included in some cases. As a result, this book often makes it unnecessary to consult the original articles for details. It also gives surveys which enable the reader to familiarize himself with the relevant material.

Discussing the isoprene derivatives, *H. J. Nicholas* describes the synthesis, degradation, occurrence, and function of vitamin A, α-tocopherols, vitamin K, ubiquinones, plastoquinone, carotinoids, squalene, and other terpenes, as well as rubber. He also discusses ecdysone and the giberellins, together with their function and the regulation of the biosynthetic cycles between organelles. The metabolism of steroid hormones and bile acids is discussed by *D. B. Gorer*, whose account includes the formation and the conversion of C_{18}, C_{19}, and C_{21} sterols, the action of ACTH and other hormones, the enzymatic hydroxylation and dehydrogenation of the steroid skeleton, and processes of conjugation and elimination. The author examines the reaction mechanisms in great detail and also discusses the secondary conversion of bile acids by intestinal microflora, though the products of this conversion are only indirectly connected with biogenetic cycles.

The phenolic substances are divided into flavonoids (*F. de Eds*), tannins (*D. G. Roux*), and lignin (*W. J. Schubert*), which is biogenetically connected with tannins in carbohydrate metabolism. The glycosides and the aglycons of flavones and flavonones are of pharmacologic interest, and their toxicology and therapeutic use therefore receive critical treatment. One finds a similarly good account of the influence of intestinal bacteria, nutritional factors, and dosage on the products of metabolism and elimination. The hydrolyzable and condensed polyphenols of the tannins are examined in a relatively short but informative section. Here and in the chapter on lignin, one encounters isocyclic polyhydroxy compounds, which occupy a central position in the metabolism of aromatic systems, and which are aromatized and – in the case of lignin – condensed into large, complex polymeric molecules. Their chemical structure is mainly hypothetical, and it is therefore too soon to discuss the general features of these molecules. By contrast, the general outlines of the biogenesis based on CO_2, carbohydrates, shikimic acid, and C_3 fragments are known. The same applies to the origin of methoxy groups and to the polymerization of monomeric phenylacrylic acid precursors by enzymatic oxidoreductase and peroxidase (laccase). The degradation by fungi that decompose wood is first hydrolytic (even ether bridges are cleaved here by etherases), and then oxidative, leading to vanillin derivatives.

A monographic study of the biosynthesis of alkaloids and other secondary nitrogen metabolites by *J. B. Spenser* represents the main part of the book. This subject is treated in biogenetic terms, and, despite the great variety of the substances, the study shows the relations between the synthetic pathways, which had been earlier proposed speculatively by organic chemists, mostly exhibiting an extraordinary insight. The syntheses involved are relatively simple (Mannich condensations and oxidative coupling of phenols), but give rise to a remarkable group of compounds, which are difficult to systematize.

One of the most fascinating chapters of the chemistry of natural products is that of secondary fungal metabolism, although the underlying principles are not clear since we do not know whether we are dealing here with elimination processes or with accumulation processes; nevertheless, about 1000 compounds have so far been isolated. *R. Bentley* and *J. M. Campbell* examine some routes for the aromatic syntheses based on glycolysis intermediates, acetate, mevalonate, and polyoxomethylene compounds, together with the formation of terpenes, sterols, and anthraquinones. The enzymatic halogenation and the regulation of these processes have also been described.

[1] Cf. Angew. Chem. *80*, 974 (1968); Angew. Chem. internat. Edit. *7*, 901 (1968).

When such a variety of fields is covered, it is understandable that the chapters cannot always be perfectly dovetailed into one another, and in fact they overlap at several places. However, the Editors have minimized this, and so ensured readability and maintained the monographic nature of the sections. The book is carefully edited, easy to use, and has a comprehensive subject index. This excellent work, "Comprehensive Biochemistry", is thus enriched by a further volume, which retains the high standard we have grown accustomed to throughout the series.

L. Jaenicke [NB 790 IE]

Carbocyclic Ring Expansion Reactions. By *C. D. Gutsche* and *D. Redmore*. Supplement 1 to Advances in Alicyclic Chemistry. Edited by *H. Hart* and *G. J. Karabatsos*. Academic Press, New York-London 1968. 1st Edit., viii, 243 pp., stitched $ 13.50.

Do you know what MLOC is? The explanation can be found in the preface to this book. It is the "*M*agnificent *L*and of *O*rganic *C*hemistry", of which carbocyclic ring expansion reactions form a part. At one time a "hamlet" in the great land of OC, the CRER (*C*arbocyclic *R*ing *E*xpansion *R*eactions) has now grown into a sprawling town, the study of which has won the interest of many chemists, and will continue to do so in the future. The present book is intended as a chemical "Guide Michelin" to the region of CRER.

The book is divided into nine sections: 1. Wagner-Meerwein rearrangements of cycloalkanecarbinyl systems; 2. Pinacol-type rearrangements of cycloalkanecarbinyl systems; 3. Diazoalkane ring expansions of cycloalkanes; 4. Ring expansions *via* anionic intermediates; 5. Ring expansion *via* carbenes as free-radical intermediates; 6. Photochemically induced ring expansions; 7. Ring expansion reactions with bicyclo[*n*.1.0]alkanes as intermediates; 8. Ring expansion by two carbon atoms; 9. Ring expansion by three or more carbon atoms.

The authors have succeeded in presenting a concise, easily readable discussion of all that is important about the course, mechanisms, substituent effects, and steric factors of these reactions without historical trimmings. Practical applications are also dealt with. The authors incorporate the discussion of their own research field fully into this framework, and lose nothing in the way of detail as a result. Clear reaction schemes are given for many of the reactions, which are of widely differing nature in some cases.

When used in conjunction with the text, the detailed and particularly up-to-date reference list (up to 1967) enables anyone interested to acquire within a short time a good knowledge of the reaction types discussed. A few printer's errors (*e.g.* 2-methyl-4- instead of 2-methyl-5-isopropylcyclohexanone and 2-methyl-6- instead of 3-methyl-5-isopropylcycloheptanone) do not detract from the value of the book, which can be wholeheartedly recommended to all organic chemists.

E. Müller [NB 797 IE]

Contact and Frictional Electrification. By *W. R. Harper*. From the series: Monographs on the Physics and Chemistry of Materials. Oxford at the Clarendon Press (Oxford Univ. Press), London 1967, 1st Edit., xii, 369 pp., numerous figures, 70 s.

This book deals with the build-up of electrostatic charges on substances as a result of mutual contact or friction. It appears in the series "Monographs on the Physics and Chemistry of Materials", which presents recent results concerning solids and in the related field of materials research.

An attempt is made in the present book to set out the numerous experimental findings relating to contact or frictional electrification in an orderly manner and to explain them with the aid of models. Terms such as surface charges, contact, and frictional electricity are introduced and explained in the first of the three parts of the book. The second part deals with physical principles, particularly from solid physics, that appear necessary for an understanding of frictional electricity. The lack of reference to physicochemical or thermodynamic aspects is regrettable. Experimental results and special systems are discussed in the third part.

The book is of particular interest to physicists and fundamental research workers who are concerned with problems of frictional electricity; however, it should also provide some stimulus to chemists and engineers, who are more interested in the practical aspects of frictional electricity.

H. Rickert [NB 795 IE]

Reagents for Organic Synthesis. By *L. F. Fieser* and *M. Fieser*. John Wiley and Sons Inc., New York-London-Sydney 1967. 1st Edit., ix, 1457 pp., $ 210

A chapter in the book "Experiments in Organic Chemistry" by the same authors was the forerunner of the present, comprehensive work, which considers 1120 reagents, arranged in alphabetical order, that are of importance to the experimental organic chemist.

The various reagents are described according to the following pattern: Structural formula, molecular weight, physical constants, most important methods for synthesis and purification, commercial sources, as well as characteristic examples for the application of the reagent, containing in most cases information regarding optimum weight ratios, reaction conditions, and yields each supplemented by copious references. The examples illustrating the application of the reagents are generally chosen to have a maximum information content. 17% of the literature references cite procedures in "Organic Syntheses".

The authors have consciously refrained from treating the common solvents and their purification in the same manner, since they contend that adequately useful literature is available on this subject. This book contains no more than commercial sources for solvents.

As an illustration of the makeup and utility of the present work let us consider the keyword "Phosgene": Here one finds the structural formula, molecular weight, boiling point, melting point, information concerning toxicity, and commercial sources. There follow data on purification and particularly on the detection and removal of chlorine. Under the heading "Use of Phosgene" the reader finds methods for the preparation of carbonic half-ester chlorides. The method of *Barton* – conversion of primary alcohols *via* carbonic half-ester chlorides and their reaction with dimethyl sulfoxide – comes next. There follows an account of the use of phosgene in the preparation of isocyanates from primary amines, which also gives the most important experimental data as well as the preparation of isocyanides from alkylformamides with phosgene and triethylamine.

The dehydration of amides with phosgene and pyridine, the preparation of cyclic carbonates and of mixed anhydrides of carbonic acids, and finally the preparation of benzyl esters of α-amino acids *via* the oxazolidines, which are obtained from the α-amino acids and phosgene, represent further examples of the application of phosgene. In total, 18 literature references and numerous structural formulas illustrating the reactions are to be found under this keyword.

Lists of the manufacturers and of the pieces of apparatus included in the text are also to be found alongside the subject and author indexes at the end of the book. An alphabetical list of the reactions and reaction types giving details of reagents required proves to be an extremely valuable feature. The book is one of the most important recent publications for organic chemists working in research establishments and in industry. It certainly closes a gap in the existing literature and will undoubtedly soon be numbered among the standard works of organic chemistry.

A number of minor defects do little to detract from the virtues of the book. For instance, the Non-American is at a certain disadvantage because only American firms are given in the list of sources. Further, the selected literature references too often concern highly specialized examples. In some cases, the examples that are given lack any general significance. This applies, *e.g.*, to the reaction of hydrazine with 1,3-cyclohexanedione mentioned on p. 449. On the other hand, no reference is made to the one-step acid cleavage and reduction of alkylated 1,3-cyclohexanediones to the reduced carboxylic acids. A critical reappraisal of the literature citations with regard to their general interest might well be appropriate in future editions. *H. Stetter* [NB 784a IE]

Physical Methods in Advanced Inorganic Chemistry. Edited by *H. A. O. Hill* and *P. Day*. Interscience Publishers, London-New York-Sydney 1968. 1st Edit. xii, 627 pp., numerous Figs. and Tables, bound, *ca.* DM 74.—.

This book contains descriptions of physical methods that are of immense value to the practical inorganic chemist. It contains eleven sections covering the following topics: 1. Diffraction methods (*C. K. Prout*), 2. X-ray spectroscopy (*C. Bonelle*), 3. Molecular photoelectron spectroscopy (*D. W. Turner*), 4. Electronic absorption spectroscopy (*H. Schmidtke*), 5. Rotatory dispersion and circular dichroism (*R. D. Gillard*), 6. Vibrational spectroscopy (*M. J. Ware*), 7. Electron spin resonance (ESR) (*E. König*), 8. Mössbauer spectroscopy (*J. Danon*), 9. Nuclear quadrupole resonance (NQR) (*H. Sillescu*), 10. Nuclear magnetic resonance (NMR) (*D. R. Eaton*), and 11. Thermochemistry in inorganic solutions (*J. J. Christensen* and *R. M. Izatt*).

To provide such a wealth of information within the confines of little more than 600 pages requires careful and clever planning of each of the sections. The authors do not give accounts of all theories, apparatus, and results but explain the application of their methods on the basis of theoretical fundamentals using numerous practical examples; and plenty of references are given for those readers who wish to gain further detailed information about the subject matter of the book. In section 12 (General conclusions), the editors show with the aid of several examples how a critical evaluation of the results obtained by each of the methods mentioned can lead to a uniform picture of the structure of a molecule even, if the results appear to be contradictory.

A general index of about 750 entries at the end of the book is very useful, even though some of the authors have made little contribution (*e.g.* for Section 2 there are only 10 entries). All the methods described excepting method 11 can be used for the elucidation of atomic or electronic structure. A different title for the book in which the word "structure" occurs would have made the reader understand why a number of elemental-analytical and kinetic methods (relaxation effects) have not been considered and why the electric and dielectric properties of solutions and gases have not been treated. Mass- and rotation spectrometry of inorganic substances, further solid-state methods, as well as electron diffraction in gases could easily have been included and the scope and usefulness of the book thus increased. However, it is a handy book containing a compact account of methods used in (molecular) structural research. It can be recommended to all inorganic chemists who wish to judge the merits of these methods and to all students of chemistry who are embarking on research work in structural chemistry.

K. Krogmann [NB 785a IE]

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 45075, Telex 461855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 6
JUNE 1969
PAGES 401–468

The Synthesis of Rare Sugars

By J. S. Brimacombe[*]

The use of new oxidation reagents, such as the Pfitzner-Moffatt reagent, dimethyl sulfoxide-acid anhydrides, and ruthenium tetroxide, has significantly improved the yields obtained on oxidation of a secondary hydroxyl group to a carbonyl group in suitably protected sugars. The application of these new oxidants in the carbohydrate field is briefly surveyed. The product ketones are convenient intermediates for syntheses of amino, branched-chain, deoxy, and other rare sugars. Some representative syntheses are illustrated.

1. Introduction

In recent years there has been a dramatic increase in the number of rare sugars isolated from natural sources and these have provided the carbohydrate chemist with new and challenging problems of structural determination and synthesis. A potentially valuable approach to the synthesis of amino, branched-chain, deoxy, and other rare sugars is based upon a class of carbohydrates systematically named as osuloses but which are better known, perhaps, by the trivial names of "keto" or "oxo" sugars. From the viewpoint of synthesis, the most important members of this group have the aldehyde group substituted either by glycosidation or by ketalation and they are normally prepared by the direct oxidation of a secondary hydroxyl group to a keto group in partially protected sugars [1–4].

One of the drawbacks to early synthetic work was the low yields of keto sugars obtained in the oxidation reaction [1,2]. Fortunately, the situation has been improved enormously by the discovery of new oxidative procedures that have given high yields of keto sugars on oxidation of "isolated" hydroxyl groups in sugar derivatives.

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[1] *K. Heyns* and *H. Paulsen*, Advances Carbohydrate Chem. *17*, 169 (1962).

[2] *O. Theander*, Advances Carbohydrate Chem. *17*, 223 (1962).

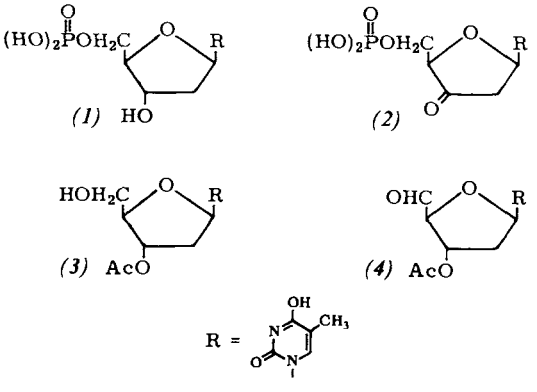
[3] *W. G. Overend*, Chem. and Ind. *1963*, 342.

[4] *J. S. Brimacombe*, Chem. in Britain *1966*, 99.

2. Oxidation

2.1. Oxidation with Dimethyl Sulfoxide-Carbodiimide

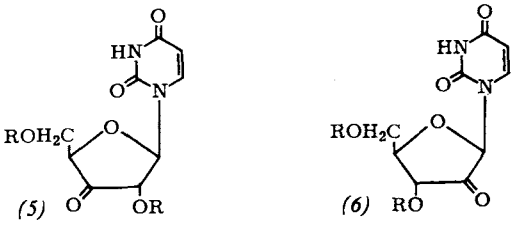
Pfitzner and *Moffatt* [5] found that attempts to polymerize thymidine 5′-phosphate *(1)* with dicyclohexylcarbodiimide in dimethyl sulfoxide led to cleavage of the *N*-glycoside and phosphate ester groups. Treatment of thymidine with *N,N*-dicyclohexylcarbodiimide-dimethyl sulfoxide in the presence of anhydrous phosphoric acid or, less effectively, trifluoroacetic acid also resulted in release of the base and this behavior was exhibited on similar treatment of other nucleotides



containing an unsubstituted hydroxyl group on C-3′. 3′-*O*-Acetylthymidine *(3)*, on the other hand, was converted into a carbonyl-containing compound formulated as the 5′-aldehydo derivative *(4)*. The

[5] *K. E. Pfitzner* and *J. G. Moffatt*, J. Amer. chem. Soc. *85*, 3027 (1963); *87*, 5661 (1965).

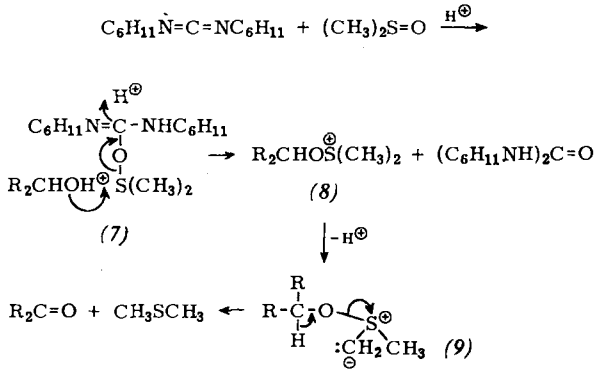
cleavage of the bonds in thymidine and its 5′-phosphate was attributed to oxidation of the 3′-hydroxyl group to a keto group, *e.g. (2)*, which was responsible for β-elimination of the base and 5′-phosphate group, if one was present. This proposal is supported by the isolation [6] of the ketones *(5)* and *(6)* from the oxidations of 2′,5′- and 3′,5′-di-*O*-trityluridine, respectively, with dimethyl sulfoxide-carbodiimide. The Pfitzner-Moffatt reagent proved to be an efficient oxidant of



(5) R = $(C_6H_5)_3C$ *(6)*

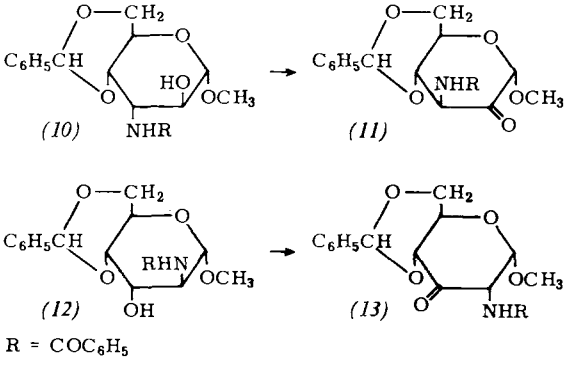
steroid and alkaloid alcohols [7] and of particular relevance to carbohydrate chemistry was the observation that oxidation could be achieved at room temperature under essentially neutral conditions (*i.e.*, by using pyridinium trifluoroacetate as a proton source). Another distinct advantage of the procedure lies in the oxidation of primary alcohols exclusively to the aldehyde stage.

The mechanism of the oxidation was elucidated [8] through isotope experiments. The oxidation proceeds with the initial formation of a sulfoxide-carbodiimide adduct *(7)* that is attacked by the alcohol to give an alkoxysulfonium ion *(8)*. This then undergoes proton abstraction and a concerted collapse of the resulting ylid *(9)* to give the carbonyl compound and dimethyl sulfide.



(7) *(8)* *(9)*

The Pfitzner-Moffatt reagent was first used in the carbohydrate field by *Dyer, McGonigal,* and *Rice* [9] to oxidize 5-deoxy-1,2-*O*-isopropylidene-β-L-arabinose *(50)* into 5-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-pentofuranos-3-ulose *(51)*, which was ultimately transformed into L-streptose *(53)* (Section 3.6). The reagent was more extensively applied to carbohydrates by *Baker* and *Buss* [10] who obtained smooth oxidations of the "isolated" hydroxyl groups of 1,2:5,6-di-*O*-isopropylidene-3-*O*-methylsulfonyl-D-mannitol, methyl 4,6-*O*-benzylidene-2-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside, methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside, and methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside. It was noted [10] that oxidation of methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside *(10)* and the isomeric altroside *(12)* gave the ketones *(11)* and *(13)*, respectively, with epimerization of the benzamido groups to the more stable equatorial positions. This presumably occurs through an acid-catalyzed enolization [11]. A number of sugar alcohols, including 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose *(14)*, methyl 3,5-*O*-isopropylidene-α-D-xylofuranoside, and



(10) *(11)* *(12)* *(13)* R = COC_6H_5

methyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside, resisted oxidation [10] and these results imply that the Pfitzner-Moffatt reagent is fairly demanding in its steric requirements.

The reagent has been applied, in one instance, to the oxidation of a carbohydrate primary hydroxyl group. Thus, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose was transformed [12] into 1,2:3,4-di-*O*-isopropylidene-6-*aldehydo*-α-D-*galacto*-hexodialdo-1,5-pyranose, an intermediate required for chain-extension reactions leading to sugar derivatives related to lincomycin.

2.2. Oxidation with Dimethyl Sulfoxide-Acid Anhydride

Mixtures of dimethyl sulfoxide and certain acid anhydrides (for example, acetic anhydride, benzoic anhydride, and phosphorus pentoxide) were found by *Albright* and *Goldman* [13] to be efficient oxidants of hindered alkaloid and steroid alcohols. The oxidation with dimethyl sulfoxide-acetic anhydride was visualized [13] as proceeding *via* the alkoxysulfonium salt *(18)*, so that the mechanism is related to that of the Pfitzner-Moffatt procedure [8]. This general mechanism is supported by the isolation of (methylthio)methyl ethers *(17)* from some oxidations, and these compounds are thought to be formed from a competitive reaction of the acyloxysulfonium intermediate *(16)*. The use of dimethyl sulfoxide containing phosphorus pentoxide as an oxidant for partially protected sugars was communicated independently by *Onodera, Hirano,*

[6] *A. F. Cook* and *J. G. Moffatt*, J. Amer. chem. Soc. *89*, 2697 (1967).

[7] *K. E. Pfitzner* and *J. G. Moffatt*, J. Amer. chem. Soc. *87*, 5670 (1965).

[8] *A. H. Fenselau* and *J. G. Moffatt*, J. Amer. chem. Soc. *88*, 1762 (1966).

[9] *J. R. Dyer, W. E. McGonigal,* and *K. C. Rice*, J. Amer. chem. Soc. *87*, 654 (1965).

[10] *B. R. Baker* and *D. H. Buss*, J. org. Chemistry *30*, 2304, 2308 (1965).

[11] *Y. Ali* and *A. C. Richardson*, Carbohydrate Res. *5*, 441 (1967).

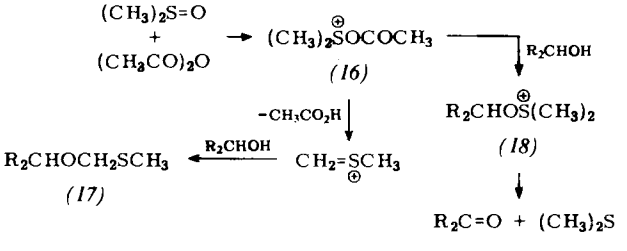
[12] *D. Horton, J. B. Hughes,* and *J. M. J. Tronchet*, Chem. Commun. *1965*, 481.

[13] *J. D. Albright* and *L. Goldman*, J. Amer. chem. Soc. *87*, 4214 (1965).

Table 1. Examples of keto sugars and lactones prepared by oxidation.

Keto sugar	Yield (%)	M.p. (°C)	$[\alpha]_D$ (°) [a]	Method [b]	Ref.
1,6-Anhydro-2,3-*O*-isopropylidene-β-D-*lyxo*-hexopyranos-4-ulose *(35)*	77	82.5—83	−76±1	A	[15]
	85—92 [c]			B	[15, 35]
1,6-Anhydro-3,4-*O*-isopropylidene-β-D-*lyxo*-hexopyranos-2-ulose *(32)*	90	92—93	−89±1	A	[16]
	85 [c]			B	[16]
	76 [c]	96—97	−110±1	B	[35]
5-*O*-Benzoyl-1,3,4-tri-*O*-benzyl-keto-D-*threo*-pentulose	84		−38.8±0.5	A	[17]
2,3,5-Tri-*O*-benzyl-D-arabino-1,4-lactone	95	67	+6.8	A	[17]
5-*O*-Benzoyl-1,2-*O*-isopropylidene-α-D-*erythro*-pentofuranos-3-ulose	31	97—98.5		A	[18]
1,3,4-Tri-*O*-benzyl-5-*O*-triphenylmethyl-keto-D-*threo*-pentulose	86		−26.2	A	[17]
1,3,4,5-Tetra-*O*-benzyl-6-*O*-triphenylmethyl-keto-L-sorbose	79		−4.2±0.4	A	[17]
1,2:4,5-Di-*O*-cyclohexylidene-β-D-*erythro*-2,3-hexodiulo-2,6-pyranose *(38)*	65	152—153	−90	A	[19]
1,2:5,6-Di-*O*-cyclohexylidene-α-D-*ribo*-hexofuranos-3-ulose *(19)*	50	65—67	+119.2	A	[19]
2,3:5,6-Di-*O*-isopropylidene-D-mannono-1,4-lactone	96	126	+50±2	A	[15]
1,2-*O*-Isopropylidene-5-*O*-(di-*O*-phenylphosphono)-α-D-*erythro*-pentofuranos-3-ulose	35	75—78	+44.5	C	[21]
1,2:4,5-Di-*O*-isopropylidene-β-D-*erythro*-2,3-hexodiulo-2,6-pyranose *(37)*	53	101.5—102.5	−126.4	A	[19]
	70	101—102	−100.4 [d]	A	[20]
1,2:5,6-Di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose *(15)*	65	118—119 [e]	+110 [e]	C	[21]
	55—60			A	[22]
	85—90 [c]			B	[32, 33]
1,2-*O*-Isopropylidene-5-*O*-tosyl-α-D-*erythro*-pentofuranos-3-ulose	31	105—106 [f]	+70.5 [f]	C	[21]
1,2-*O*-Isopropylidene-α-D-*xylo*-hexofuranurono-6,3-lacton-5-ulose	47	146—148	+88 [g]	C	[21]
Methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose	58—71	222	+128 [h]	C	[21]
Methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose	64	153—155	+550	A	[11]
Methyl 4,6-*O*-benzylidene-2-*O*-tosyl-α-D-*ribo*-hexopyranosid-3-ulose *(22)*	82—92	162—164	+44.6	C	[21, 22]
	49			A	[22]
Methyl α-D-*erythro*-pentopyranosid-3-ulose [i]	50—60	80—82	+191 [j]	A	[23, 24]
Methyl β-D-*erythro*-pentopyranosid-3-ulose [i]	70—80	85—88	−77 [j]	A	[23, 24]
Methyl α-D-*ribo*-hexopyranosid-3-ulose [k]	6	91—92	+155 [l]	A	[24]
6-*O*-Benzoyl-1,2:4,5-di-*O*-isopropylidene-keto-DL-*xylo*-hex-3-ulose	100 [c]	67.5—68.5 [36]		B	[33]
6-Deoxy-1,3:2,5-di-*O*-methylene-keto-L-*lyxo*-hex-4-ulose	100 [c]	151—152 [37]	+3.3 [37]	B	[33]
1,2-*O*-Isopropylidene-α-L-*glycero*-tetrofuranos-3-ulose	70—75 [c]			B	[33]
Methyl 3,4,6-tri-*O*-benzyl-α-D-*arabino*-hexopyranosid-2-ulose	50 [c]	150—151	+52.7	B	[32]
Methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose	35 [c]	171—172	+159 [m]	B	[32]
Methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*threo*-hexopyranosid-3-ulose	47 [c]	132—133	+150	B	[32]
Methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose	100 [c]	b.p. 78—80 °C/ 0.45 torr	−107 [n]	B	[33]
Methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-2-ulose	45 [c]	73—74	−111 [39]	B	[32]
Methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosid-2-ulose	40 [c]	97—98	+166 [p]	B	[32]
	80 [c, o]			B	[33]

[a] Usually measured on 1—2% chloroform solutions. [b] A: Acetic anhydride in dimethyl sulfoxide; B: Ruthenium tetroxide; C: Phosphorus-pentoxide in dimethyl sulfoxide. [c] Maximum yields. [d] In acetone. [e] Data for crystalline hydrate. [f] Methanolate. [g] In dimethyl sulfoxide. [h] In dimethylformamide. [i] From oxidation of the methyl D-xyloside-2,4-phenylboronate. [j] $[\alpha]_{Hg}$ in water. [k] From oxidation of methyl α-D-glucopyranoside. [l] In water. [m] In ethyl acetate, taken from [38]. [n] In ethanol, taken from [39]. [o] Data for the D-enantiomer. [p] In ethanol, taken from [40].



and *Kashimura* [14]. Oxidations using these procedures give good yields and can be conducted at room temperature; the reagents are inexpensive. The dimethyl sulfoxide-acetic anhydride method is particularly suited to the carbohydrate field because the excess of reagents and by-products can be removed simply by evaporation at low temperature [15] or by straightforward extraction procedures.

A number of the keto sugars that have been prepared by these procedures are listed in Table 1. Studies by *Onodera*, *Hirano*, and *Kashimura* [21] have shown that oxidations with dimethyl sulfoxide-phosphorus pentoxide are not markedly influenced by the orientation of the hydroxyl group in pyranoid and furanoid ring systems. The same applies to oxidations using dimethyl sulfoxide-acetic anhydride.

Oxidation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose *(14)*, for example, is achieved only with great difficulty with most other reagents [2], but it was readily converted into 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose

[14] *K. Onodera*, *S. Hirano*, and *N. Kashimura*, J. Amer. chem. Soc. *87*, 4651 (1965).

[15] *D. Horton* and *J. S. Jewell*, Carbohydrate Res. *2*, 251 (1966).

[16] *D. Horton* and *J. S. Jewell*, Carbohydrate Res. *5*, 149 (1967).

[17] *Y. Rabinsohn* and *H. G. Fletcher*, J. org. Chemistry *32*, 3452 (1967).

[18] *G. L. Tong*, *W. W. Lee*, and *L. Goodman*, J. org. Chemistry *32*, 1984 (1967).

[19] *K. James*, *A. R. Tatchell*, and *P. K. Ray*, J. chem. Soc. (London) *(C) 1967*, 2681.

[20] *E. J. McDonald*, Carbohydrate Res. *5*, 106 (1967).

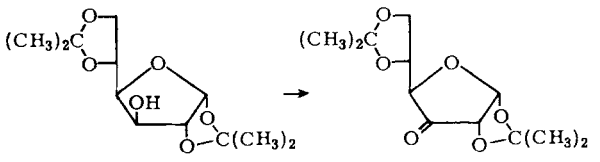
[21] *K. Onodera*, *S. Hirano*, and *N. Kashimura*, Carbohydrate Res. *6*, 276 (1968).

[22] *J. S. Brimacombe*, *J. G. H. Bryan*, *A. Husain*, *M. Stacey*, and *M. S. Tolley*, Carbohydrate Res. *3*, 318 (1967).

[23] *B. Lindberg* and *K. N. Slessor*, Carbohydrate Res. *1*, 492 (1966).

[24] *B. Lindberg* and *K. N. Slessor*, Acta chem. scand. *21*, 910 (1967).

(15) by using either acetic anhydride[22,25] or phosphorus pentoxide[14,21,22] in dimethyl sulfoxide. It is pertinent to note that methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside was oxidized with methyl sulfoxide-acetic anhydride to methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose[11].



(14) *(15)*

Oxidation with dimethyl sulfoxide-acetic anhydride has been of value[23,24] in the synthesis of unsubstituted glycopyranosiduloses which, hitherto, have been obtained from glycopyranosides, either by non-specific oxidation[2] or by selective catalytic oxidation of axial hydroxyl groups[1,26]. The method takes advantage of the stability of phenylboronate esters[27] under the conditions of oxidation and of their ready removal in hydroxylic solvents. The methyl D-*erythro*-pentopyranosid-3-uloses were prepared[24], in high yield, following oxidation of the anomeric methyl D-xylopyranoside 2,4-phenylboronates with dimethyl sulfoxide-acetic anhydride.

Attempts to oxidize the primary hydroxyl group of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose with acetic anhydride-dimethyl sulfoxide gave[28] a mixture of 1,2:3,4-di-*O*-isopropylidene-6-*O*(methylthio) methyl-α-D-galactopyranose and 6-*O*-acetyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, but the anticipated 6-aldehydo compound was not formed. (Methylthio)methyl ethers have been isolated[19] as by-products from similar oxidation of other carbohydrates.

(For reviews of oxidations employing dimethyl sulfoxide see Ref.[29].)

2.3. Oxidation with Ruthenium Tetroxide

Oxidation of partially protected sugars with ruthenium tetroxide[30] was reported by *Overend et al.*[31,32] to give better yields than those generally obtained with the chromium trioxide-pyridine complex[2].

Oxidations are conducted in carbon tetrachloride at room temperature by using a slight excess of ruthenium tetroxide, prepared by oxidation of the dioxide with sodium metaperiodate, or, with a catalytic quantity of the tetroxide in the presence of sodium metaperiodate[32,33]. It is important that the dihydrate $RuO_2 \cdot 2H_2O$ is used for oxidation to the tetroxide since other modifications are not oxidized under the mild conditions employed[34].

A number of keto sugars that have been prepared by these procedures are listed in Table 1. Axial and equatorial hydroxyl groups on an otherwise protected pyranoid ring appear to be oxidized with equal ease[34].

2.4. Other Methods

Lead tetraacetate is a good oxidant[41] of certain simple alcohols in pyridine solution but low yields of glycopyranosiduloses were afforded on oxidation of glycosides, such as methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranoside[32], and the procedure has been unsatisfactory with other partially protected sugars[15,42].

Rearrangement of certain methyl 4,6-*O*-benzylidene-3-deoxy-3-phenylazo-aldohexopyranosides with sodium methoxide yield the 3-phenylhydrazones[43], which are converted into the hexopyranosid-3-ulose on reaction with benzaldehyde in acetic acid solution.

3. Keto Sugars as Intermediates

A number of rare sugars have become available through syntheses which use the new oxidative procedures described above. It should be remembered that nucleophilic additions to keto sugars can lead to two diastereoisomeric products and this is clearly disadvantageous from a synthetic viewpoint. In many cases, however, the addition is markedly stereoselective and, with certain fused-ring systems, a stereospecific addition is often achieved. In any event, the successful application of the method requires a definitive establishment of the stereochemistry of the product(s). Similar considerations apply to the reduction of keto-sugar oximes and hydrazones.

3.1. D-Allose and its Derivatives

Both 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose *(15)*[44] and 1,2:5,6-di-*O*-cyclohexyl-

[25] *W. Sowa* and *G. H. S. Thomas*, Canad. J. Chem. *44*, 836 (1966).

[26] *K. Heyns*, Stärke *1963*, 432.

[27] *R. J. Ferrier*, J. chem. Soc. (London) *1961*, 2325; *R. J. Ferier, D. Prasad, A. Rudowski*, and *I. Sangster, ibid. 1964*, 3330.

[28] *J. L. Godman* and *D. Horton*, Carbohydrate Res. *6*, 229 (1968).

[29] *W. W. Epstein* and *F. W. Sweat*, Chem. Reviews *67*, 247 (1967); *N. Kharasch* and *B. S. Thyagarajan*, Quart. Rep. Sulfur Chem. *1*, 16 (1966).

[30] *C. Djerassi* and *R. R. Engle*, J. Amer. chem. Soc. *75*, 3838 (1953); *L. M. Berkowitz* and *P. N. Rylander, ibid. 80*, 6682 (1958).

[31] *P. J. Beynon, P. M. Collins*, and *W. G. Overend*, Proc. chem. Soc. (London) *1964*, 342.

[32] *P. J. Beynon, P. M. Collins, P. T. Doganges*, and *W. G. Overend*, J. chem. Soc. (London) *(C) 1966*, 1131.

[33] *V. M. Parikh* and *J. K. N. Jones*, Canad. J. Chem. *43*, 3452 (1965).

[34] *P. J. Beynon, P. M. Collins, D. Gardiner*, and *W. G. Overend*, Carbohydrate Res. *6*, 431 (1968).

[35] *K. Heyns, J. Weyer*, and *H. Paulsen*, Chem. Ber. *100*, 2317 (1967).

[36] *G. U. Yuen* and *J. M. Sugihara*, J. org. Chemistry *26*, 1598 (1961).

[37] *J. W. Bird* and *J. K. N. Jones*, Canad. J. Chem. *41*, 1877 (1963).

[38] *B. Flaherty, W. G. Overend*, and *N. R. Williams*, J. chem. Soc. (London) *(C) 1966*, 398.

[39] *P. M. Collins* and *W. G. Overend*, Chem. and Ind. *1963*, 375; J. chem. Soc. (London) *1965*, 1912.

[40] *J. S. Burton, W. G. Overend*, and *N. R. Williams*, Chem. and Ind. *1961*, 175; J. chem. Soc. (London) *1965*, 3433.

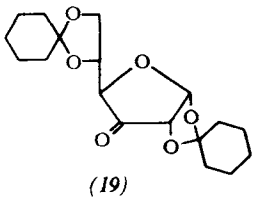
[41] *R. E. Partch*, Tetrahedron Letters *1964*, 3071; J. org. Chemistry *30*, 2498 (1965).

[42] *J. S. Brimacombe* and *J. G. H. Bryan*, unpublished results.

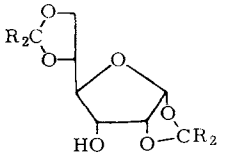
[43] *G. J. F. Chittenden* and *R. D. Guthrie*, Proc. chem. Soc. (London) *1964*, 289; J. chem. Soc. (London) *(C) 1966*, 695.

[44] *O. Theander*, Acta chem. scand. *18*, 2209 (1964).

idene-α-D-*ribo*-hexofuranos-3-ulose *(19)* [19] are reduced stereospecifically, with $NaBH_4$, to the allose diacetals *(20)* and *(21)*, respectively, which afford D-allose on removal of the acetal groups with acid. $LiAlH_4$ reduction of ketone *(19)* is also stereospecific [19] but similar reduction of ketone *(15)* produced [45]



(19)

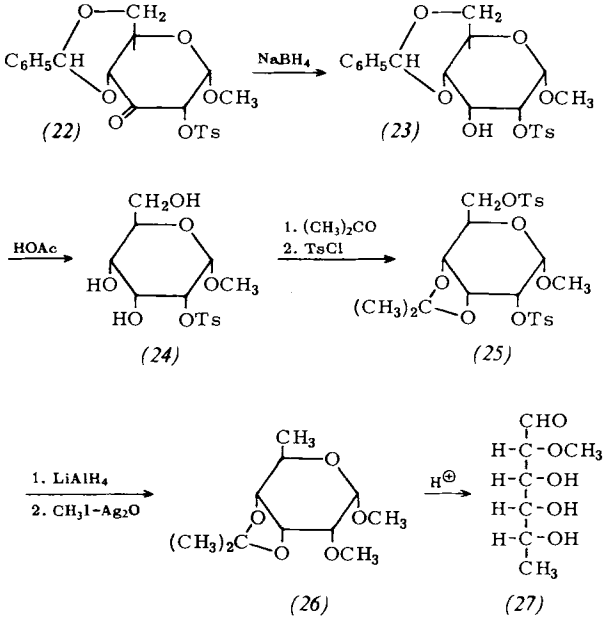


(20), R = CH_3
(21), R-R = $-(CH_2)_5-$

a mixture containing the allose and glucose diacetals in a ratio of 7:3.

Reduction of methyl 4,6-*O*-benzylidene-2-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranosid-3-ulose *(22)*, with $NaBH_4$, yielded [10] exclusively methyl 4,6-*O*-benzylidene-2-*O*-*p*-tolylsulfonyl-α-D-allopyranoside *(23)*. Methyl-α-D-allopyranoside is formed [46] on successive treatments of compound *(23)* with dilute acid and sodium methoxide, while methanolysis of the α-alloside afforded a mixture of glycosides from which methyl β-D-allopyranoside was crystallized. Thus, D-allose and the anomeric allopyranosides are available from straightforward procedures.

Alloside *(23)* is a key intermediate in syntheses of 6-deoxy-3-*O*-methyl-D-allose [47], a component of the sarcostin glycosides of *Ascelepias lilacina* Weimarck [48] and *A. swynnertonii* S. Moore [49], and 6-deoxy-2-*O*-

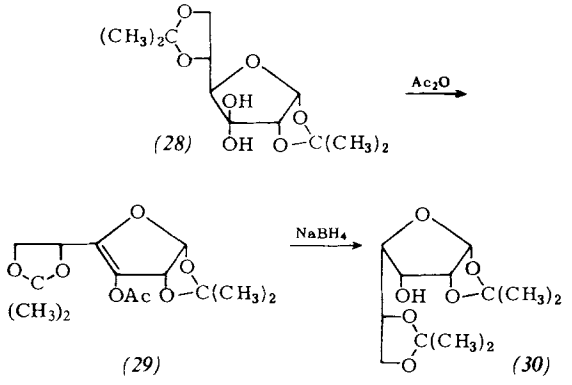


(22) *(23)* *(24)* *(25)* *(26)* *(27)*

methyl-D-allose (D-javose) [50], a constituent of two cardenolide glycosides found in the seeds of *Antiaris toxicaria* Lesch [51]. One synthesis of D-javose *(27)*, for example, used the route illustrated *(22)* → *(27)*.

3.2. D-Gulose

The crystalline hydrate *(28)* derived from compound *(15)* is converted [52] into the enol-acetate *(29)* on treatment with acetic anhydride in pyridine at 60 °C.

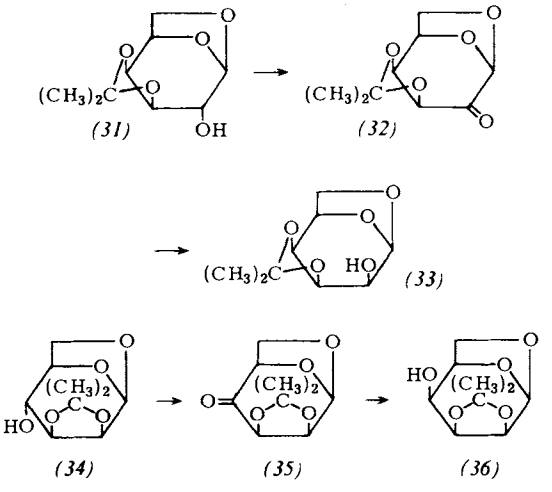


(28) *(29)* *(30)*

Reduction of *(29)* with $NaBH_4$ in methanol afforded 1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose *(30)*, in approximately 30% yield [53], which was then converted into D-gulose by acid hydrolysis.

3.3. D- and L-Talose and their Derivatives

Oxidation of 1,6-anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose *(31)* and 1,6-anhydro-2,3-*O*-isopropylidene-β-D-mannopyranose *(34)* is readily accomplished with either dimethyl sulfoxide-acetic anhydride [15,16] or ruthenium tetroxide [15,16,35] to give the ketones *(32)* and *(35)*, respectively.



(31) *(32)* *(33)* *(34)* *(35)* *(36)*

[45] *P. M. Collins*, Tetrahedron *21*, 1809 (1965).

[46] *J. S. Brimacombe* and *A. Husain*, Carbohydrate Res. *6*, 491 (1968).

[47] *J. S. Brimacombe* and *D. Portsmouth*, J. chem. Soc. (London) *(C) 1966*, 499.

[48] *L. Sawlewicz*, *E. Weiss*, and *T. Reichstein*, Helv. chim. Acta *50*, 530 (1967).

[49] *K. Jaeggi*, Dissertation, Universität Basel 1966.

[50] *J. S. Brimacombe* and *A. Husain*, J. chem. Soc. (London) *(C) 1967*, 1503.

[51] *P. Mühlradt*, *E. Weiss*, and *T. Reichstein*, Liebigs Ann. Chem. *685*, 253 (1965).

[52] *W. Meyer zu Reckendorf*, Angew. Chem. *79*, 151 (1967); Angew. Chem. internat. Edit. *6*, 177 (1967).

[53] *W. Meyer zu Reckendorf*, private communication.

These ketones can be reduced quantitatively and stereospecifically with metal hydrides to yield 1,6-anhydro-3,4-*O*-isopropylidene-β-D-talopyranose *(33)* and the 2,3-isopropylidene derivative *(36)*, respectively. Both compounds afforded the previously unknown 1,6-anhydro-β-D-talopyranose [16,35] on mild acid treatment while more vigorous treatment gave a mixture of products from which D-talose was crystallized [16].

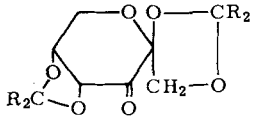
Reduction of methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-2-ulose and methyl 2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose, either catalytically or with $LiAlH_4$, yields [39] predominantly products having the L-*talo* configuration. Deacetonation and acetylation of the product mixtures permits the isolation of methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-taloside which gives crystalline 6-deoxy-L-talose on deacetylation and acid hydrolysis.

The stereochemical outcome of reduction of the foregoing keto sugars has been rationalized [16,39] on the basis of the reagent's approach from the less hindered side of the carbonyl function.

1,2:5,6-Di-*O*-isopropylidene-α-D-allofuranose *(20)* has been transformed [54] into L-acovenose (6-deoxy-3-*O*-methyl-L-talose) by a sequence involving methylation, graded acidic hydrolysis, periodate oxidation, and addition of methylmagnesium bromide.

3.4. D-Psicose (D-*ribo*-hexulose)

Two groups [19,20] have shown that D-psicose can be readily prepared by a route involving stereoselective reduction of 1,2:4,5-di-*O*-isopropylidene-β-D-*erythro*-2,3-hexodiulo-2,6-pyranose *(37)* or the dicyclohexylidene ketone *(38)* to the related psicopyranose diacetals. Ketones *(37)* and *(38)* are obtained by oxidation of 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose

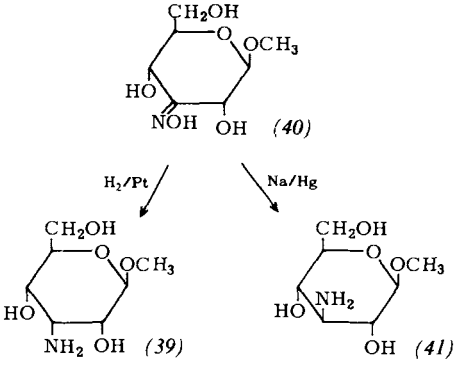


(37), R = CH_3
(38), R-R = $-(CH_2)_5-$

and 1,2:4,5-di-*O*-cyclohexylidene-β-D-fructopyranose, respectively, with dimethyl sulfoxide-acetic anhydride.

3.5. Amino Sugar Derivatives

Keto sugars have been utilized in syntheses of amino sugar derivatives in three ways. Firstly, the reduction of oximes or hydrazones derived from keto sugars provides a now well-established route [3] to amino sugars and a parallelism has been noted [55] between the steric course of metal hydride reduction of ketones and their oximes. This is particularly true of metal hydride reductions of ketones and oximes attached to fused-ring systems (for example, ketones *(32)* and *(35)* and their oximes) where the geometry of the molecule favors attack of the reagent from one direction only. In less substituted systems, the choice of reducing agent can often lead to a preponderance of one epimer over the other. Catalytic reduction of methyl β-D-*ribo*-hexopyranosid-3-ulose oxime *(40)* gave [56] exclusively methyl 3-amino-3-deoxy-β-D-allopyranoside *(39)*, while reduction with sodium amalgam yielded predominantly methyl 3-amino-3-deoxy-β-D-glucopyranoside *(41)*.



A number of amino sugars and their derivatives including 2-amino-2-deoxy-L-ribose [3], 2-amino-2,6-dideoxy-L-talose [57,58] (pneumosamine) *(43)*, 2-amino-2,6-dideoxy-L-galactose [58] (L-fucosamine) *(44)*, 2-amino-2,6-dideoxy-L-mannose [59] (L-rhamnosamine), 2-amino-2,6-dideoxy-L-glucose [59], 3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose [14,21], methyl 4-acetamido-4,6-dideoxy-α-L-talopyranoside [60], 4-amino-1,6-anhydro-4-deoxy-β-D-talopyranose [61], and 3-amino-1,6-anhydro-3-deoxy-β-D-galactopyranose [62] have been prepared by the oxime route.

The method offers some advantages for the synthesis of 2-amino-2-deoxy sugars since bimolecular nucleophilic displacement of sulfonic esters at C-2 with azide ion and hydrazine is extremely difficult to effect. For example, the absolute configuration of pneumosamine was established [63] by a synthesis of the D-enantiomer which involved the reaction of anhydrous hydrazine on methyl 6-deoxy-3,4-*O*-isopropylidene-2-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside. An improved procedure [57] for the naturally occurring L-sugar *(43)* utilized the catalytic reduction of methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-2-ulose oxime *(42)* even though chromatographic separation of the epimeric amino sugars *(43)* and *(44)* was necessary at the final stage of the synthesis.

[54] *B. M. Kapur* and *H. Allgeier*, Helv. chim. Acta *51*, 89 (1968).

[55] *P. M. Collins* and *W. G. Overend*, J. chem. Soc. (London) *1965*, 3448.

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[57] *J. S. Brimacombe* and *M. J. How*, J. chem. Soc. (London) *1963*, 3886.

[58] *J. S. Brimacombe, J. G. H. Bryan*, and *M. Stacey*, Carbohydrate Res. *1*, 258 (1965).

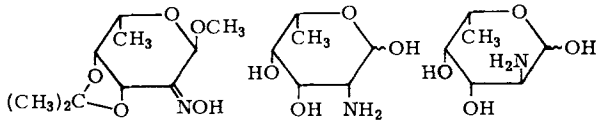
[59] *J. S. Brimacombe* and *M. C. Cook*, J. chem. Soc. (London) *1964*, 2663.

[60] *S. W. Gunner, W. G. Overend*, and *N. R. Williams*, Carbohydrate Res. *4*, 498 (1967).

[61] *D. Horton* and *J. S. Jewell*, Carbohydrate Res. *3*, 255 (1966).

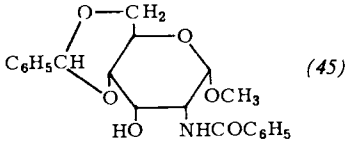
[62] *K. Heyns, J. Weyer*, and *H. Paulsen*, Chem. Ber. *98*, 327 (1965).

[63] *J. S. Brimacombe* and *M. J. How*, J. chem. Soc. (London) *1962*, 5037.



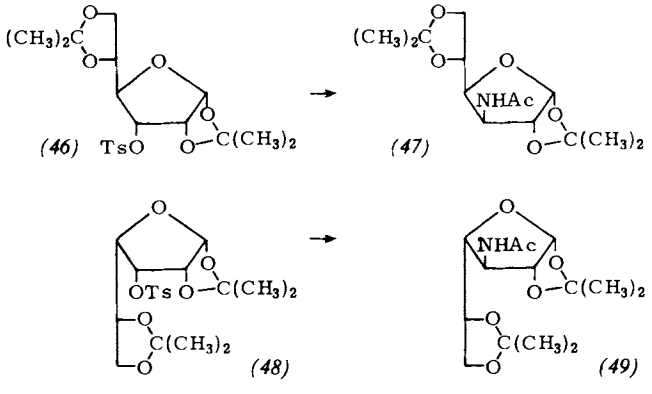
(42) (43) (44)

Secondly, configurational inversions can be effected by oxidation of partially protected acetamido sugars and reduction of the resulting ketone. Oxidation of methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside, with the Pfitzner-Moffatt reagent, afforded the ketone *(13)* which is reduced stereospecifically to methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-allopyranoside *(45)* with $NaBH_4$[10]. Since ketone *(13)* is also the product of similar oxidation[10] of methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside *(12)*, the altroside *(12)* can be converted into the alloside *(45)* *via* the ketone *(13)*.



(45)

Finally, a route to certain 3-acetamido-3-deoxy sugars is based upon the ready displacement of *endo*-sulfonyloxy groups attached to trioxabicyclo[3.3.0]octane ring-systems such as occur in 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-allofuranose *(46)* and 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-gulofuranose *(48)*. Sulfonates *(46)* and *(48)* were prepared from the parent alcohols *(20)* and *(30)*.



(46) (47) (48) (49)

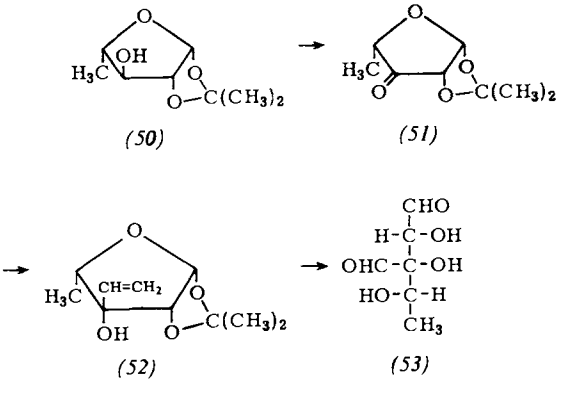
Whereas the *exo*-sulfonyloxy group of 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranose is generally unreactive[64] towards bimolecular nucleophilic displacement, the epimeric D-allose sulfonate *(46)* (*endo*-substituent) undergoes ready displacement with a variety of nucleophiles[22,65] due to the more favorable approach of the nucleophile from the *exo*-direction. The sulfonyloxy groups of compounds *(46)*[22,65] and *(48)*[66] are smoothly displaced with azide ion in dimethylformamide to give, after reduction and *N*-acetylation, 3-acetamido-3-deoxy diacetals possessing the D-*gluco* *(47)* and D-*galacto* *(49)* configurations, respectively. The free acetamido sugars were afforded on mild acid hydrolysis of these compounds. 3-Amino-3-deoxy-D-xylose can be synthesized[22] from 3-acetamido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose *(47)* by selective removal of the 5,6-*O*-isopropylidene group, followed by a conventional chain-shortening sequence and acid hydrolysis.

Other nucleophiles have been used in displacement reactions of sulfonate *(46)*. With tetrabutylammonium fluoride, for example, the method has led[67] to excellent syntheses of 3-deoxy-3-fluoro-D-glucose and 3-deoxy-3-fluoro-D-xylose.

3.6. Branched-Chain Sugars

Branched-chain sugars of the type R–$\overset{|}{\underset{|}{C}}$OH and R–$\overset{|}{\underset{|}{C}}$H are found in Nature[3]. Treatment of glycopyranosiduloses with Grignard reagents[3,40], organolithium reagents[68], diazomethane[69,70], or dimethylsulfoxonium methylide[71] provides access to the former type of branched-chain sugar. The two latter reagents yield epoxides which can be opened either with lithium aluminum hydride to give a glycoside having a *C*-methyl substituent, or, with alkali to give a *C*-hydroxymethyl substituent.

A constitutional synthesis of streptose (5-deoxy-3-formyl-L-lyxose) *(53)* was achieved[9] by way of the reaction of 5-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-



(50) (51) (52) (53)

pentofuranos-3-ulose *(51)* with vinylmagnesium bromide. The addition appeared to be stereospecific and afforded 5-deoxy-1,2-*O*-isopropylidene-3-*C*-vinyl-β-L-lyxofuranose *(52)*, which was converted into L-streptose *(53)* following ozonolysis and deacetonation. Methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyr-

[64] *M. L. Wolfrom, J. Bernsmann,* and *D. Horton,* J. org. Chemistry *27,* 4505 (1962); *B. R. Baker* and *A. H. Haines, ibid. 28,* 438 (1963); *K. J. Ryan, H. Arzoumanian, E. M. Acton,* and *L. Goodman,* J. Amer. chem. Soc. *86,* 2497 (1964); *N. C. Jamieson* and *R. K. Brown,* Canad. J. Chem. *39,* 1765 (1961).

[65] *D. T. Williams* and *J. K. N. Jones,* Canad. J. Chem. *45,* 8 (1967).

[66] *J. S. Brimacombe, P. A. Gent,* and *M. Stacey,* J. chem. Soc. (London) *(C) 1968,* 567.

[67] *K. W. Buck, A. B. Foster, R. Hems,* and *J. M. Webber,* Carbohydrate Res. *3,* 137 (1966); *5,* 292 (1967).

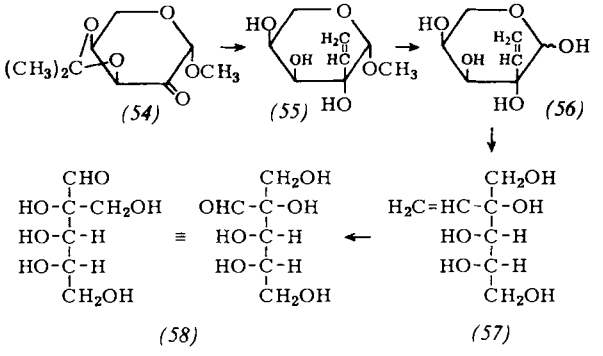
[68] *A. A. J. Feast, W. G. Overend,* and *N. R. Williams,* J. chem. Soc. (London) *(C) 1966,* 303.

[69] *W. G. Overend* and *N. R. Williams,* J. chem. Soc. (London) *1965,* 3446.

[70] *R. J. Ferrier, W. G. Overend, G. A. Rafferty, H. M. Ware,* and *N. R. Williams,* J. chem. Soc. (London) *(C) 1968,* 1091.

[71] *R. D. King, W. G. Overend, J. Wells,* and *N. R. Williams,* Chem. Commun. *1967,* 726.

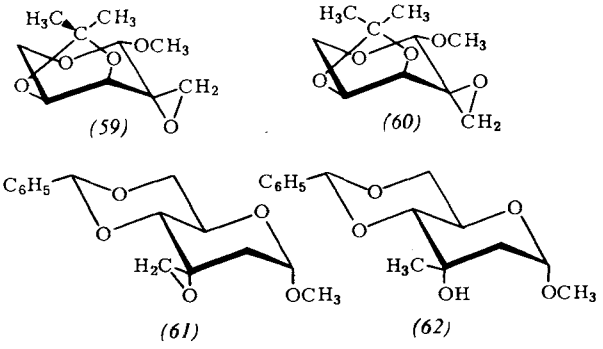
anosid-2-ulose *(54)* has been reacted[40] with a range of Grignard reagents (RMgHal, where R = CH_3, C_6H_5, $C\equiv C-C_6H_5$, $CH_2=CH$) and, after further conversions, it was possible to obtain L-arabinopyranoside derivatives possessing either a methyl, hydroxymethyl, or formyl side chain. Acid hydrolysis of methyl 2-*C*-vinyl-β-L-arabinopyranoside *(55)*, so obtained[40], gave 2-*C*-vinyl-L-arabinose *(56)* which was reduced to the alditol *(57)* and thence, on ozonolysis, to 2-*C*-hydroxymethyl-L-ribose (L-hamamelose) *(58)*.



(54) *(55)* *(56)* *(58)* *(57)*

Grignard additions to glycopyranosiduloses have been used to prepare the enantiomers of a number of antibiotic, branched-chain sugars. D-Mycarose (2,6-dideoxy-3-*C*-methyl-D-*ribo*-hexose)[38], D-cladinose (2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-D-*ribo*-hexose)[38], and D-arcanose (2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-D-*xylo*-hexose)[72] have been synthesized for the purpose of establishing the structures of the naturally-occurring L-forms.

Whereas the reaction of ketone *(54)* with Grignard reagents afforded branched-chain glycosides having the L-*arabino* configuration, addition of either methyllithium or *trans*-β-styryllithium[68] yielded branched-chain glycosides having the L-*ribo* configuration. Treatment of ketone *(54)* with a slight excess of diazomethane, followed by reduction of the mixture of epoxides *(59)* and *(60)* with $LiAlH_4$, gave[70] two isomeric 2-*C*-methylpentoside derivatives: the preponderant product had the L-*ribo* configuration. If the ketone *(54)* is epoxidized with dimethylsulfoxonium methylide[71], the major product obtained on treatment of the epoxide mixture with $LiAlH_4$ and partial acid hydrolysis is methyl 2-*C*-methyl-β-L-arabinopyranoside. Methyl 4,6-benzylidene-2-deoxy-3-*C*-methyl-α-D-*ribo*-hexopyranoside *(62)* is obtained analogously[71] on reduction of the epoxide *(61)*, formed on treatment of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose with dimethylsulfoxonium methylide. These additions follow the generalization of *Corey* and *Chaykovsky*[73] that, with cyclic ketones, dimethylsulfoxonium methylide gives preferentially an equatorial addition product.



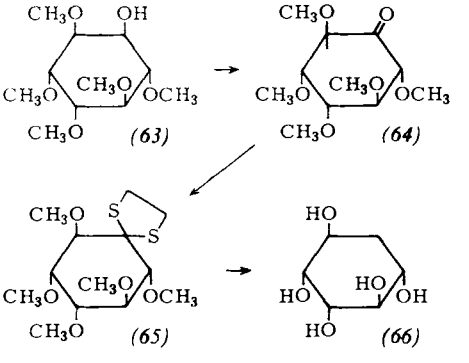
(59) *(60)* *(61)* *(62)*

3.7. Deoxy Sugars

There are several possible ways in which keto sugars might be transformed into deoxy sugars but none of these procedures appears to have been extensively investigated.

The carbonyl group in 2,4,6/3,5-pentahydroxycyclohexanone (*myo*-inosose-2) is reduced to a methylene group on treatment with Adams' catalyst and H_2 in acid solution[74]. Similar reductions of 2,3,5/4,6-pentahydroxycyclohexanone [(+)*vibo*-inosose][75] and (±)-2,3,4,5/6-pentahydroxycyclohexanone [*epi*-inosose-2][76] yielded the related methylene compounds but, additionally, cyclohexanetetrols and cyclohexanetriols were formed by reductive removal of hydroxyl groups. This procedure gave[56] methyl 3-deoxy-β-D-*ribo*-hexopyranoside when applied to methyl β-D-*ribo*-hexopyranosid-3-ulose but was unsuccessfully applied[3] to methyl 2,3-di-*O*-benzyl-α-D-*xylo*-hexopyranosid-4-ulose.

An alternative approach was used[77] in synthesizing 1,3,4/2,5-cyclohexanepentol [(−)*proto*-quercitol] *(66)*. Thus, (−)*proto*-inosose pentamethyl ether *(64)*, prepared by oxidation of the alcohol *(63)* with ruthenium dioxide-sodium periodate, was converted into the thioketal *(65)* on reaction with ethane-1,2-dithiol and, thence, by successive disulfurization over Raney nickel and demethylation into (−)*proto*-quercitol *(66)*.



(63) *(64)* *(65)* *(66)*

Methyl 4-deoxy-α-D-*xylo*-hexopyranoside was obtained[3] from methyl 2,3-di-*O*-benzyl-α-D-*xylo*-hexopyranosid-4-ulose by a route involving mercaptalation with ethanethiol and desulfurization of the thioketal thus formed.

[72] *G. B. Howarth, W. A. Szarek,* and *J. K. N. Jones,* Chem. Commun. *1968*, 62.

[73] *E. J. Corey* and *M. Chaykovsky,* J. Amer. chem. Soc. *87*, 1353 (1965).

[74] *T. Posternak,* Helv. chim. Acta *33*, 350 (1950).

[75] *G. G. Post* and *L. Anderson,* J. Amer. chem. Soc. *84*, 471 (1962).

[76] *P. A. J. Gorin,* Canad. J. Chem. *42*, 1748 (1964).

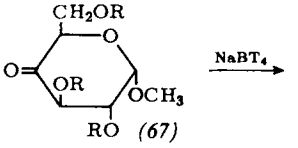
[77] *G. E. McCasland, M. O. Naumann,* and *L. J. Durham,* Carbohydrate Res. *4*, 516 (1967).

Treatment of *p*-tolylsulfonylhydrazones with either $LiAlH_4$, $NaBH_4$, or KBH_4 affords[78] a mild method for reducing carbonyl groups to methylene groups. This procedure was used to convert[79] D-glucose and L-arabinose *p*-tolylsulfonylhydrazones into 1-deoxy-D-glucitol and 1-deoxy-L-arabinitol, respectively, but failed[80] to achieve a similar conversion with 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose *p*-tolylsulfonylhydrazone. This hydrazone was unreactive towards the Wolff-Kishner conditions and it was suggested[80] that, in both cases, the approach of the base is sterically hindered.

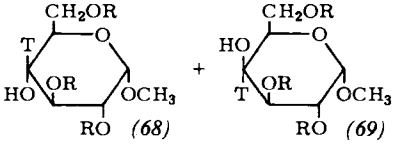
3.8. Specifically-Labeled Sugars

Sugars in which one or more of the hydrogen atoms are replaced by either deuterium or tritium are increasingly used in metabolic experiments, in studies of enzymic reactions, and are also of potential interest for nuclear magnetic resonance and mass spectroscopic studies. Reduction to the epimeric pair of glycosides is routinely used to establish the location of the carbonyl group in unsubstituted glycopyranosiduloses and is applied equally well to more highly substituted keto sugars[2,3]. Reduction with deuterated or tritiated reductants ($NaBD_4$, $NaBT_4$, $LiAlT_4$) would appear to offer worthwhile syntheses of specifically-labeled sugars. Methyl 2,3,6-tri-*O*-benzoyl-α-D-*xylo*-hexopyranosid-4-ulose *(67)*, for example, was reduced with $NaBT_4$ in ethanol to give[81] a mixture of the tritiated glucopyranoside *(68)* and galactopyranoside *(69)* derivatives, which was converted into a mixture of [4-T]-D-glucose and [4-T]-D-galactose by debenzoylation and acid hydrolysis.

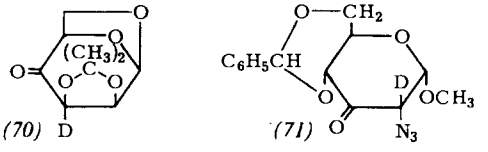
Horton and *Jewell*[61] applied the principle of stereochemical control of base-catalyzed enolization to introduce deuterium specifically into 1,6-anhydro-2,3-*O*-isopropylidene-β-D-*lyxo*-hexopyranos-4-ulose *(35)*. The ketone is deuterated rapidly at C-3 on treatment with NaOD in D_2O without change of configuration. The ring strain in the [3.2.1]bicyclic system prohibits the formation of the intermediate 4,5-enol, necessary for exchange with H-5, and the stereospecificity of the exchange at C-3 is predictable on the expectation of the thermodynamically more stable, *cis*-fused acetal *(70)* preponderating at equilibrium. Appropriate reduction of ketones *(35)* and *(70)* provides a route



(67)



(68) *(69)*



(70) *(71)*

R = COC_6H_5

to derivatives of D-talose that are deuterated at C-3, at C-4, or at both positions. An acid-catalyzed enolization effected[11] the introduction of deuterium at C-2 of methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose to give the deuterated azido-ketone *(71)*. This compound should be a valuable intermediate for the synthesis of specifically-labeled amino sugars.

I am grateful to my co-workers M. C. Cook, M. J. How, D. Portsmouth, A. Husain, J. G. H. Bryan, and (Miss) P. A. Gent for their work on keto and amino sugars. Thanks are also due to Professors M. Stacey and B. Lindberg, and Dr. O. Theander for their sustained interest in these investigations.

Received: July 8, 1968 [A 699 IE]
German version: Angew. Chem. *81*, 415 (1969)

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[80] *J. Defaye* and *J. Hildesheim*, Carbohydrate Res. *4*, 145 (1967).
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Sigma-Pi Rearrangements of Organotransition Metal Compounds

By M. Tsutsui, M. Hancock, J. Ariyoshi, and M. N. Levy[*]

σ-Bonded organic groups in transition-metal complexes can rearrange to π-bonding ligands and vice versa: the classic example is the formation of π-arenechromium complexes from σ-arylchromium compounds. Rearrangements of this kind can be induced, inter alia, by reactions of the metal or of the ligand, as well as by migration or insertion of a ligand. Rearrangements play a role in many industrial processes, including the polymerization and isomerization of olefins and the hydroformylation of olefins.

1. Introduction

Sigma (σ)-pi(π) rearrangements involve the rearrangement of an organic group that is σ-bonded to a transition metal to the corresponding π-bonded species. Not only these, but also the reverse, π-σ, rearrangements will be covered in this review. All rearrangements occur *intra*molecularly; it is possible that *inter*molecular rearrangements may occur but none have been reported.

A sigma compound involves ligand to metal bonding utilizing σ-orbitals (a sp^n hybrid) on the ligand and dσ-orbitals on the metal; in a π-complex bonding occurs by a σ-overlap between the ligand π-orbitals and dσ-acceptor metal orbitals and a "back-bond" resulting from flow of electron density from filled metal d_{xy} or other d_π-p_π hybrid orbitals into antibonding orbitals on the carbon atoms. The π-complex thus involves a certain amount of double bond character in the metal-ligand interaction.

The first example of this rearrangement in organometallic chemistry came with the characterization of the π-arenechromium complexes [1] (*Hein*'s complexes) and the isolation of the intermediate in their preparation, tri(σ-phenyl)chromium 3-tetrahydrofuran [2]. Since then such rearrangements have been observed in organometallic compounds of almost all the transition metals and with a large variety of ligands, including groups bound through an element other than carbon. Possibly the most important application of σ-π rearrangements is in the field of homogeneous catalytic reactions such as Ziegler-Natta polymerization of olefins (cf. Section 2.3.1) and the Oxo process (hydroformylation of olefins, cf. Section 2.3.3).

As will be seen later, the oxidation state and the stereochemistry of the metal atom change little during a rearrangement and thus the difference in ligation, lattice, and solvation energies (if any) will make only a small contribution to the energy difference between initial and final states. The stability of one state with respect to the other will therefore depend considerably upon the difference in ligand field stabilization energies. For σ-bonded compounds a correlation [3] has been drawn between their stability and the possibility of transition of electrons from the relatively high-energy filled d-orbitals into the lowest antibonding orbitals (here, the anti-bonding σ-orbitals) corresponding to the first step in the rupture of the metal-carbon bond. Thus, to get the most stable σ-organometallic compound, the energy of this transition, ΔE, should be maximized, and the best way to achieve this is to lower the energy of the d-nonbonding orbitals by combining them with π-type orbitals of low energy in suitable ligands (Fig. 1).

In the π-complexes, ΔE is increased by the interaction of the antibonding π-orbitals on the ligand and the nonbonding metal orbitals.

It can be seen that the σ-state will be destabilized with respect to the π-state on losing a ligand and a σ-π rearrangement can occur; the reverse will occur on addition of a ligand to a π-complex. In the latter case it has been pointed out that ligands with a large donor capacity increase the electron density on the metal thereby causing a rise in the energy of the d-orbitals. As a result, the π-group may also acquire a more negative charge, which leads to destabilization of the π-mode of bonding in favor of the σ-form. There may also be a relationship [4] between ligands effecting π-σ rearrangements and the *trans*-effect series [5].

The relative ease of the rearrangement can also be correlated in terms of the concept of "hard" and "soft" bases [6]. σ-Bonded organic groups are "harder" than corresponding π-bonded moieties because of the greater polarizability of the delocalized π-electron cloud compared with the localized σ-orbitals [7]. Thus "hardening" the metal will favor the σ-compound and "softening" it will favor the π-complex. "Hardening"

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[7] *J. O. Edwards* and *R. G. Pearson*, J. Amer. chem. Soc. *84*, 16 (1962).

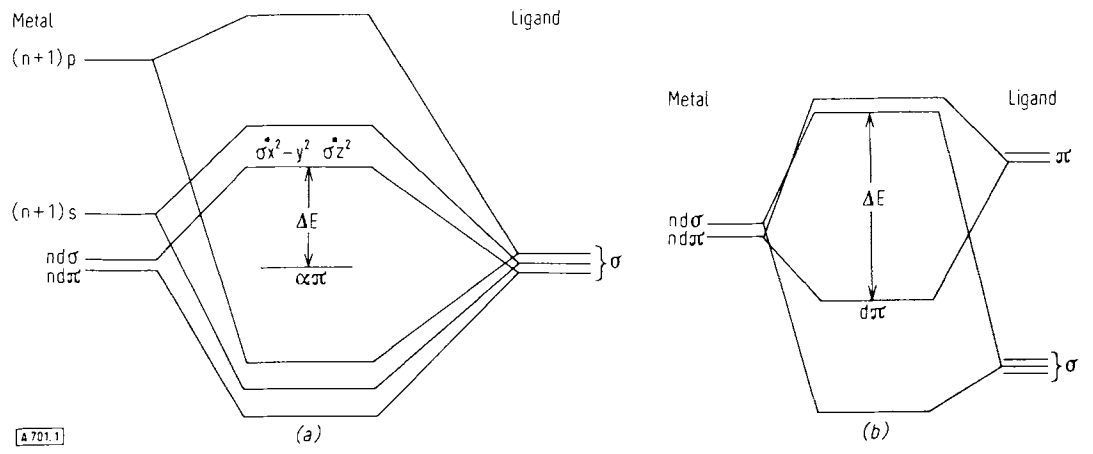


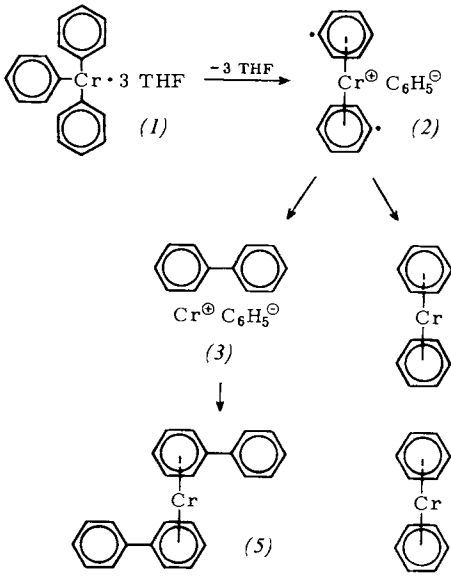
Fig. 1. Schematic representation of energy levels for organotransitionmetal compounds, a) without π-bonding, b) with π-bonding.

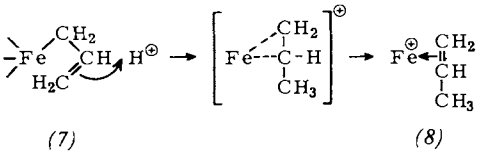
or "softening" the organic moiety can also initiate rearrangement.

Both approaches lead to the same conclusion, *i.e.* that addition of ligands which are strong π-bonders, *e.g.*, CO, CN^-, PR_3, dimethyl sulfoxide, will result in a π- to σ-rearrangement and removal of such ligands cause the reverse.

2. Mechanism of σ–π Rearrangements

The only mechanism which is well established is the rearrangement of σ-arylchromium compounds to π-arene complexes. Tri(σ-phenyl)chromium-3-tetrahydrofuran *(1)* at 60 °C, under high vacuum or on washing with ether, gives a black pyrophoric solid which on treatment with deoxygenated water gives the π-arene complexes, bis(biphenyl)chromium(0) *(5)* and benzene(biphenyl)chromium(0) *(6)*. The formation of radical intermediates (the black pyrophoric solid) *(2)*, *(3)*, and *(4)* has been proposed [9] and hydrolysis of these gives *Hein*'s π-complexes. The existence of a transition state involving π-radical hybridization has been postulated [10], the metal-carbon σ-bonds cleaving homolytically with a corresponding three-electron reduction of Cr^{III} to Cr^0. EPR investigations show homolytic fission of the chromium-carbon bond and possibly the formation of radical π-complexes [11]. π-radical formation, hydrogen abstraction, and hydrogen transfer all occur within the confines of the intermediate organochromium complexes [12, 13].





σ-Bonded allyl metal compounds *(7)* are readily protonated by hydrogen chloride or mineral acids to give π-allene complexes *(8)*. In the case of σ-allyliron compounds a bimolecular reaction is proposed; experiments with DCl show protonation to occur at C-3 [14].

2.1. Rearrangements Induced by Reactions on the Metal

As pointed out earlier (Section 1), groups capable of coordinating should be capable of inducing rearrangements by means of the *trans*-effect. However, only ligands high in the *trans*-effect series and able to participate in metal to ligand π-bonding can stabilize a σ-state or shift an equilibrium sufficiently towards the σ-compounds.

Tetrahydrofuran is a comparatively weak π-bonding ligand and stabilization of a σ-compound has only been reported with those organic groups which are themselves capable of π-bonding. The rearrangement of arylchromium compounds on losing tetrahydrofuran have already been discussed fully. When the σ-bonded ligand is a cyclopentadienyl group stabil-

[8] See, *e.g.*, *P. Cossee*, Recueil Trav. chim. Pays-Bas *85*, 1151 (1966).

[9] *W. Herwig* and *H. H. Zeiss*, J. Amer. chem. Soc. *81*, 4798 (1959).

[10] *M. Tsutsui*, Ann. New York Acad. Sci. *93*, 33 (1961).

[11] *P. Kasai*, *M. Tsutsui*, and *J. Ariyoshi*, unpublished results.

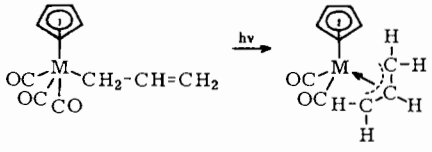
[12] *R. P. Sneeden*, *F. Glockling*, and *H. H. Zeiss*, J. organometallic Chem. *6*, 149 (1966).

[13] *M. Tsutsui* and *M. N. Levy*, Z. Naturforsch. *21b*, 823 (1966).

[14] *J. K. P. Ariyartine*, *M. L. H. Green*, and *P. L. I. Nagy*, Proc. chem. Soc. (London) *1963*, 107.

zation is reduced. Chlorobis(σ-cyclopentadienyl)iron(III)-tetrahydrofuran rearranges to the ferrocinium cation on losing the solvent ligand, this occurring above −50 °C, under vacuum at −60 °C, or on treatment with an organic solvent at −60 °C[15].

Diethyl ether has also been reported as a ligand in the alkali-metal salts of σ-bonded phenylchromate. Reactions of $Na_2[Cr(C_6H_5)_5(C_2H_5)_2O] \cdot 2\,(C_2H_5)_2O$ and $Li_3[Cr(C_6H_5)_6] \cdot 2.5\text{-}(C_2H_5)_2O$ with chromium trichloride 3-tetrahydrofuran in ether give black amorphous products which yied π-arene complexes on hydrolysis, the transformation taking place through σ-phenylchromium intermediates[16].

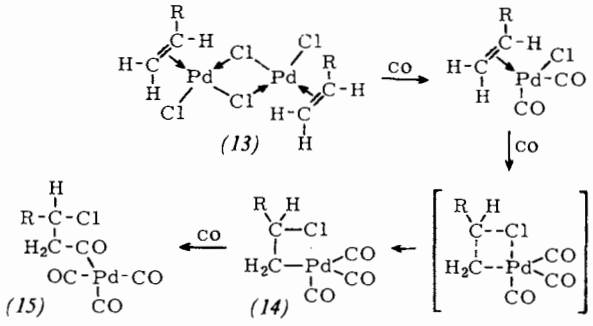


(9), M = Mo *(10)*, M = Mo
(11), M = W *(12)*, M = W

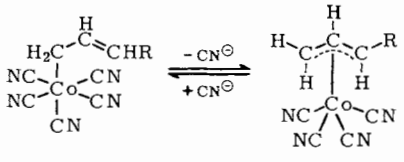
Loss of carbon monoxide from a σ-complex is induced by irradiation with ultraviolet light or by heating, and the reverse is achieved under a pressure of carbon monoxide. On irradiation with UV, the σ-allyltricarbonyl-π-cyclopentadienylmolybdenum[17] *(9)* and -tungsten[18] *(11)* give the π-allene complexes *(10)* and *(12)* with the loss of one molecule of carbon monoxide. On heating or irradiating with UV, tricarbonyl-π-cyclopentadienyl-σ-methylthiomethylmolybdenum rearranges with loss of carbon monoxide to give a π-complex, the structure of which could not be determined unambiguously[19]. The reaction between sodium tricarbonyl-π-cyclopentadienylmolybdate and benzyl chloride gives a σ-benzyl derivative. Irradiation in hexane gives, concurrent with loss of CO, a low yield of π-benzyl dicarbonyl-π-cyclopentadienylmolybdenum. The benzyl group is bonded through an allylic system involving three of the carbon atoms, and variable-temperature NMR measurements show that the molecule is stereochemically dynamic[20].

The reaction of allyl chloride with sodium (or lithium) pentacarbonylmanganate at room temperature gives σ-allylpentacarbonylmanganese which at 100 °C evolves one mol. equiv. of carbon monoxide leaving the π-allyltetracarbonylmanganese[21,22].

The reaction of π-olefinpalladium complexes such as *(13)* and carbon monoxide gives a β-chloroacylpalladium complex *(15)*. Initially, bridge cleavage takes place and on further carbonylation, rearrangement

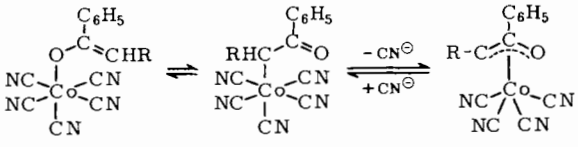


occurs to the σ-complex *(14)* followed by alkyl migration to give *(15)*[23].



(16) *(17)*

Because of the formal similarity of RNC, CN^-, and NO^+ to CO, compounds containing these groups might be expected to undergo similar rearrangements, but only rearrangements involving addition and abstraction of CN^- have been reported. The σ-bonded compound *(16)* loses a cyanide ion to give the π-bonded complex *(17)*, the rearrangement being reversed on addition of cyanide ion.



(18) *(19)*

Rearrangement of the phenacyl group has also been observed, although the π-complexes *(18)* and *(19)* were not obtained in a pure state[24].

Analogous σ-π structures have been proposed as determining the stereoselectivity of the butene products obtained in the pentacyanocobaltate(II)-catalyzed hydrogenation of butadiene. In the presence of an excess of cyanide ion, 1-butene is the major product derived exclusively from a σ-butenyl intermediate. *trans*-2-Butene is the main product in the absence of an excess of cyanide and may derive from either a π-butenyl complex or an isomeric σ-butenyl compound in equilibrium with π-structures[25].

In the presence of Lewis acids π-allylhalogenonickel compounds catalyze the dimerization of propylene; the structure of the catalyst can be varied by addition of phosphines, NMR studies showed that 1:1 and 1:2 derivatives of triphenylphosphine and triphenylphosphite contain a π-allyl group, but the 1:2 complex

[15] *M. Tsutsui, M. Hancock, J. Ariyoshi*, and *M. N. Levy*, J. Amer. chem. Soc., in press.

[16] *F. Hein* and *K. Schniedeknecht*, J. Organometallic Chem. *6*, 45 (1966).

[17] *M. L. H. Green* and *P. L. I. Nagy*, J. Chem. Soc. London, 189 *(1963)*.

[18] *M. L. H. Green* and *A. N. Stear*, J. organometallic Chem. *1*, 230 (1964).

[19] *R. B. King* and *M. B. Bisnette*, Inorg. Chem. *4*, 486 (1965).

[20] *R. B. King* and *A. Fronzaghia*, J. Amer. chem. Soc. *88*, 709 (1966).

[21] *W. R. McClellan, H. H. Hoehn, H. N. Crips, E. L. Muetterties*, and *B. W. Howk*, J. Amer. chem. Soc. *83*, 1601 (1961).

[22] *H. D. Kaesz, R. B. King*, and *F. G. A. Stone*, Z. Naturforsch. *15b*, 682 (1960).

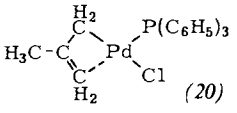
[23] *J. Tsuji, M. Morkawa*, and *J. Kiju*, J. Amer. chem. Soc. *86*, 485 (1964).

[24] *J. Kwiatek* and *J. K. Seyler*, J. organometallic Chem. *3*, 421 (1965).

[25] *J. Kwiatek, I. L. Mador*, and *J. K. Seyler*, Advances Chem. Ser. *37*, 201 (1963).

with triethylphosphine exists in a dynamic σ-bonded equilibrium whereas the 1:1 complex is π-bonded [26].

Considerable discussion on the nature of the stereochemically non-rigid allylmetal complexes has arisen from variable-temperature NMR measurements. Internal rotation [27,28] and σ-π rearrangements have been suggested for the palladium complexes. Allylchloropalladium is dimeric in the solid state [29] but in benzene and dioxane solution it is found from cryoscopic and dipole moment measurements that an equilibrium exists with about 75% dimer and 25% monomer [30]. NMR spectra of solutions of allylchloropalladium in dimethyl sulfoxide require that the allylic ligand be σ-bonded to the metal. Only one peak is found and a rapid equilibrium is therefore deduced between two equivalent σ-forms. The other coordination sites are probably occupied by one chloride and two dimethyl sulfoxide ligands [31]. During preparations of allylic palladium complexes, the same σ-π changes are noted [32].



(20)

Addition of triphenylphosphine to chloro-π-methallylpalladium (up to 2 moles $(C_6H_5)_3P$ per 1 g-atom Pd) has been followed by NMR. During reaction, changes observed in the spectrum indicate formation of a σ-allylic compound that undergoes a rapid exchange. The NMR spectrum of the product, chloromethallyltriphenylphosphinepalladium, suggest structure *(20)* with two carbons only weakly bonded to the palladium [33]. X-ray analysis of the compound supports the structure given in *(20)* [34]. NMR variable-temperature

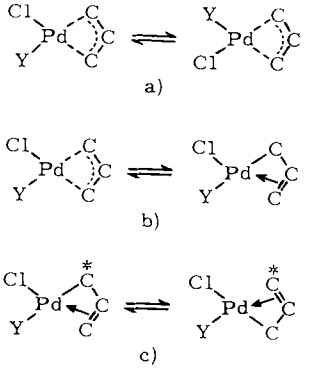
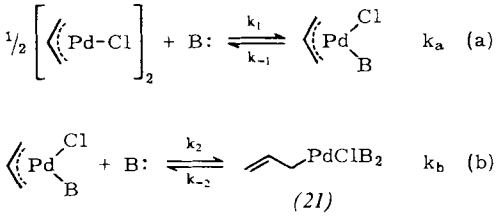


Fig. 2. Possible reactions of allylpalladium complexes (schematic): a) ligand exchange; b) π-σ equilibration; c) head-over-tail equilibration.

measurements from 25 °C to 65 °C suggest that allylchloropalladium in DMSO has a π-bonded structure in which hindered rotation of the CH_2 groups about the C–C bonds occurs at a rate dependent on the temperature [35]. The temperature dependence of the NMR spectra of a number of allylic complexes of palladium has been studied and the results explained by ligand exchange, followed by π- to σ-equilibration, which may then be followed by a head-over-tail equilibration [36].

Further work casts doubt upon the structure of the intermediate *(20)* proposed by *Shaw et al.* [33]. It is suggested from variable-temperature NMR studies on reactions between allylchloropalladium and the ligands $P(C_6H_5)_3$, $P(n\text{-}C_4H_9)_3$, 4-methyl-2,6,7,1-trioxaphosphabicyclo[2.2.2]octane, $As(C_6H_5)_3$, $Sb(C_6H_5)_3$ that an equilibrium is established even at low temperatures between σ- and π-bonded compound with the equilibrium being almost completely to the side of π-bonding. At higher temperatures, rotation of the π-allyl group is inferred for all ligands and at very high temperatures and high ligand to metal ratio, rapid formation of a σ-allyl group has to be postulated to explain the NMR spectra [37].

Temperature dependence studies of the NMR spectra recorded during reactions between π-allyl complexes and the ligands (B:) triphenylphosphine, dimethyl sulfoxide, and dimethyl sulfide show that σ-π rearrangements are occurring as in reactions (a) and (b). The disappearance of coordinated allyl and the appearance



(21)

of uncoordinated olefin absorptions in the infrared spectra demonstrate the formation of σ-bonded allyls, as in *(21)*. Equilibrium lies far to the right with $(C_6H_5)_3P$, but with DMSO and DMS it lies to the left [38].

The reaction between chloro-π-methylallylpalladium and triphenylarsine has also been studied by variable-temperature NMR. Three equilibria are occurring [eq. (c)–(e)]. In (e) two mechanisms are involved: between −70 °C and −40 °C triphenylarsine exchange is occurring and between +10 °C and +80 °C, ligand exchange occurs along with the formation of a σ-allyl compound or an activated state involving the σ-bonded compound [39].

$$\pi\text{-}C_4H_7PdCl(C_6H_5)_3As \rightleftharpoons \pi\text{-}C_4H_7PdCl + (C_6H_5)_3As \quad (c)$$

$$[\pi\text{-}C_4H_7PdCl]_2 + 2\,(C_6H_5)_3As \rightleftharpoons 2\,\pi\text{-}C_4H_7PdCl(C_6H_5)_3As \quad (d)$$

$$\pi\text{-}C_4H_7PdCl(C_6H_5)_3As + (C_6H_5)_3As^* \rightleftharpoons \pi\text{-}C_4H_7PdCl(C_6H_5)_3As^* + (C_6H_5)_3As \quad (e)$$

[26] *D. Walter* and *G. Wilke*, Angew. Chem. *78*, 941 (1966); Angew. Chem. internat. Edit. *5*, 897 (1966).

[27] *J. K. Becconsall* and *S. O'Brien*, Chem. Commun. *1966*, 302.

[28] *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).

[29] *A. E. Smith*, Acta crystallogr. *18*, 331 (1965); *W. E. Oberhansli*, and *L. F. Dahl*, J. organometallic Chem. *3*, 43 (1965).

[30] *I. I. Moiseev, E. A. Fedorovskaya*, and *Ya. K. Syrkin*, Ž. neorg. Chim. *4*, 2641 (1959), cited in ref. [31].

[31] *T. C. W. Chien* and *H. C. Diem*, Chem. and Ind. *1961*, 745.

[32] *R. Schultz*, Tetrahedron Letters *1964*, 301.

[33] *J. Powell, S. D. Robinson*, and *B. L. Shaw*, Chem. Commun. *1965*, 78.

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[35] *J. K. Becconsall* and *S. O'Brien*, Chem. Commun. *1966*, 302.

[36] *K. C. Ramey* and *G. L. Statton*, J. Amer. chem. Soc. *88*, 1327, 4387 (1966).

[37] *K. Vrieze, C. Maclean, P. Cossee*, and *C. W. Hilbers*, Recueil Trav. chim. Pays-Bas *85*, 1077 (1966).

[38] *F. A. Cotton, J. W. Faller*, and *A. Musco*, Inorg. Chem. *6*, 179 (1967).

[39] *K. Vrieze, P. Cossee, C. W. Hilbers*, and *A. P. Praat*, Recueil Trav. chim. Pays-Bas *86*, 769 (1967).

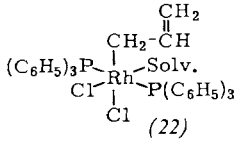
A study of NMR was carried out at 34 °C on aseries of complexes PdX(all)L where X = halogen, all = allylic ligand, and L = *tert.*-phosphine, triphenyl arsine, or triphenylstibine. As the ratio of L/Pd is varied from 0 to 2 several fast processes occur involving π-allylic to σ-allylic rearrangement, during which rotations about the C–C bond and Pd–C bond and exchange of coordinated ligand with free ligand occur. Carbon monoxide also coordinates to the palladium in $[PdClCH_2-C(CH_3)=CH_2]_2$ and the NMR spectrum in $CHCl_3$ corresponds to that of a dynamic σ-methallyl system [40].

A diastereoisomeric mixture is prepared in ethyl acetate by cleaving the chlorine bridge of dimeric 1-acetyl-2-methylallylchloropalladium with (*S*)-α-phenethylamine. Resolution is achieved by crystallizing the crude diastereoisomeric mixture from CCl_4. Optical-activity measurements performed on acetone solutions at very low and higher temperatures indicate that:

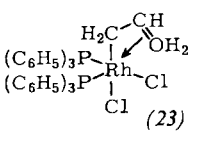
(a) Only one of the two diastereoisomers is quantitatively obtained in the CCl_4 crystallization through a "second-order asymmetric transformation"; (b) Epimerization of the pure (–)-diastereomer takes place very rapidly at temperatures above –20 °C.

The epimerization can only occur through a rotation around the C-2–C-3 bond, *i.e.* through a σ-bonded intermediate [41].

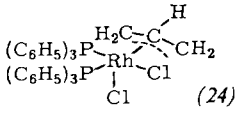
A similar rearrangement is reported for allylic platinum complexes on addition of triphenylphosphine. A variable-temperature study of the NMR spectrum indicates that σ-π equilibria are occurring [42]. Other studies on dichloro-π-methylallylbis(triphenylphosphine)rhodium or the triphenylarsine analog show that allyl interchange is occurring *via* a short lived σ-allyl intermediate [43].



(22)

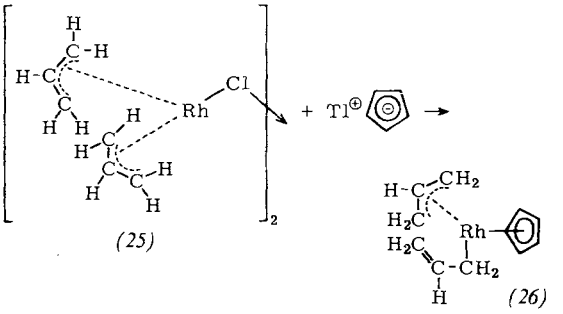


(23)



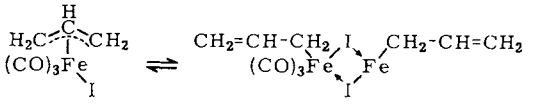
(24)

The reaction of chlorotris(triphenylphosphine)rhodium with allyl chloride at 25 °C produces yellow crystals. In solution, the NMR spectrum agrees with the σ-bonded structure *(22)* but an infrared spectrum taken in a mull shows no band attributable to an uncoordinated double bond so that in the solid state the structure may be *(23)*. On refluxing the yellow crystals, a π allylic compound *(24)* is obtained whose structure is assigned on the basis of spectral data [44].



(25) *(26)*

Cyclopentadienide ion would be expected to exhibit a similar effect to carbonyl and especially to cyanide ion in ability to cause a π-σ rearrangement [45]. Allyl chloride reacts with a methanolic solution of carbonylchlororhodium in the presence of a little water to give a compound with the structure *(25)*. On addition of thallium cyclopentadienide the complex *(26)* is obtained, the NMR spectra of which indicates that one allyl group is π-bonded and one is σ-bonded [46].



(27) *(28)*

All the ligands reported to affect π–σ or σ–π rearrangements show a strong *trans*-effect and it might be expected that iodide ion would show a similar although weaker effect [47]. The reaction between allyl iodide and pentacarbonyliron gives a compound with an empirical formula $C_3H_5Fe(CO)_3I$. No olefin stretching frequency is observed in the infrared and so the structure would be expected to be *(27)*. In cyclohexane, however, a considerable degree of dimerization is found and a complicated NMR is obtained which could not be interpreted on the basis of structure *(28)*. Four carbonyl stretching frequencies are also found in the infrared rather than the expected three. It is suggested that an equilibrium occurs between *(27)* and *(28)* in solution [48].

A suspension of carbonylchlorobis(π-cyclooctene)iridium undergoes an oxidative addition in allyl chloride to give a white solid π-allylcarbonyldichloro-π-cyclooctene iridium, which decomposes above 14 °C but when dissolved in chloroform-methanol gives the more stable dimer. NMR and IR spectra are very complex and it is suggested that the dimer has σ-allyl groups and bridging chlorine atoms. The π-methallyl complex does not dimerize and hence no rearrangement is observed [49].

2.2. Rearrangements Induced by Reactions on the Ligand

This case differs from that discussed in Section 2.1 in that the basic stereochemistry of the metal is not changed and the metal remains coordinatively satu-

[40] *J. Powell* and *B. L. Shaw*, J. chem. Soc. (London) *A 1967*, 1839.

[41] *P. Corradini*, *G. Maglio*, *A. Musco*, and *G. Paiaro*, Chem. Commun. *1966*, 618.

[42] *H. G. Volger* and *K. Vrieze*, J. organometallic Chem. *6*, 297 (1966).

[43] *H. C. Volger* and *K. Vrieze*, J. organometallic Chem. *9*, 537 (1967).

[44] *D. N. Lawson*, *J. A. Gibson*, and *G. Wilkinson*, J. chem. Soc. (London) *A 1966*, 1733.

[45] *R. S. G. Phillips* and *R. J. P. Williams*: Inorganic Chemistry. Oxford University Press, New York 1966, p. 339.

[46] *J. L. Powell* and *B. L. Shaw*, Chem. Commun. *1966*, 236.

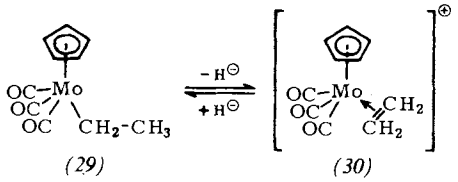
[47] See, e.g. *F. Cotton* and *B. Wilkinson*: Advanced Inorganic Chemistry. 2nd Edit., Interscience New York 1966, p. 176.

[48] *R. A. Plowman* and *F. G. A. Stone*, Z. Naturforsch. *17b*, 575 (1962).

[49] *B. L. Shaw* and *E. Singleton*, J. chem. Soc. (London) *A 1967*, 1683.

rated. Therefore any π-group formed will only be a two-electron donor: no delocalized π-systems are formed in the cases described below. The π-compounds, because the π-group is "softer" than te σ, will be the thermodynamically stable form but if the equilibrium is shifted chemically then one can stabilize the σ-compound.

Ethyltricarbonyl(π-cyclopentadienyl)molybdenum *(29)* on treatment with triphenylmethyl perchlorate yields the ethylene π-complex *(30)* while the abstraction is



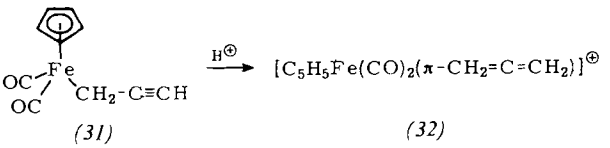
(29) *(30)*

reversed on treatment with $NaBH_4$ [50]. Small amounts of π-ethylenepentacarbonylmanganese tetrafluoroborate are obtained on treating ethylpentacarbonylmanganese with triphenylmethyl tetrafluoroborate. The reaction is also reversed on addition of $NaBH_4$ [51].

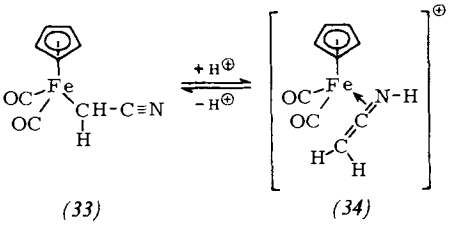
It is also found that when a σ-alkyl-dicarbonyl-π-cyclopentadienyliron compound (alkyl = ethyl, *n*-propyl, and isopropyl) is treated with a stoichiometric amount of triphenylmethyl perchlorate, a fast reaction occurs giving a good yield of the corresponding π-complex [52]. In the above case when the alkyl group is primary, the abstraction is found to be reversible, reduction of the π-complex with $NaBH_4$ giving the σ-alkyl [53].

Protonation of σ-allyl compounds gives the corresponding π-olefins [19, 54, 55]. Dilute mineral acids or hydrogen chloride effect these protonations and rearrangements, but in the case of σ-allylpentacarbonylmanganese it has been found that the π-allyl is only obtained when perchloric acid is employed. Cleavage of the σ compound to give $(CO)_5MnA$ occurs when A is Cl, NO_3, CF_3COO, or SO_4H [56].

Using this reaction several unusual π-bonded groups have been obtained. The σ-propargyliron compound *(31)* gives a hexachloroantimonate *(32)* in concentrated hydrochloric acid which gives acetone on hydrolysis. The formation of acetone indicates that there may be a π-allene system present in the cation [57]. The π-

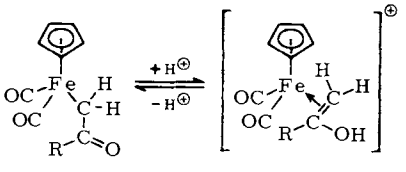


(31) *(32)*



(33) *(34)*

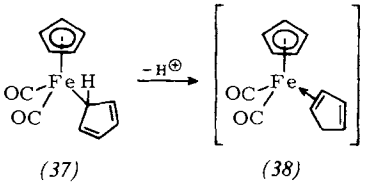
allene complex would be expected if the course of the protonation were similar to that of the isoelectronic compound *(33)*, which undergoes a reversible rearrangement to give a π-imine cation *(34)* [58]. Protonation of a σ-bonded α-ketone *(35)* "traps vinyl alcohol" in the rearranged product *(36)* [59]. Polyvinyl alcohol is becoming quite important industrially and thus this rearrangement could have considerable significance.



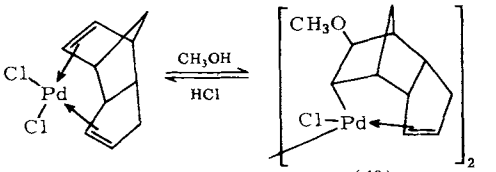
(35) *(36)*

Protonation of dicarbonyl-π-cyclopentadienyl-σ-cyclopentadienyliron *(37)* in concentrated hydrochloric acid gives a π-olefin complex *(38)* [60]; thus *(37)* shows the same behavior as the σ-bonded allyl compounds.

In recent years many complexes have been reported in which large ring diolefins are chelated to transition metals, particularly to platinum and palladium. These π-diolefin complexes undergo addition reactions to one double bond giving σ-bonded complexes. The



(37) *(38)*



(39) *(40)*

[50] *M. L. H. Green* and *M. Cousins*, J. chem. Soc. (London) *1963*, 889.

[51] *M. L. H. Green* and *P. L. I. Nagy*, J. organometallic Chem. *1*, 58 (1963).

[52] *M. L. H. Green* and *P. L. I. Nagy*, Proc. chem. Soc. (London) *1962*, 74.

[53] *M. L. H. Green* and *P. L. I. Nagy*, J. Amer. chem. Soc. *84*, 1310 (1962).

[54] *M. L. H. Green*, Proc. 7. Int. Conf. Coordinat. Chem., Stockholm 1962, p. 301.

[55] *M. L. H. Green* and *P. L. I. Nagy*, Proc. chem. Soc. (London) *1961*, 378.

[56] *M. L. H. Green, A. G. Massey, J. T. Moelwyn-Hughes*, and *P. L. I. Nagy*, J. organometallic Chem. *8*, 511 (1967).

[57] *J. K. P. Ariyartine* and *M. L. H. Green*, J. organometallic Chem. *1*, 90 (1963).

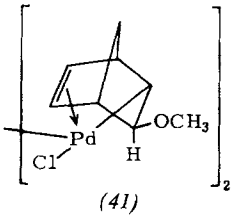
[58] *J. K. P. Ariyartine* and *M. L. H. Green*, J. chem. Soc. (London) *1963*, 2976.

[59] *J. K. P. Aiyartine* and *M. L. H. Green*, J. chem. Soc. (London) *1964*, 1.

[60] *M. L. H. Green* and *P. L. I. Nagy*, Z. Naturforsch. *18b*, 162 (1963).

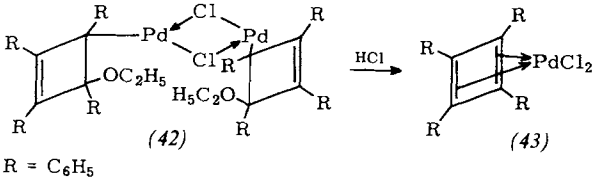
reaction of palladium dichloride with *endo*-dicyclopentadiene gives a monomeric π-complex *(39)*, which reacts with methoxide to give a dimeric σ-bonded compound[61] *(40)*. The reverse (elimination) is brought about by treatment with hydrochloric acid. 1,5-Cyclooctadiene reacts with sodium tetrachloropalladate(II) in methanol to give the π-complex, which then reacts with methanol in the presence of sodium bicarbonate to give a σ-bonded compound[62].

A similar reaction to that of the palladium complex *(39)* is reported for the analogous platinum complex, a reversible π-σ reaction occurring on treatment with methoxide or hydrochloric acid[63]. The reaction between π-dienemetal dihalides and an organic anion appears to be fairly general. It has been reported for cases with the diene being 1,5-cyclooctadiene, norbornadiene, 4-vinylcyclohexene, 1,5-hexadiene, dicyclopentadiene, and dipentene; rearrangements occurring with alcohols[64] in the presence of anhydrous sodium carbonate, acetate and propionate ions[65], diketones[66], and primary amines[67]. The reaction of methoxide ion with dichloro(norbornadiene)palladium proceeds *via* addition – as in all the above examples – to form the complex *(41)* in which the methoxy group has the *exo*-configuration, thus establishing that *trans* addition to the olefin has occurred[68].



(41)

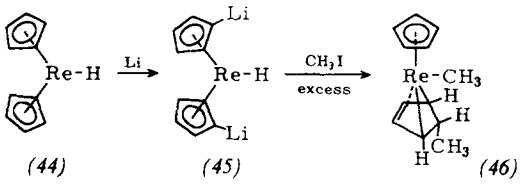
We can consider, in the above category, *Malatesta*'s synthesis of π-cyclobutadienepalladium complexes. The reaction between diphenylacetylene and alcoholic palladium chloride gives a σ-bonded compound *(42)* which reacts with hydrogen halides to give dichloro-(tetraphenylbutadiene)palladium *(43)*[69].



(42) *(43)*

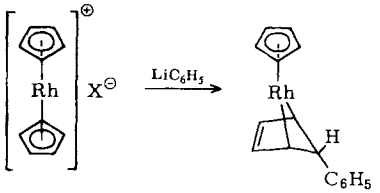
R = C_6H_5

It is also reported that the reaction of diphenylacetylene with palladium chloride in ethanol gives, *inter alia*, a compound $Pd(C_{28}H_{20}OC_2H_5)Cl$ assigned a structure with σ- and π-bonding. Refluxing this in an ethanol-hydrochloric acid (90:10) mixture again gives compound *(43)*[70].



(44) *(45)* *(46)*

π-Cyclopentadienyl rings appear to be resistant to rearrangement, although two reactions leading to σ-bonded compounds have been reported. Treatment of bis(π-cyclopentadienyl)hydridorhenium *(44)* with lithium gives the dilithium compound *(45)* which reacts with an excess of methyl iodide to form *(46)*, a compound in which the rhenium is σ-bonded to two carbon atoms and π-bonded to the ring double bond[71]. Compound *(47)* reacts similarly with phenyllithium to give a compound with the formula C_5H_5Rh-1-*exo*-$C_6H_5C_5H_5$. This compound is assigned the structure *(48)* on the basis of its NMR spectrum and



(47) *(48)*

its X-ray powder diffraction pattern, which showed that it is isomorphous with the corresponding cobalt compound, the structure of which had been elucidated by detailed X-ray analysis[72, 73].

2.3. Migration or Insertion Reactions

Migration reactions involve initially a coordinatively unsaturated organometallic compound, with one group σ-bonded. Coordination of a π-molecule occurs followed by rearrangement with the σ-group migrating to the olefin and then π-σ rearrangement of the olefin[8]. This mechanism is industrially important, being postulated for such processes as the polymerization of olefins (Ziegler-Natta catalysis) and the hydroformylation of olefins (Oxo process).

2.3.1. Olefin Polymerization

Ziegler and *Natta*[74, 75] found that a catalyst consisting of a transition metal halide, *e.g.*, $TiCl_4$, and a non-

[61] *J. K. Stille* and *R. A. Morgan*, J. Amer. chem. Soc. *88*, 5135 (1966).

[62] *R. A. Schultz*, J. organometallic Chem. *6*, 435 (1966).

[63] *F. Paiaro, A. Paninzi*, and *A. Direinzi*, Tetrahedron Letters *1966*, 3905.

[64] *J. Chatt, L. M. Vallerino*, and *L. M. Venanzi*, J. chem. Soc. (London) *1957*, 2496.

[65] *J. Tsuji* and *M. Takahashi*, J. Amer. chem. Soc. *87*, 3275 (1965).

[66] *B. F. T. Johnson, J. Lewis*, and *M. S. Subramanian*, Chem. Commun. *1966*, 117.

[67] *G. Paiaro, A. DeRenzi*, and *R. Palumbo*, Chem. Commun. *1967*, 1150.

[68] *M. Green* and *R. I. Hancock*, J. chem. Soc. (London) *A 1967*, 2054.

[69] *L. Malatesta, A. Santarella, L. M. Vallarino*, and *F. Zingales*, Angew. Chem. *72*, 34 (1960).

[70] *L. M. Vallarino* and *A. Santarella*, Gazz. chim. ital. *94*, 252 (1964).

[71] *R. L. Cooper, M. L. H. Green*, and *J. T. Moelwyn-Hughes*, J. organometallic Chem. *3*, 261 (1965).

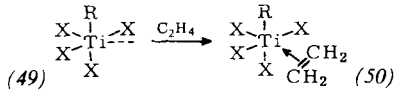
[72] *R. J. Angelici* and *E. O. Fischer*, J. Amer. chem. Soc. *85*, 3233 (1963).

[73] *M. R. Churchill* and *R. Mason*, Proc. chem. Soc. (London) *1963*, 112.

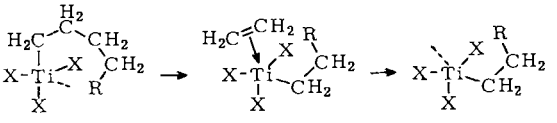
[74] *K. Ziegler, E. Holzkamp, H. Briel*, and *H. Martin*, Angew. Chem. *67*, 541 (1955).

[75] *G. Natta* and *I. Pasquoi*, Advances in Catalysis and Related Subjects *11*, 1 (1959).

transition metal alkyl, *e.g.*, $Al(C_2H_5)_3$ [76,77], readily causes polymerization of olefins. Propagation of the polymerization involves alkylation of the titatinum by the aluminum alkyl to give *(49)*. Formation of a π-



(49) *(50)*

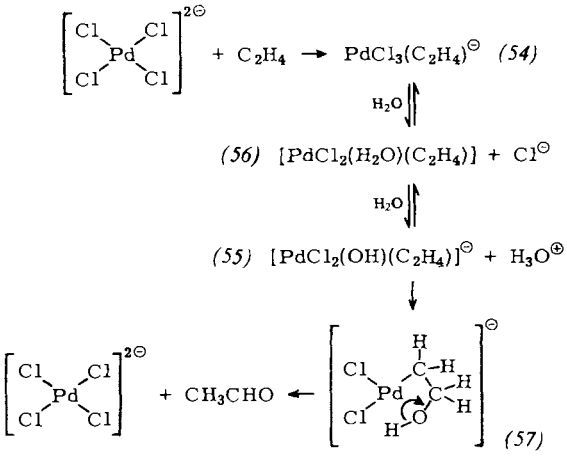


(51) *(52)* *(53)*

complex *(50)* between the olefin and the organotitanium compound *(49)* then occurs followed by "insertion" of the olefin into the titanium-carbon bond giving another σ-bonded compound *(53)*. This migration process leaves a vacant coordination site on the titanium which will act as an active center for the formation of another π-complex *(52)*. Again "insertion" occurs to give a σ-bonded compound with the growing polymer chain attached to either of two octahedral positions on the same metal atom [formula *(51)*].

2.3.2. Wacker Process

The oxidation of ethylene in aqueous solution to acetaldehyde using a palladium chloride-cupric chloride catalyst constitutes the Wacker process. The mechanism of the reaction is complicated but initially a π-olefin complex *(54)* is probably formed. Hydrolysis of the chloro complex occurs to give eventually the π-olefin hydroxy complex *(55)*. Subsequent migration of the coordinated OH^- group gives a σ-β-hydroxy compound *(57)*. This undergoes a hydride shift with rearrangement and elimination of acetaldehyde [78–81].



(54) *(56)* *(55)* *(57)*

[76] *E. O. Fischer*, Int. Conf. Coordinat. Chem., London 1959; Chem. Soc. Spec. Publ. *13*, 73 (1959).

[77] *J. C. W. Chien*, J. Amer. chem. Soc. *81*, 86 (1959).

[78] *J. Schmidt*, Chem. and Ind. *1962*, 54.

[79] *I. I. Mosseau, M. N. Worshafrig*, and *J. H. Sirkin*, Doklady Akad. Nauk SSSR *130*, 820 (1960); *133*, 377 (1960).

[80] *R. M. Henry*, J. Amer. chem. Soc. *86*, 3246 (1964).

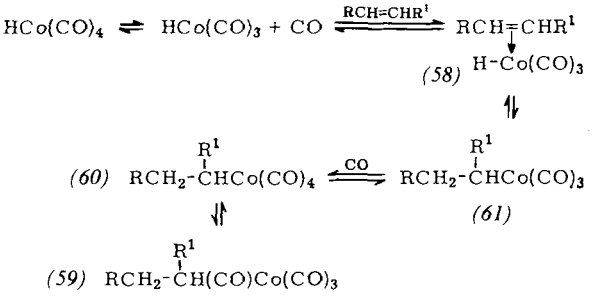
[81] *J. Halpern*, Proc. 3. Int. Congr. Catalysis, North-Holland Publ. Co., Amsterdam 1965, p. 146.

2.3.3. Oxo Reaction

The catalytic addition of hydrogen and carbon monoxide to olefins to give higher alcohols *via* the aldehyde (usually C_6–C_9) constitutes the important hydroformylation of the "oxo" process and has the overall stoichiometry.

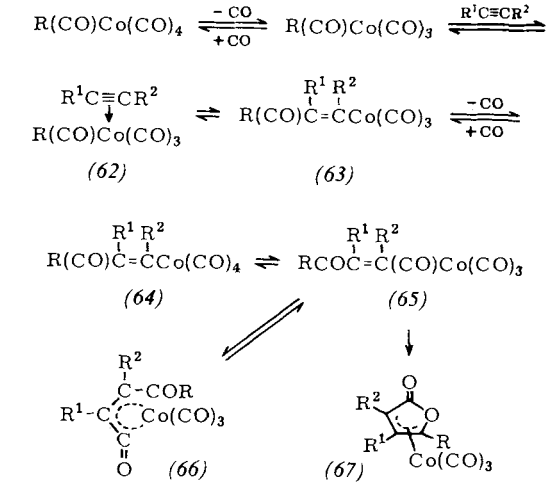
$$R\text{–}CH{=}CH_2 + CO + H_2 \rightarrow R\text{–}CH_2\text{–}CH_2\text{–}CHO$$

The reaction is usually carried out at high pressure and temperatures of 150 °C or above using a carbonylcobalt catalyst. Initially monomeric tetracarbon-



(58) *(60)* *(61)* *(59)*

ylhydridocobalt is formed, which loses carbon monoxide to give the tricarbonyl. Olefin addition occurs to give a π-complex *(58)*, which rearranges to the 5-complex *(61)*. Addition of CO to *(61)* gives *(60)*, which rearranges to *(59)* [82,83]. The complex *(60)* was isolated as the triphenylphosphine derivative.



(62) *(63)* *(64)* *(65)* *(66)* *(67)*

Closely allied to the hydroformylation of olefins is the reaction of acetylenes with acylcarbonylcobalt complexes. Formation of a π-complex *(62)*, is followed by rearrangement to the σ-compound *(63)*. Finally the π-allyl systems *(66)* and *(67)* are formed *via* the intermediates *(64)* and *(65)* [84].

A similar σ-π rearrangement is postulated for the thermal decomposition of alkenoyltetracarbonylcobalt *(68)* in solution [85]. In dilute etheral solution *(68)* decomposes to give several products, including a π-allyltricarbonylcobalt *(70)*, a

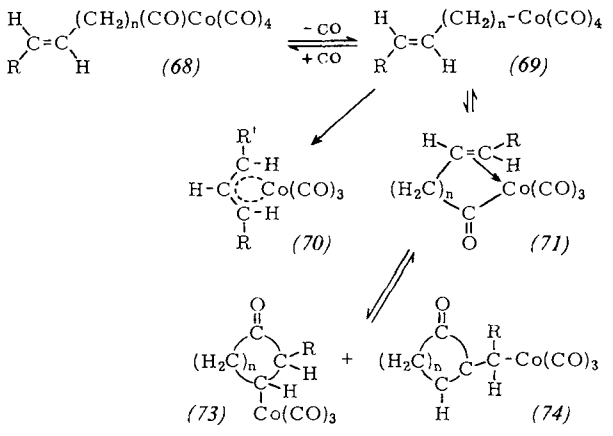
[82] *R. F. Heck* and *D. S. Breslow*, Chem. and Ind. *1960*, 467.

[83] *R. F. Heck* and *D. S. Breslow*, J. Amer. chem. Soc. *83*, 4023 (1961).

[84] *R. F. Heck*, J. Amer. chem. Soc. *86*, 2819 (1964).

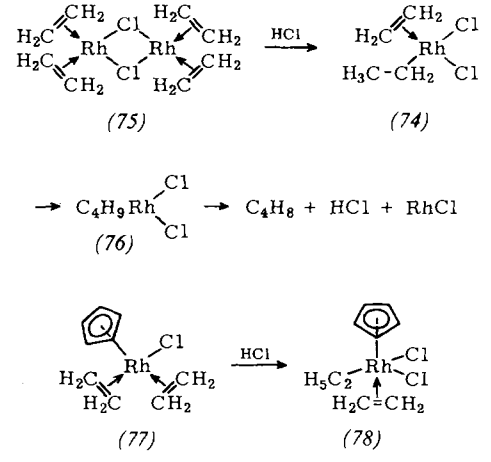
[85] *R. F. Heck*, J. Amer. chem. Soc. *87*, 4117 (1965).

π-alkenoyl tricarbonylcobalt *(71)*, and the σ-bonded complexes *(72)* and *(73)*. A σ-bonded tetracarbonyl *(69)* is postulated as forming initially[86].

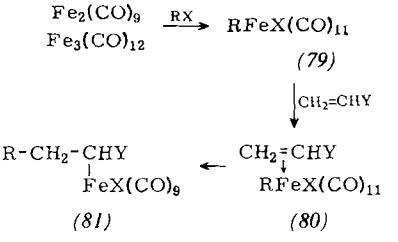


In favorable cases, the hydrogenation of olefins may be achieved through a π-σ-rearrangement by hydrogen transfer from a transitory hydridotransition metal complex. The homogeneous catalytic hydrogenation of fumaric acid in aqueous solution with ruthenium(II) chloride as catalyst proceeds *via* formation of a π-olefinhydridoruthenium-complex with subsequent insertion of the olefin into the metal-hydride bond giving a σ-alkyl compound. The hydrogenation is completed by an electrophilic attack on the metal-bonded carbon atom by a proton[87].

Hydration of unsaturated compounds catalyzed by transition metal complexes appears also to proceed *via* a π-σ mechanism. The catalytic hydration of acetylenic compounds by ruthenium(III) chloride involves the formation of an intermediate π-complex of the hydrated ruthenium compound followed by insertion of the acetylene across the metal-oxygen bond to give the σ-bonded compound, which then rearranges to give ruthenium(III) chloride and a ketone[88].

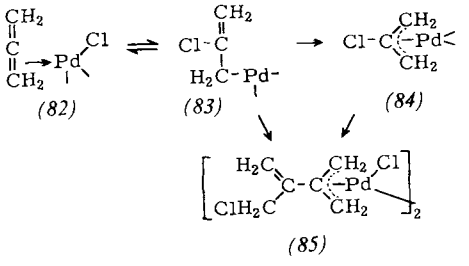


Studies on the rhodium-catalyzed dimerization of ethylene to linear butenes indicate (from NMR studies below −10 °C) that a σ-ethyl-π-ethylene compound *(74)* is formed by reaction of hydrogen chloride with the π-complex *(75)*. Ethyl migration then occurs to give the butyldichlororhodium *(76)* which collapses to give butene and Rh^I. Compound *(77)* reacts with hydrogen chloride to give σ-ethyl-π-ethylenedichlororhodium *(78)*[89].

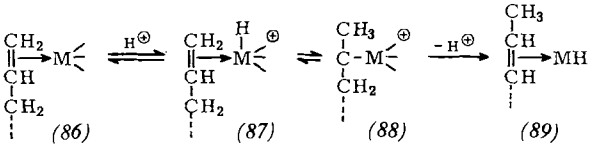


The reaction of olefins with nonacarbonyldiiron or dodecacarbonyltriiron in the presence of organic halides gives initially a σ-compound *(79)*. Olefin addition then occurs to give the π-complex *(80)* followed by alkyl migration with the formation of another σ-compound *(81)*[90].

A σ-π insertion rearrangement is proposed to explain the formation of the π-complex *(85)* when allene is bubbled into a methanolic solution of sodium chloropalladite, or its formation, together with chlorobis(π-2-chloroallyl)palladium *(84)*, on passing allene into a benzene solution of bis(benzonitrile)dichloropalladium. A π-σ-π mechanism involving intermediates *(82)* and *(83)* is proposed to explain the formation of these compounds[91].



Double bond migration in olefins is catalyzed by a wide variety of Group VIII transition metal complexes and in many cases has been shown to involve formation of π-olefin complexes, such as *(86)*, which can be protonated to metal hydride intermediates *(87)*. Addition of M–H to the olefin double bond then occurs to give a σ-bonded alkyl metal compound *(88)*, and finally rearrangement to the isomeric olefin and the metal hydride *(89)*. With normal olefins the isomerization is catalyzed by, for example, hydrated rhodium trichloride, bis(benzonitrile)dichloropalladium, and rhodium heptanoate[92]. Using deuterated olefins, it



is found that the mechanism involved in this isomerization varies with the metal. With rhodium(III) compounds, the rearrangement proceeds *via* the π-olefin

[86] *R. F. Heck*, J. Amer. chem. Soc. *85*, 3115 (1963).

[87] *J. Halpern, J. F. Harrold*, and *B. R. James*, J. Amer. chem. Soc. *88*, 5150 (1966).

[88] *J. Halpern, B. R. James*, and *A. L. Kemp*, J. Amer. chem. Soc. *83*, 4097 (1961).

[89] *R. Cramer*, J. Amer. chem. Soc. *87*, 4717 (1965).

[90] *I. Rhee, M. Ryang*, and *S. Tsutsumi*, J. organometallic Chem. (Amsterdam) *9*, 361 (1967).

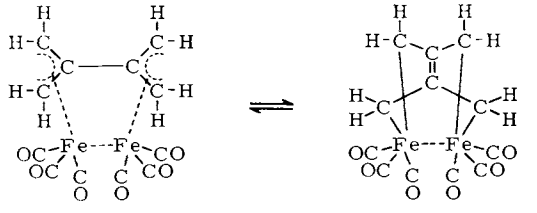
[91] *M. S. Lupin, J. Powell*, and *B. L. Shaw*, J. chem. Soc. (London) *A 1966*, 1687.

[92] *J. H. Harrold* and *A. J. Chalk*, J. Amer. chem. Soc. *86*, 1776 (1964).

to the σ-alkyl compound, but for the corresponding palladium-catalyzed reaction the rearrangement appears to go through a π-allyl intermediate [93].

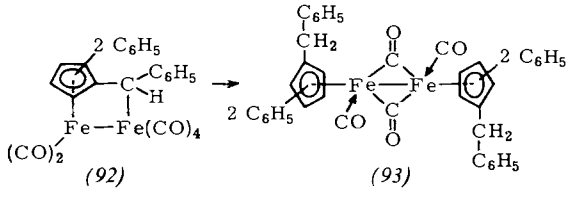
2.4. Other Rearrangements

Dicarbonyl(π-cyclopentadienyl)(σ-cyclopentadienyl)-iron *(37)* not only undergoes rearrangement on protonation but is thermally unstable, giving ferrocene and tetracarbonylbis(π-cyclopentadienyl)iron [94]. *(37)* is a member [95] of the rapidly growing group of compounds (including the allyl compounds discussed previously) that are stereochemically dynamic.



(90) *(91)*

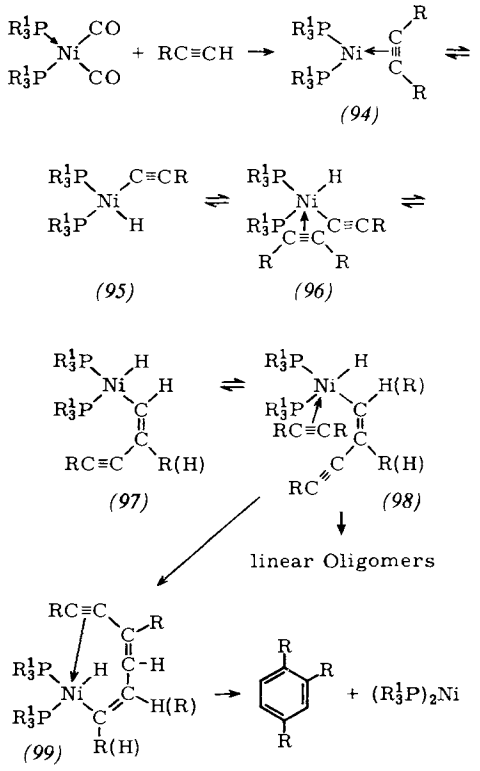
The π-bonded complex *(90)* is found to be in equilibrium with the σ-compound, even at −10 °C in solution [96]. The reaction of phenylacetylene with dodecacarbonyltriiron gives, in addition to other products, a π-bonded compound *(92)* which rearranges to the π-complex *(93)* [97].



(92) *(93)*

Vinylcyclopropanes bearing *para*-substituted phenyl groups react with iron pentacarbonyl to yield π-complexes in which the cyclopropane ring has opened. The mechanism proposed involves formation of π- and σ-bonded intermediates [98].

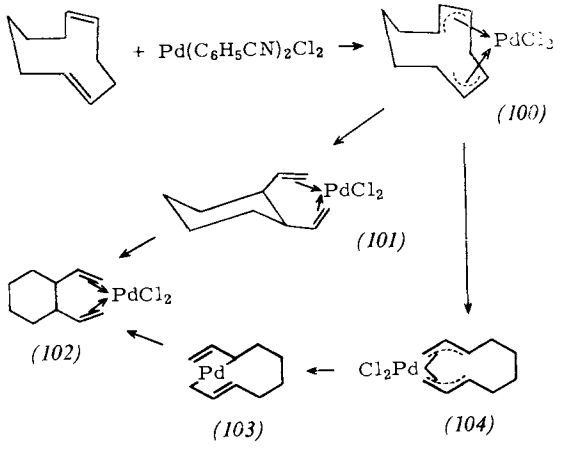
In 1940 *Reppe* and *Schweckendick* found that carbonylphosphinenickel compounds catalyze the trimerization of acetylenes to aromatic compounds [99]. Later researchers have shown that linear oligomers of monosubstituted acetylenes are also formed [100]. Initial formation of a π-complex *(94)* is postulated and this undergoes oxidative addition to give a σ-compound *(95)*. Compound *(95)* reacts with more acetylene to



(94) *(95)* *(96)* *(97)* *(98)* *(99)*

linear Oligomers

form *(96)* and this π-complex undergoes a migration to give *(97)*. Repetition of this step [*(98)*, *(99)*] and subsequent ring closure lead to the benzene derivative. The linear oligomers are formed from *(98)*.



(100) *(101)* *(102)* *(103)* *(104)*

Cope arrangements can occur on thermal excitation. photolysis, and by reaction with metal compounds. A σ-π mechanism has been proposed for the metal-induced rearrangement. The reaction of bis(benzonitrile)dichloropalladium with *cis,trans*-1,5-cyclodecadiene gives a palladium complex *(102)* of 1,2-divinylcyclohexane. Initially, a π-allylic-complex *(100)* is postulated, the ring then opening to complex *(104)* or *(101)*. Rearrangement of *(104)* proceeds *via (103)* to give *(102)*, whereas *(101)* gives *(102)* directly [101].

A Cope rearrangement of *cis*-1,2-divinylcyclobutane catalyzed by nickel complexes with tri(2-biphenyl)-phosphite, triphenylphosphine, and tricyclohexyl-

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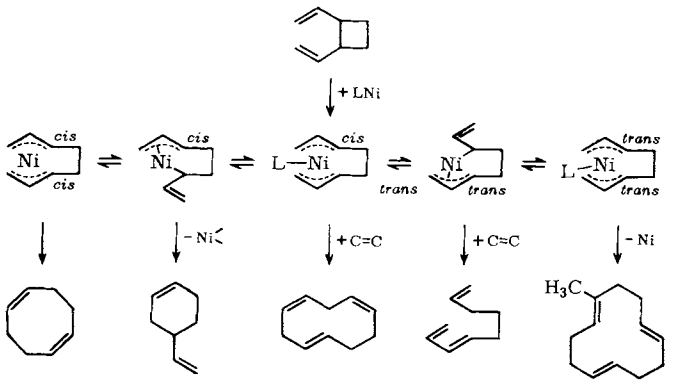
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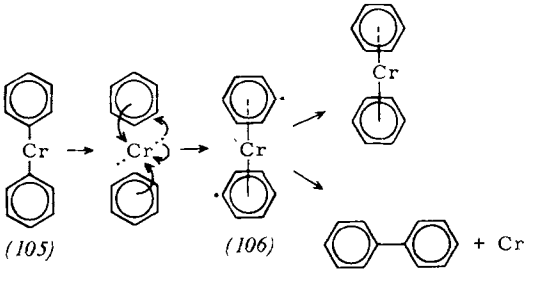
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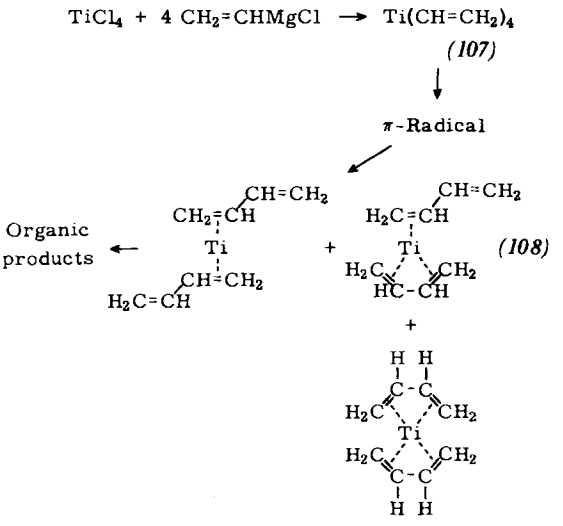
phosphine is reported to go *via* a σ-π rearrangement [102].

Coupling reactions between Grignard reagents and various substrates are catalyzed by polyvalent transition metal salts in stoichiometric amounts or in traces. These free radical processes are characterized by dimerization of the radical from the organic halide. Such reactions have long been a mechanistic source of debate [103, 104] but with the elucidation of the structures of *Hein*'s complexes [1, 2] came the realization that coupling probably goes *via* a σ-π rearrangement and π-radical hybridization.



(105) *(106)*

In 1914, *Bennett* and *Turner* [105] obtained biphenyl, instead of the expected triphenylchromium, in good yield from the reaction of phenyl magnesium chloride with chromic chloride. It is now known that the σ-bonded compound *(105)* is initially formed but the chromium-carbon bond cleaves homolytically to give the π-radical complex *(106)* [106] which then, under the rigorous conditions used, couples to give biphenyl and chromium. Under milder conditions, as used by *Hein*, *(106)* gives dibenzenechromium(0) by hydrolysis [105, 106]. (Chromium(II) is shown rather than chromium(III) for simplicity.)



(107) *(108)*

cis- or *trans*-α-Phenyl-α-styrylmagnesium bromide reacts with chromium(III) chloride or cobalt(II) chloride to give *cis,cis*-1,2,3,4-tetraphenylbutadiene, but the reaction with nickel(II) bromide or palladium(II) chloride gives the *trans,trans* isomer, *i.e. cis*-coupling occurs with those transitional metal complexes that normally have an octahedral (d^2sp^3 hybridization) configuration, while *trans* coupling occurs with those that normally take a square planar form [107].

Double coupling occurs during the reaction of vinylmagnesium bromide with titanium tetrachloride yielding four organic compounds: 4-vinyl-1-cyclohexene, 2,6-octadiene, 3-methyl-1,5-heptadiene, and 3-methyl-1,4,6-heptatriene. Initially, σ-bonded tetravinyltitanium *(107)* is probably formed which yields the observed products *via* a π-radical complex and several π-bonded intermediates [108].

Corresponding to the stoichiometric coupling reaction of vinyl groups on titanium outlined above is the catalytic coupling of vinylmagnesium chloride by titanium tetrachloride in the presence of bromoethane, the reaction products being 3-methyl-1,5-heptadiene and 3-methyl-1,4,6-heptatriene. The mechanism proposed [108] again involves initial formation of σ-tetravinyltitanium which undergoes radical hybridization and coupling. Activated titanium is formed which reacts with the bromoethane to give ethyl radicals and titanium tetrabromide which re-enters the reaction cycle.

Our research mentioned in this article was supported by the Air Force Office of Scientific Research, AF-AFOSR 824-67. We thank Dr. K. Suzuki, Dr. H. Gysling, Dr. R. Velapoldi, E. Manda, and *M. Haya for helpful discussions and assistance.*

Received: May 14 1968 [A 701 IE]
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Phosphorus Isocyanates

By G. I. Derkatsch[*]

Compounds containing the PNCO grouping can be obtained e.g. from phosphorus halides and silver cyanate or esters of N-chloroiminocarbonic acid and by thermal decomposition of alkoxycarbonylimino-phosphoranes. The phosphorus(v) isocyanates resemble the "carbon" isocyanates in their chemical properties, whereas the phosphorus(III) isocyanates resemble the phosphorus(III) chlorides. Some of the compounds discussed have insecticidal or cytostatic actions.

Aryl, alkyl, and acyl isocyanates have been known for more than a century, and have been very extensively studied. On the other hand, compounds in which the NCO groups are bound to an element other than carbon (P, As, Si, Sn, B, *etc.*) have only recently been prepared.

The first phosphorus isocyanates were actually obtained as early as 1940, but until 1954 the substances in this class were difficult to prepare, and practically no investigations had been carried out on them. The rapid development of this field began only with the discovery of simpler and more convenient methods of preparation.

Phosphorus isocyanates are used, *inter alia*, for the preparation of phosphorylated urethanes and ureas. Some of them are physiologically very active, and have found practical use as insecticides and drugs (see Section 4).

The following types are known at present:

Phosphorus(III) isocyanates: X_2PNCO and $XP(NCO)_2$ with X = Hal, alkoxy, aryloxy, alkyl, and aryl; also $P(NCO)_3$ and $P_2(NCO)_4$.

Phosphorus(v) isocyanates: $X^1X^2P(O)NCO$ with $X^1 = X^2$ = Hal, alkyl, aryl, alkoxy, aryloxy, dialkylamino, diarylamino; X^1 = Hal, X^2 = alkoxy, aryloxy, alkyl, or aryl; X^1 = alkyl or aryl, X^2 = alkoxy, aryloxy, dialkylamino, diarylamino; $XP(O)(NCO)_2$ with X = Hal, alkoxy, aryloxy, alkyl, aryl; $(RO)_2P(X)NCO$ with R = alkyl or aryl, X = S, NCOR; also $P(O)(NCO)_3$, $P(S)(NCO)_3$, and $P_3N_3Cl_4(NH_2)NCO$ (2-amino-2,4,6,6-tetrachloro-4-isocyanato-1,3,5-triaza-2,4,6-triphospha^{V}cyclohexane).

The phosphorus isocyanates are very reactive, and they can be prepared from readily obtainable starting materials. Alcohols, phenols, amines, and other substances containing active hydrogen atoms add readily to the NCO group in these compounds. In some cases the NCO group reacts as a pseudohalogen, and can be replaced as a unit by other groups. Phosphorus isocyanates in which halogen atoms are also attached to the phosphorus atom can react at two points in the molecule.

1. Preparation of Phosphorus Isocyanates

1.1. Reaction of Cyanic Acid and its Salts with Phosphorus Halides

Alkyl and acyl isocyanates were until recently obtainable only from halogeno-alkanes or acyl halides and metal cyanates[1,2]. More convenient preparation methods were proposed only during the last few years[3–6], and the first phosphorus(III) isocyanates were prepared by a reaction based on the old method, *i.e.* from phosphorus halides and silver cyanate. *Anderson* and *Forbers*[7] showed that phosphorus triisocyanate is formed on reaction of silver cyanate with phosphorus trichloride in boiling benzene:

$$PCl_3 + 3\,AgOCN \rightarrow P(NCO)_3 + 3\,AgCl$$

This compound is also formed from silver cyanate and phosphorus triiodide in nitromethane[8,9].

When silver cyanate is slowly introduced into an excess of phosphorus trichloride Cl_2PNCO and $ClP(NCO)_2$ are obtained[10]. Cl_2PNCO can also be prepared by heating a mixture of phosphorus trichloride and phosphorus triisocyanate vapors[11]. Alkyl- and aryldichlorophosphines[12–14] and methyldibromophosphine[15] react similarly:

$$RPCl_2 + 2\,AgOCN \rightarrow RP(NCO)_2 + 2\,AgCl$$

Phosphorus(III) isocyanates (such as phosphorus triisocyanate) have recently been obtained from phos-

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phorus chlorides and potassium, sodium, and lithium cyanates in benzene or sulfur dioxide [16–19].

The action of silver cyanate on phosphoryl or thiophosphoryl trichloride yields mixtures of phosphoryl triisocyanate and phosphoryl tricyanate or the corresponding thio compounds.

$$POCl_3 + 3\,AgOCN \rightarrow PO(NCO)_3 + PO(OCN)_3 + 3\,AgCl$$

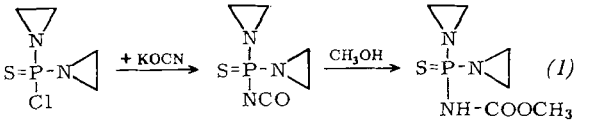
The liquid isocyanates can be separated very readily from the solid cyanates by distillation [20, 21].

Alkyl- and arylphosphonic dichlorides react with silver cyanate to give only isocyanates [12, 22, 23]:

$$RPOCl_2 + 2\,AgOCN \rightarrow RPO(NCO)_2 + 2\,AgCl$$

Isocyanates can similarly be obtained from diphenylphosphinic chloride [24, 25] and tetraiodobiphosphine [26], whereas the reactions of $RO(CH_3)P(O)Cl$ [27], $ROP(O)ClF$ [28], and $RP(O)ClF$ [29] with NaOCN lead only to replacement of the chlorine atoms by the isocyanate group.

Potassium cyanate reacts with bis(aziridin-1-yl)thiophosphoryl chloride in methanol to form methyl *N*-[bis(aziridin-1-yl)-phosphoryl]-carbamate *(1)*. An isocyanate is probably formed as an intermediate. Compound *(1)* is very unstable, and readily forms polymers in the presence of water [30].



(1)

In the presence of triethylamine or pyridine alkoxydichlorophosphines react very readily with cyanic acid to form alkoxydicyanatophosphines in yields of about 50 to 60 %.

$$AlkOPCl_2 + 2\,HNCO \xrightarrow{2\,(C_2H_5)_3N} AlkOP(NCO)_2 + 2\,(C_2H_5)_3NHCl$$

Phosphoryl chlorides give only polymers on reaction with cyanic acid, and in many cases do not react at all [5].

1.2. Reaction of Difluorophosphoric Anhydride with Potassium Cyanate

Difluorophosphoric anhydride reacts with potassium cyanate to form phosphoryl difluoride isocyanate:

$$(F_2PO)_2O + KOCN \rightarrow F_2P(O)NCO + K(PO_2F_2)$$

After filtration of the reaction mixture, the product can be distilled off under normal pressure (yield 50 to 55 %) [31].

1.3. Thermal Decomposition of Alkoxycarbonyliminophosphoranes

Kirsanov found in 1955 that phosphorus pentachloride reacts very readily with alkyl carbamates. The reaction yields alkoxycarbonyliminotrichlorophosphoranes, which lose alkyl chloride when heated to form phosphoryl dichloride isocyanate [32–37]:

$$AlkOCONH_2 + PCl_5 \rightarrow 2\,HCl + AlkOCON{=}PCl_3 \rightarrow Cl_2P(O)NCO + AlkCl$$

The decomposition of the methyl and ethyl compounds begins at 21–25 °C, and proceeds to completion at 65–70 °C. The mixture must be heated very slowly since the reaction is strongly exothermic and much gas is evolved so that explosions may occur if heating is fast. The higher the molecular weight of the alkyl groups, the more stable are the phosphoranes and the less vigorous their decomposition. The methyl and ethyl compounds are the most suitable for the preparation of phosphoryl dichloride isocyanate. The intermediate of the reaction, which proceeds almost quantitatively, need not be separated [32, 34, 36].

The reaction of methyl carbamate with alkyl and aryltetrachlorophosphoranes such as CCl_3PCl_4, CH_3PCl_4, and $C_6H_5PCl_4$ yields mixtures of phosphonic chloride isocyanates and phosphonic dichlorides [38, 39].

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All chlorophosphazo compounds $AlkOCON{=}PX_2Cl$ with at least one chlorine atom attached to the phosphorus can decompose as follows [38–45]:

$$AlkOCON{=}PX_2Cl \rightarrow X_2P(O)NCO + AlkCl$$
(X = Alk, Ar, ArO, Cl, *etc.*)

However, unlike the trichlorophosphorane derivatives $AlkOCON{=}PCl_3$, the monochloro and dichloro compounds are obtained only in low yields or not at all by the Kirsanov reaction. In 1963 we found a new general and convenient method for the preparation of similar compounds [40–45], *i.e.* the reaction of *N*-chloroiminocarbonates with phosphorus(III) halides.

$$(AlkO)_2C{=}NCl + X_2PCl \rightarrow [(AlkO)_2C{=}NPX_2Cl]^{\oplus}Cl^{\ominus} \rightarrow AlkCl + AlkOCON{=}PX_2Cl \rightarrow X_2P(O)NCO + AlkCl$$

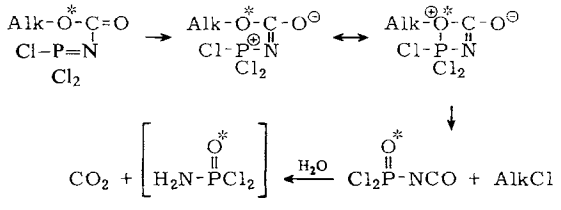
The intermediates need not be isolated.

This method is not suitable for the preparation of alkylphosphonic chloride isocyanates Alk(Cl)P(O)NCO, since the decomposition of the phosphorane proceeds in two directions simultaneously:

$$C_2H_5OCON{=}P(Alk)Cl_2 \rightarrow \begin{cases} AlkP(O)Cl_2 + (C_2H_5OCN)_n \\ Cl(Alk)P(O)NCO + C_2H_5Cl \end{cases}$$

The products can be separated only with great difficulty by distillation [45].

Phosphoryl dichloride isocyanate, $Cl_2P(O)NCO$, is obtained only in low yields from diethyl *N*-chloroiminocarbonate; the main product is a polymer of unknown structure [46].



The thermal decomposition of alkoxycarbonyliminotrichlorophosphoranes has also been studied with the aid of compounds labeled with ^{18}O [32, 33, 42, 47].

1.4. Thermal Decomposition of Alkyl Phosphorylcarbamates

Alkyl dialkoxy- or diaryloxyphosphorylcarbamates can be converted into phosphorus(v) isocyanates by heating to eliminate alcohol [48–50], the products in this case being diesters of isocyanatophosphoric acid. Since the reaction

$$(RO)_2P(O)NHCOOAlk \rightleftharpoons (RO)_2P(O)NCO + AlkOH$$

is reversible, the alcohol must be removed.

Several phosphorus(v) isocyanates can be prepared in good yields from the readily obtainable phosphoryl dichloride isocyanates (*via* the carbamates):

$$AlkOCONHP(S)(OR)_2 \rightarrow (RO)_2P(S)NCO + AlkOH \quad [51]$$

$$AlkOCONHP(O)[N(C_2H_5)_2]_2 \rightarrow [(C_2H_5)_2N]_2P(O)NCO + AlkOH \quad [45, 52]$$

$$AlkPO(NHCOOAlk)_2 \rightarrow AlkP(O)(NCO)_2 + 2\,AlkOH \quad [53]$$

1.5. Action of Oxalyl Chloride on Phosphoric Ester Amides

Carbonamides and sulfonamides react with oxalyl chloride to form acyl and sulfonyl isocyanates [2–4]. We found in 1965 that phosphoric and thiophosphoric diester amides react in a similar manner with oxalyl chloride to form diesters of isocyanatophosphoric and isocyanatothiophosphoric acids, frequently together with small quantities of phosphorylated oxalic amides:

$$(RO)_2P(X)NH_2 + (COCl)_2 \rightarrow (RO)_2P(X)NCO + 2\,HCl + CO \quad (X = O, S)$$

In the reaction of oxalyl chloride with diaryl phosphoramidates, it is possible to isolate the intermediate *(2)*:

$$(ArO)_2P(O)NH_2 + (COCl)_2 \rightarrow HCl + \underset{(2)}{(ArO)_2P(O)NHCOCOCl} \rightarrow HCl + CO + (ArO)_2P(O)NCO$$

Very reactive and thermally unstable *N*-phosphoryloxalamide chlorides probably also occur in the other cases. Depending on the substituents on the phosphorus atom, they decompose completely into phosphorus isocyanates or undergo partial reaction with the starting compound to form *N,N*-diphosphoryloxamides *(3)*.

Phosphorus(v) isocyanates can be prepared very conveniently by this method in yields of up to 70 to 80 % [54,55].

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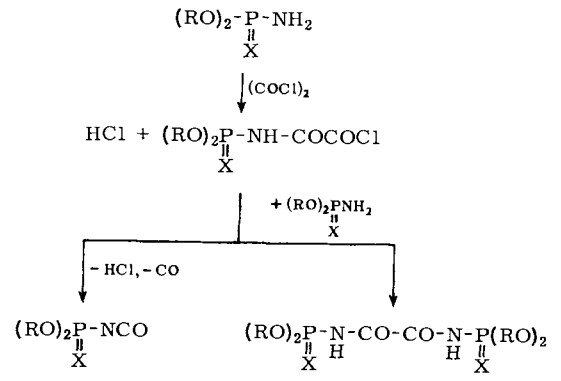
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[54] *L. I. Samaray* and *G. I. Derkatsch*, Ž. obšč. *35*, 755 (1965).

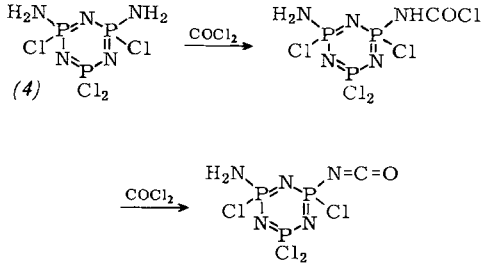
[55] *L. I. Samaray* and *G. I. Derkatsch*, Ž. obšč. Chim. *36*, 1433 (1966).



X = O, S
R = Alkyl, Aryl

(3)

The cyclotriphosphazene derivative *(4)* also reacts similarly with phosgene[56].



1.6. Other Syntheses of Phosphorus(v) Isocyanates

Alkyl and aryl isothiocyanates react very readily with mercuric oxide or silver oxide to form alkyl and aryl isocyanates[1,57]. The phosphorus(v) isothiocyanates, on the other hand, decompose under these conditions to give mercury dithiocyanate and esters of diphosphoric acid:

$$2(RO)_2P(O)NCS + HgO \rightarrow Hg(SCN)_2 + (RO)_2P(O)-O-P(O)(OR)_2$$

Phosphorus(v) isothiocyanates are converted by the action of chlorine into the very reactive *N*-dichloromethylenephosphoric diester amides, which react with formic acid to give phosphorus(v) isocyanates.

$$(RO)_2P(O)NCS + Cl_2 \rightarrow [(RO)_2P(O)NC(Cl)-SCl] \xrightarrow[-SCl_2]{+\ Cl_2}$$

$$(RO)_2P(O)N=CCl_2 \xrightarrow{+\ HCOOH} (RO)_2P(O)NCO + 2HCl + CO$$

N-Dichloromethylenealkylphosphonic amide chloride and *N*,*N*-bis(dichloromethylene)alkylphosphonamide react similarly with formic acid or acetic acid to give phosphorus(v) isocyanates[58–60]:

$$AlkP(O)(Cl)N=CCl_2 + HCOOH \rightarrow Alk(Cl)P(O)NCO + 2HCl + CO$$

Trialkyl and triaryl phosphites react with phosphorus triisocyanate and phosphoryl triisocyanate in accordance with the following scheme[61]:

$$(RO)_3P + P(NCO)_3 \rightarrow ROP(NCO)_2 + (RO)_2PNCO$$
$$(RO)_3P + PO(NCO)_3 \rightarrow ROP(O)(NCO_2) + (RO)_2P(O)NCO$$

The reaction of alkoxydiisocyanatophosphine with chlorine leads to phosphoryl chloride diisocyanate in a yield of about 70 %:

$$AlkOP(NCO)_2 + Cl_2 \rightarrow [AlkOP(NCO)Cl_2] \rightarrow ClP(O)(NCO)_2 + AlkCl$$

Bromine reacts similarly[62].

Alkyl chloroisocyanatophosphates are formed from dialkoxyisocyanatophosphine and chlorine.

$$(AlkO)_2PNCO + Cl_2 \rightarrow AlkO(Cl)P(O)NCO$$

These products can also be obtained by the reaction of dialkyl isocyanatophosphates with phosphorus(v) chloride or from the corresponding thio compound and chlorine[63].

The reaction of tetraisocyanatosilane with phosphoryl fluoride yields phosphoryl difluoride isocyanate[64]:

$$Si(NCO)_4 + POF_3 \rightarrow F_2P(O)NCO$$

(for further information on the preparation and/or properties of phosphoryl isocyanates, see[101,104–116]).

2. Properties of Phosphorus Isocyanates

All phosphorus isocyanates are highly reactive. The phosphorus(v) isocyanates behave similarly to "carbon" isocyanates. They react very readily with alcohols, phenols, some amines, and other compounds bearing active hydrogen atoms, and can therefore serve as important starting materials for the synthesis of derivatives of phosphoric acid, phosphonic acid, and phosphinic acid.

Phosphorus(III) isocyanates often exhibit chemical properties similar to those of phosphorus(III) chloride. The NCO groups show only a slight, if any, tendency to enter into addition reactions.

2.1. Chemical Properties of Phosphorus(III) Isocyanates

2.1.1. Stability

Phosphorus(III) isocyanates decompose even in the absence of air and moisture. Their stability increases in the series $P(NCO)_3 < ClP(NCO)_2 < Cl_2PNCO$.

$ClP(NCO)_2$ can be distilled under vacuum and kept for some time in a sealed vessel. On distillation under normal pressure

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[58] *G. I. Derkatsch*, *N. I. Liptuga*, and *A. V. Kirsanov*, Ž. obšč. Chim. *34*, 2812 (1964).

[59] *G. I. Derkatsch* and *N. I. Liptuga*, Ž. obšč. Chim. *36*, 461 (1966).

[60] *G. I. Derkatsch* and *N. I. Liptuga*, Sbornik Ž. obšč. Chim.: Chemistry of Organophosphorus Compounds. Izdanije Akad. Nauk SSSR *1967*, 102.

[61] *H. C. Fielding*, Brit. Pat. 968886 (1964); Ref. Ž. Chim. 7 H 113 (1966).

[62] *G. I. Derkatsch* and *E. I. Slussarenko*, Ž. obšč. Chim. *37*, 2069 (1967).

[63] *A. V. Narbut* and *G. I. Derkatsch*, Ž. obšč. Chim., in press.

[64] *O. Glemser*, *U. Biermann*, and *M. Field*, Chem. Ber. *100*, 1082 (1967).

it is completely converted into phosphorus triisocyanate and phosphorus dichloride isocyanate[7,11].

$$2ClP(NCO)_2 \rightarrow Cl_2PNCO + P(NCO)_3$$

2.1.2. Substitution of the NCO Groups

The reaction of phosphorus triisocyanate with antimony trifluoride yields phosphorus difluoride isocyanate and phosphorus fluoride diisocyanate[65]. The reaction of phosphorus triisocyanate and benzoyl chloride or aluminum chloride proceeds similarly[66]:

$$P(NCO)_3 + 2C_6H_5COCl \rightarrow Cl_2PNCO + 2C_6H_5CONCO$$
$$P(NCO)_3 + AlCl_3 \rightarrow PCl_3 + Al(NCO)_3$$

Phosphorus triisocyanate reacts very readily with chlorine to give phosphorus dichloride triisocyanate, and with iodine to give $P(NCO)_3 \cdot I$[67]. Other phosphorus(III) isocyanates (*e.g.* Cl_2PNCO, $(ArO)_2PNCO$, and Ar_2PNCO) can also add chlorine.

The reaction of sulfur tetrafluoride with phosphorus triisocyanate or phosphorus fluoride diisocyanate leads to $F_2S{=}NCOF$[68]. Phosphorus triisocyanate reacts with tetracarbonylnickel to form $Ni[P(NCO)_3]_4$[69] and with ethylene oxide to form isocyanato-bis(β-isocyanatoethoxy)phosphine. This reaction can also be carried out with other phosphorus isocyanates[70,71]:

$$P(NCO)_3 + (CH_2)_2O \rightarrow OCNP(OCH_2CH_2NCO)_2$$

2.1.3 Other Reactions

The reaction of alkoxy- or aryloxyisocyanatophosphines with alcohols leads to substitution or addition[72].

$$ROP(NCO)_2 \xrightarrow{R'OH} ROP(OR')_2$$

$$ROP(NCO)_2 \xrightarrow{R'OH} ROP(NHCOOR')_2$$

Other phosphorus(III) isocyanates, like their phosphorus(V) analogs, undergo only addition with alcohols, amines, or ketones[12,13,73,74].

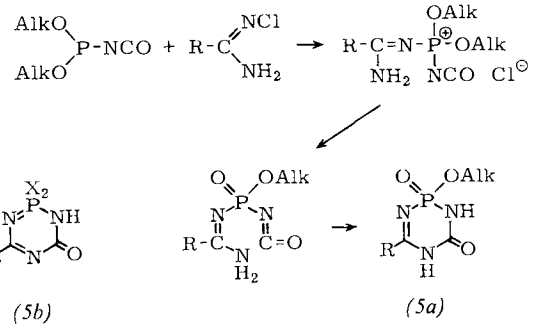
On reaction with SO_2Cl_2 or sulfur, the phosphorus(III) isocyanates are oxidized to phosphorus(V) compounds[20,75]:

$$C_6H_5OP(NCO)_2 + SO_2Cl_2 \rightarrow C_6H_5OP(O)(NCO)_2 + SOCl_2$$
$$P(NCO)_3 + S \rightarrow PS(NCO)_3$$

Dialkoxy- or diaryloxyisocyanatophosphines react with alkyl iodides in accordance with the Arbusov scheme to give alkylphosphonic ester isocyanates[76].

$$(RO)_2PNCO + AlkI \rightarrow RI + Alk(RO)P(O)NCO$$

whereas dialkoxyisocyanatophosphines and *N*-chloroamidines give very unstable phosphonium compounds, which are readily converted into phospha^{V}triazine derivatives *(5a)*.



(5b) *(5a)*

Diaryloxyisocyanatophosphines and dichloroisocyanatophosphines, on the other hand, react with *N*-chloroamidines *via* similar intermediates to form 2,2-diaryloxy- and 2,2-dichloro-3,4-dihydrophospha^{V}triazin-4-ones *(5b)*[76].

2.2 Chemical Properties of Phosphorus(V) Isocyanates

2.2.1. Reaction with Water

Phosphoryl dichloride isocyanate is very readily decomposed by water into carbon dioxide, hydrogen chloride, and ammonium dihydrogen phosphate; with concentrated hydrochloric acid at −20 °C, on the other hand, it forms *N*-(dichlorophosphoryl)carbamic acid, which slowly loses hydrogen chloride at room temperature and reacts with alcohols to give trialkyl phosphates. Reaction with phosphorus(V) chloride regenerates the starting material:

$$Cl_2P(O)NCO + H_2O \xrightarrow[HCl]{} Cl_2P(O)NHCOOH$$
$$Cl_2P(O)NHCOOH + PCl_5 \rightarrow Cl_2P(O)NCO + 2HCl + POCl_3$$

N-(Dichlorophosphoryl)corbomic acid changes under vacuum at 160 °C into phosphoryl dichloride isocyanate, hydrogen chloride, and polymers[77].

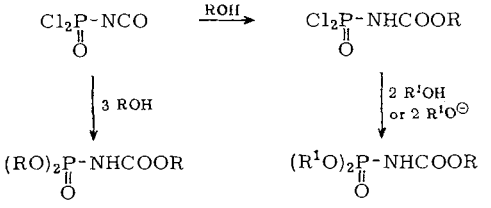
Diesters of isocyanatophosphoric acid are decomposed by water into phosphoric diester amides. The reaction probably proceeds *via* very unstable carbamic acid derivatives[35,49].

2.2.2. Reaction with Alcohols and Phenols

Phosphoryl isocyanates react very readily with equimolar quantities of alcohols and phenols to form phos-

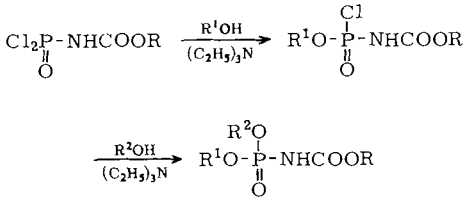
[65] *H. H. Anderson*, J. Amer. chem. Soc. *69*, 2495 (1947).
[66] *H. H. Anderson*, J. Amer. chem. Soc. *75*, 1576 (1963).
[67] *E. Colton* and *L. S. Cyr*, Nature (London) *183*, 1042 (1959).
[68] *A. Clifford* and *C. Kolayashi*, Inorg. Chem. *4*, 571 (1965).
[69] *G. Wilkinson*, Z. Naturforsch. *9b*, 446 (1954).
[70] *Houben-Weyl-Müller:* Methoden der organischen Chemie, Vol. XII/2, Thieme-Verlag, Stuttgart 1964, p 110.
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[72] *P. R. Steyermark*, J. org. Chemistry *28*, 3570 (1963).
[73] *H. C. Fielding*, Brit. Pat. 982931 (1965); Ref. Ž. Chim. 8 H 103 (1966).
[74] *H. C. Fielding*, *J. M. Pollock*, and *N. H. Pay*, Brit. Pat. 933482 (1963); Chem. Abstr. *60*, 731 g (1964).
[75] *P. R. Steyermark*, US-Pat. 3177239 (1965); Ref. Ž. Chim. 14 H 162 (1966).
[76] *G. I. Derkatsch*, *E. S. Gubnitskaya*, *M. V. Kolotilo*, and *A. G. Matyusha*, Ž. obšč. Chim. *36*, 2215 (1966); *E. S. Gubnitskaya* and *G. I. Derkatsch ibid.*, in press.
[77] *A. V. Kirsanov* and *L. P. Zuravlyova*, Ž. obšč. Chim. *31*, 598 (1961).

phorylcarbamic esters [12, 13, 23, 34, 38, 53–55, 73, 75, 77–82]. The reaction is carried out in benzene, dioxane, petroleum ether, or ether [78, 79] (see also [35, 41, 49]).



Reaction with an excess of alcohol yields *N*-(dialkoxyphosphoryl)carbamic esters, which can also be prepared from *N*-(dichlorophosphoryl)carbamic esters and alcohols or alkoxides.

This stepwise reaction is recommended for the preparation of *N*(-(dialkoxyphosphoryl)carbamic esters with different alkyl groups [36, 78]. The phosphoryl dichloride isocyanate is first allowed to react with an equimolar quantity of one alcohol and then, without isolation of the carbamic ester, with two molar equivalents of another alcohol or alkoxide. Esters of *N*-(dialkoxyphosphoryl)carbamic acids with different alkoxy groups on the phosphorus can also be prepared [50].



N-(Dichlorophosphoryl)carbamic esters also react very readily with ammonia and with primary and secondary amines to form *N*-(diaminophosphoryl)carbamic esters [83–85].

Compounds with several phosphorylcarbamic acid groups in the molecule can be prepared by the action of polyhydroxy compounds on diesters of isocyanatophosphoric acid [80], *e.g.*:

$$2(RO)_2PONCO + p\text{-}HOC_6H_4OH \rightarrow p\text{-}[(RO)_2PONHCOO]_2C_6H_4$$

When *N*-(dialkoxyphosphoryl)carbamic esters are heated with aniline, urea derivatives are formed [87].

$$(AlkO)_2P(O)NHCOOAlk + C_6H_5NH_2 \rightarrow AlkOH + (AlkO)_2P(O)NHCONHC_6H_5$$

2.2.3. Reaction with Nitrogen Bases

Phosphoryl isocyanates react with amines and hydrazines to form phosphorylated urea and semicarbazide derivatives [86, 93]:

$$>P(O)NCO + HN< \rightarrow >P(O)NHCON<$$
$$>P(O)NCO + H_2NN< \rightarrow >P(O)NHCONHN<$$

If halogen atoms as well as NCO groups are bound to the phosphorus atom, these can also react with amines, though rather more slowly. Thus, reaction of these compounds with equimolar quantities of nitrogen bases leads almost exclusively to addition of NCO groups.

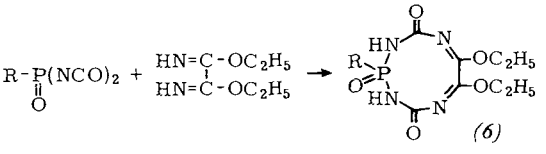
Phosphoryl dichloride isocyanate, phosphoryl difluoride isocyanate, and the mixed compound react with equimolar quantities of amines to form *N*-dihalogenophosphorylureas [86, 93]. Primary amines react with NCO groups more readily than do secondary amines.

Amidines and alkyl esters of imidic acids react only very slowly with phosphoryl isocyanates to form the expected products [35, 88–91].

The action of 2 mol. equiv. of *N*,*N*-dimethylhydrazine or an excess of hydrazine on phosphoryl dichloride isocyanate yields salts of dichlorophosphorylsemicarbazides [92]:

$$Cl_2P(O)NCO + 2(CH_3)_2NNH_2 \rightarrow (CH_3)_2N\overset{\oplus}{N}H_3Cl_2P(O)\overset{\ominus}{N}\text{–}CONHN(CH_3)_2$$
$$2Cl_2P(O)NCO + 3NH_2NH_2 \rightarrow 2NH_2\overset{\oplus}{N}H_3Cl_2P(O)\overset{\ominus}{N}\text{–}CONHNHCO\text{–}\overset{\ominus}{N}P(O)Cl_2$$

Esters of chloroisocyanatophosphoric acid and phosphonic chloride isocyanates react much more slowly than phosphoryl dihalide isocyanates with amines to give urea derivatives [38, 39]. Both isocyanate groups in phosphonic diisocyanates can react with amines to give cyclic compounds such as *(6)* [12, 13, 53, 62, 80].



(6)

The reaction of isocyanatophosphoric diesters with amines or ammonia yields *N*-phosphorylureas [53, 55, 59, 88, 89] or phosphoric ester amides [49, 75], whereas reaction with hydrazines leads to *N*-phosphorylsemicarbazides [92].

[78] *A. V. Kirsanov* and *I. N. Shmurova*, Ž. obšč. Chim. *26*, 2642 (1956).

[79] *A. V. Kirsanov*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1954*, 646.

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[83] *T. J. Bardos*, *A. K. Barua*, *L. F. Chmielewicz*, *G. E. Crevar*, *J. P. Dailey*, *S. Divald*, and *Z. B. Papanastassiou*, J, pharmac. Sci. *54*, 187 (1965).

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[85] *L. D. Prozenko* and *K. A. Kornev*, Ukrainskij chim. Ž. *27*, 243 (1961).

[86] *S. J. Kühn* and *G. A. Olah*, Canad. J. Chem. *40*, 1951 (1962).

[87] *Ch. Yosioka* and *T. Chorie*, Jap. Pat. 11125 (1962).

[88] *A. V. Kirsanov* and *E. S. Levshchenko*, Ž. obšč. Chim. *26*, 2285 (1956).

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[92] *A. V. Kirsanov* and *L. P. Zuravlyova*, Ž. obšč. Chim. *31*, 210 (1961).

[93] *G. I. Derkatsch* and *A. V. Narbut*, Ž. obšč. Chim. *37*, 1364 (1967).

[94] *V. I. Shevshchenko*, *A. S. Stepanek*, and *A. V. Kirsanov*, Ž. obšč. Chim. *32*, 150 (1962).

2.2.4. Other Reactions

When phosphoryl dichloride isocyanate is heated with PCl_5 in a closed ampoule at 200 °C, cyanogen chloride and phosphoryl chloride are formed [94].

Phosphoryl isocyanates behave in the same way as alkyl and aryl isocyanates in reactions with diesters of phosphorous acid in the presence of organic bases [95]. Phosphorylcarbamic acid derivatives are formed [96]:

$$(RO)_2P(O)NCO + (RO)_2POH \rightarrow (RO)_2P(O)NHCOP(O)(OR)_2$$

Phosphoryl triisocyanate reacts with acetone or acetophenone in boiling toluene to form acylamides [74]:

$$RCOCH_3 + P(O)(NCO)_3 \rightarrow P(O)(NHCOCH_2COR)_3$$

When treated with SbF_3, phosphoryl dichloride isocyanate gives a mixture of phosphoryl chloride fluoride and difluoride (5–10 and 50% yield respectively) [35,86,97]. The reaction of phosphoryl chloride diisocyanate with SbF_3 leads to phosphoryl fluoride diisocyanate and phosphoryl difluoride isocyanate [62].

2.3. IR and NMR Spectra of Phosphorus Isocyanates

In the IR spectra of phosphorus isocyanates, the NCO bands occur between 2430 and 2260 cm^{-1} [14,15,25,26,31,56,62,82,86].

In 1964, *Fluck* investigated the ^{31}P-NMR spectra of phosphorus isocyanates and phosphorus isothiocyanates. According to this work the NCO and NCS groups lie between Cl and Br on the electronegativity scale.

3. Organophosphorus Compounds Containing NCO Groups that are Not Directly Bound to the Phosphorus

The reaction of tris(chloromethyl) phosphate with AgOCN yields tris(isocyanatomethyl) phosphate [98]:

$$PO(OCH_2Cl)_3 + 3\,AgOCN \rightarrow 3\,AgCl + PO(OCH_2NCO)_3$$

Tris(*p*-nitrophenyl)phosphate, which can be obtained by nitration of triphenyl phosphate with concentrated nitric acid, can be hydrogenated in the presence of Raney nickel to form tris(*p*-aminophenyl) phosphate, which is converted into the isocyanate in the presence of phosgene.

$$PO(OC_6H_5)_3 \xrightarrow{HNO_3} PO(OC_6H_4NO_2\text{-}p)_3 \xrightarrow{H_2} PO(OC_6H_4NH_2\text{-}p)_3 \xrightarrow{COCl_2} PO(OC_6H_4NCO\text{-}p)_3$$

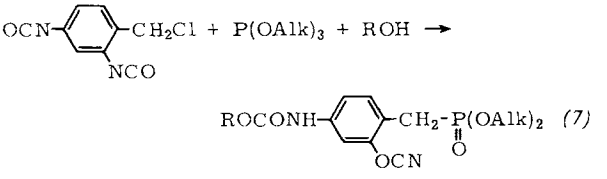
Ester amides of phosphoric acid are not all resistant to phosgene. Whereas bis(*p*-aminophenyl) *N*-methylanilidophosphate is smoothly converted into the diisocyanate on phosgenation, the *N,N*-dimethylamido derivative is cleaved under the same conditions into *N,N*-dimethylcarbamoyl chloride and bis(*p*-isocyanatophenyl) chlorophosphate.

$$C_6H_5N(CH_3)PO(OC_6H_4NH_2\text{-}p)_2 \xrightarrow{COCl_2} C_6H_5N(CH_3)PO(OC_6H_4NCO\text{-}p)_2$$

$$(CH_3)_2NPO(OC_6H_4NH_2\text{-}p)_2 \xrightarrow{COCl_2} (CH_3)_2NCOCl + ClPO(OC_6H_4NCO\text{-}p)_2$$

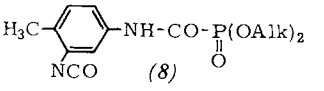
Diethyl *p*-aminophenyl thiophosphate and (particularly smoothly) tris(*p*-aminophenyl) thiophosphate also react with phosgene to form the isocyanates. Bis(3-amino-4-methylphenyl) styrylphosphonate can also be readily converted into the corresponding isocyanato ester by reaction with phosgene [99,100].

Isocyanates containing phosphonic ester groups can be prepared by the Arbusov reaction. Thus the simultaneous action of equimolar quantities of trialkyl phosphite and alcohol on 2,4-diisocyanatobenzyl chloride yields phosphorylated isocyanates *(7)*. Reaction with trialkyl phosphite alone gives only polymers.

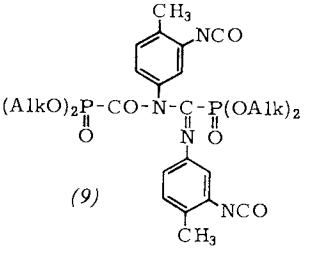


(7)

Similarly, *N*-(3-isocyanato-4-methylphenyl)carbamoyl chloride can be converted into the phosphonic esters *(8)* by reaction with trialkyl phosphites. The compound *(9)* has been obtained by a multistage process from1,3-bis(chlorocarbonylamino)-4-methylbenzene.



(8)



(9)

Esters of phosphoric acid containing isocyanate groups are used as starting materials for the production of polymers containing phosphorus [99,100]. Alkylphosphonic diisocyanates also react very readily with aliphatic and aromatic diols to give polyurethanes with phosphorus in the main chain. The reaction with diamines proceeds similarly (see Table 1) [12,13].

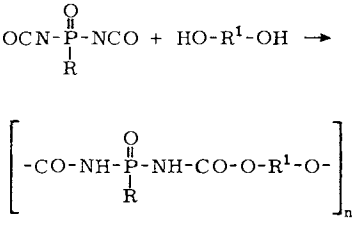


Table 1. Polymers from $C_2H_5P(O)(NCO)_2$ and diols or diamines.

Reactant	Product
1,6-Hexanediol	Colorless tacky mass, sparingly soluble in boiling ethanol, insoluble in water
Resorcinol	Solid, m.p. 75 °C, soluble in acetone, insoluble in toluene and chloroform
Hydroquinone	Vitreous, m.p. 200 °C, incombustible
p-Phenylenediamine	Solid, m.p. 300 °C, insoluble in water, ethanol, pyridine, 6N HCl

[95] *A. N. Pudovik, I. V. Konovalova,* and *R. B. Krivonossova,* Ž. obšč. Chim. *26*, 3110 (1956).

[96] *A. V. Kirsanov* and *L. P. Zuravlyova,* Ž. obšč. Chim. *30*, 3038 (1960).

[97] *G. A. Olah* and *S. J. Kuhn,* US-Pat. 3096371 (1963).

[98] *H. C. Fielding* and *J. M. Pollock,* Brit. Pat. 968109 (1964).

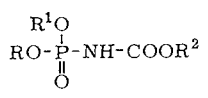
[99] *H. Holtschmidt* and *G. Oertel,* Angew. Chem. *74*, 795 (1962).

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4. Physiological Action of Phosphorus Isocyanates

Phosphorus isocyanates hydrolyze very readily, and this limits their use as physiologically active substances. Only one phosphorus isocyanate derivative has so far been marketed as a herbicide [97]. It is quite possible that the action of the preparation is due not to the phosphorus isocyanate itself, but to its reaction products. *N*-Phosphorylated urethanes and ureas are accordingly of great interest as potential physiologically active substances [35, 42].

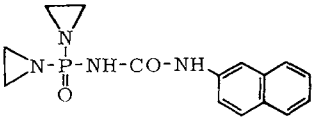


(10), R = R^1 = R^2 = CH_3
(11), R = R^1 = $(CH_3)_2CH$, R^2 = CH_3
(12), R = C_2H_5, R^1 = $(CH_3)_2CH$, R^2 = CH_3
(13), R = CH_3, R^1 = R^2 = $(CH_3)_2CH$
(14), R = C_2H_5, R^1 = R^2 = $(CH_3)_2CH$
(15), R = CH_3, R^1 = C_2H_5, R^2 = $(CH_3)_2CH$

N-Phosphorylated urethanes of the AlkOCONHPO-$(OR)_2$ type are systemic insecticides. *N*-(Dimethoxyphosphoryl)carbamic-acid methyl (K-20-35) *(10)* and isopropyl esters (avenin) *(11)* have proved to be particularly effective, and are completely harmless to warm-blooded animals. According to *Kagan*, rats fed with 15 daily doses of K-20-50 at a rate of 500 mg/kg showed no ill effects. A single peroral administration of more than 5000 mg and an intravenous administration of 500 mg of preparation per kg of body weight were also found to be harmless [102].

K-20-35 and avenin have a high toxicity for sugar-beet weevils (*Bothynoderes*) and some insects of the order Diptera; on the other hand, both preparations are practically ineffective against sucking insects. If the preparations are applied to sugar-beet seeds before sowing or to shoots, they provide protection during the dangerous early period of about two weeks. Avenin is more active and remains effective for a longer time (12–15 days) than K-20-35 (about 14 days). Some analogs of avenin with different alkoxy groups on the phosphorus atom have a contact action as well as an internal action. The activity of these compounds is strongly dependent on the nature and stage of development of the insect. The strongest contact action is shown by the compounds *(12)–(14)*, while *(13)* and *(15)* have the greatest internal activity.

N-[Bis(aziridin-1-yl)phosphoryl]urethanes and *N*-[bis-(aziridin-1-yl)phosphoryl]-*N'*-arylureas have a cytostatic action [103]. Thus the development of experimental tumors in animals is strongly hindered *e.g.* by *N*-[bis(aziridin-1-yl)phosphoryl]-*N'*-β-naphthylurea *(16)* (Preparation No. 484, BNMPh, dinaphthimine).



(16)

Dinaphthimine has a very low toxicity; its lethal dose (LD_{50}) for rats is 79.0 mg/kg by subcutaneous injection, and the therapeutic dose is 15 mg/kg. Dinaphthimine in therapeutic doses also has only a slight homotoxicity (the total quantity of leukocytes in the peripheral blood of the animal has fallen by not more than 50 % at the end of the treatment, and rapidly returns to the normal value). Unlike the azirine derivatives of phosphoric acid, which are suitable only for intravenous or intramuscular injection, the new preparation can be administered subcutaneously.

Dinaphthimine has proved to be a very active agent for the treatment of leukemia in rats and mice. When 15 mg of the preparation per kg of body weight were injected subcutaneously six or even eleven days after production of the disease, all the animals examined were cured after 10–15 injections, whereas control animals survived for only 13–18 days. The blood of the experimental animals was practically free from leukoblasts at the end of the treatment, and morbid changes in other organs had also disappeared. No harmful effect of dinaphthimine on other organs could be observed.

Received: April 8, 1968 [A 696 IE]
German version: Angew. Chem. *81*, 407 (1969)
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Synthesis of Alkynes from Enol Esters

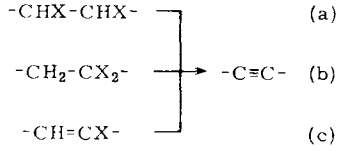
By J. Cymerman Craig, M. D. Bergenthal, I. Fleming, and J. Harley-Mason[*]

Eliminations leading from enol sulfonates, enol phosphates, and enol phosphonium salts to alkynes are reviewed. Olefin eliminations are usually the rate-determining step in the formation of the triple bond. Enol esters may also play a role in the biosynthesis of alkynes.

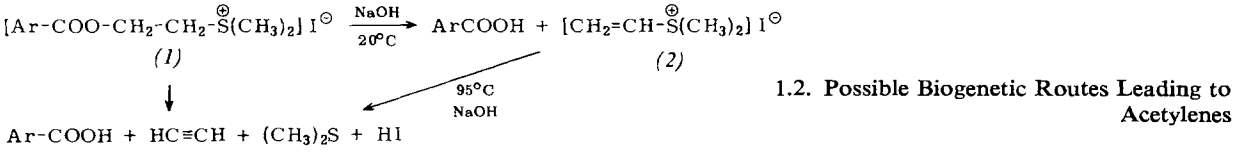
1. Introduction

1.1. General Elimination Methods Leading to Acetylenes

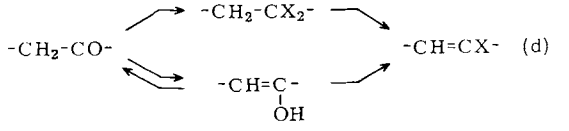
In the laboratory, acetylenes are usually prepared by elimination reactions according to equations (a), (b), or (c), where X = halogen or an equivalent "leaving group" (*e.g.*, tosylate), and the reagent is a strong base [1–5].



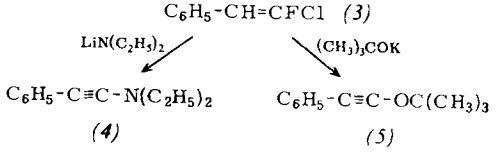
The alkaline fission of 2-aroyloxyethyldimethylsulfonium iodides *(1)*, which were found [6] to undergo double elimination to give acetylene, was regarded as an example of method (a). However, later studies revealed [7] that the reaction actually proceeds in two stages, of which the first leads to elimination of benzoate ion and the formation of dimethylvinylsulfonium iodide *(2)* which breaks down only at 95 °C. The step by which the triple bond is formed is therefore, in fact, an example of method (c).



The starting material in method (b) is generally the ketone; this may either be transformed into the dihaloderivative, and thence (by ready loss of hydrogen halide) into the halo-olefin, *or* halogenation of the enol form of the ketone may lead directly to the halo-olefin [equation (d)]. In either case it is clear that the acetylene-forming step is again an example of reaction (c).



The dehydrohalogenation of the fluoro-olefin 2-chloro-2-fluorostyrene *(3)* affords [8] the inamine *(4)* and the ethynyl ether *(5)*.



The present article will survey only the methods of carrying out the elimination reaction by procedure (c) when the olefinic derivative is an enol ester or a closely related compound.

1.2. Possible Biogenetic Routes Leading to Acetylenes

Whereas in 1950 only about seven naturally occurring acetylenes were known, this figure has now risen to a total of more than 450 and several valuable reviews exist [9–14]. All known natural acetylenes and polyacetylenes are long-chain compounds, sometimes cyclized in various ways, but never branched, and ranging in carbon content from C-8 to C-18. A relationship to the fatty acids therefore suggests itself

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immediately, and direct experimental evidence testifying to the correctness of this assumption has been obtained.

It has been shown that the molecules of natural acetylenes are built up from acetyl-coenzyme A. Thus alternate carbon atoms of C-10 and C-18 acetylenes were found to be uniformly labeled when [1-^{14}C]acetate is incorporated, showing that the molecule is built up from acetate units in a regular fashion [15,16].

It has been demonstrated that the synthesis involves the repeated condensation of acyl-coenzyme A derivatives with malonyl-coenzyme A (formed by carboxylation of acetyl-coenzyme A). Thus it was shown by using [2-^{14}C]malonate, that the C-10 alcohol *(6)* from *Tricholoma grammopodium* (dehydromatricarianol) contained ^{14}C only in the C-1–C-8 part of the chain,

$$OH-CH_2-CH=CH-C\equiv C-C\equiv C-C\equiv C-CH_3$$
(6)

and not in the terminal two-carbon unit comprising C-9 and C-10, which was presumably formed directly from acetyl-coenzyme A [17,18]. This pattern may be described as the "acetate + *n*-malonate pathway", in which the overall reaction can be represented as in equation (e).

$$H_3C(C=O)X + CH_2(COO^{\ominus})-C(=O)X \rightarrow X^{\ominus} + CH_3-C\equiv C-C(=O)X + CO_2 + H_2O \quad (e)$$

X = SCoA

Whereas the overall reaction in fatty acid synthesis is as in equation (f).

$$H_3C(C=O)X + CH_2(COO^{\ominus})-C(=O)X \xrightarrow{4\,H} X^{\ominus} + CH_3-CH_2-CH_2-C(=O)X + CO_2 + H_2O \quad (f)$$

X = SCoA

In both cases the common intermediate is the acetylmalonate derivative *(7)*, and this led to the attractive suggestion [19] that acetylenes such as *(8)* might arise by the simultaneous decarboxylation and elimination reaction of enol derivatives of acylmalonic acid [equation (g)].

$$CH_3-C(=O)-CH(COO^{\ominus})-C(=O)X \quad (7)$$

The leaving group could be *e.g.* the pyrophosphate anion [19], and the resulting acetylenic coenzyme A derivative could then react further with malonyl-coenzyme A and repeat the process to build up a diacetylenic derivative, and then a polyacetylenic acid. This pathway for polyacetylene synthesis *via* acylmalonate enols could therefore be visualized as a variation on the mechanism of fatty acid biosynthesis, in which the decarboxylation of the acylmalonyl thiolester is delayed until an enol phosphate or pyrophosphate has been formed, when the concerted decarboxylation-elimination step occurs.

$$CH_3-C(OY)=C(O^{\ominus})-C(=O)X \rightarrow OY^{\ominus} + CH_3-C\equiv C-C(=O)X + CO_2 \quad (g)$$
(8)

$$CH_3-CO-CH_2-C(=O)X \quad (9)$$

If, however, the initial "acetate + malonate" condensation were also accompanied by a simultaneous decarboxylation (and the experimental evidence is not conclusive on this point [20]), then the product of the condensation would be the acylacetate *(9)* instead of the acylmalonate *(7)*, and the formation of the acetylene *(8)* would then have to proceed by a process equivalent to the dehydration of the acylacetate *(9)*. The hydration of the triple bond is well known both in the laboratory and also enzymically, *e.g.*, in the conversion of acetylenedicarboxylic acid into oxaloacetic acid [21]. However, in view of the high energy required for the direct dehydration of $-COCH_2-$ to $-C\vdots C-$, this conversion could be expected to occur more easily in 2 steps, through an enol ester leaving group with prior or simultaneous loss of a proton from the adjacent carbon of the double bond [equation (h)].

The phosphate ion was early suggested [9] as a possible leaving group for such a process, and the pyrophosphate ion involved in the acylmalonate model [19] would be even better for this purpose. The feasibility of such elimination reactions was supported, *e.g.*, by the ready transesterification of vinyl esters [22], which implies a degree of reversibility of the addition reaction to the triple bond [equation (i)].

$$CH_3-C(H)(OY)-C(=O)X \rightarrow HOY + CH_3-C\equiv C-C(=O)X \quad (h)$$
(8)

$$R^1-COO-C(R)=CH_2 + R^2-COOH \xrightarrow{Hg(OAc)_2} R^1-COOH + R^2-COO-C(R)=CH_2 \quad (i)$$

$$CH_3-C(OPO(OC_2H_5)_2)=CH-PO(OC_2H_5)_2 \xrightarrow{NaOC_2H_5} HOPO(OC_2H_5)_2 + CH_3-C\equiv C-PO(OC_2H_5)_2 \quad (k)$$
(10) *(11)*

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The only transformation of an enol phosphate into an acetylene recorded prior to 1961 was[23] the formation of diethyl propynephosphonate *(11)* by the action of sodium ethoxide on 2-(diethoxyphosphoryl)-1-methylvinyl diethyl phosphate *(10)* [equation (k)].

The close correspondence between the two pathways (e) and (f) suggested the possibility[13] that dehydrogenation of the fatty acids could lead to the corresponding acetylenes, as in equation (l).

$$CH_3-CH_2-CH_2-\underset{X}{C}=O \rightarrow CH_3-CH=CH-\underset{X}{C}=O \rightarrow CH_3-C\equiv C-\underset{X}{C}=O \quad (1)$$

The first step in this sequence represents a demonstrated pathway in the biosynthesis of long-chain monounsaturated fatty acids, where it has been shown[24,25] that the enzyme-catalyzed conversion of stearic acid to oleic acid takes place with positional and geometrical specificity. The second step would represent a similar thermodynamic sequence, and the first experimental proof of such a conversion has been recently provided[26,27] by the isolation of labeled crepenynic acid *(14)*, together with linolenic acid *(13)*, from *Trichoma grammopodium* supplied with [10-^{14}C]oleic acid *(12)*.

$CH_3-(CH_2)_7-CH=CH-(CH_2)_7-COOH$ *(12)*

$CH_3-(CH_2)_4-CH=CH-CH_2-CH=CH-(CH_2)_7-COOH$ *(13)*

$CH_3-(CH_2)_4-C\equiv C-CH_2-CH=CH-(CH_2)_7-COOH$ *(14)*

Both the acylmalonate [equation (g)] and the acylacetate [equation (h)] pathways to acetylene compounds have been realized in the laboratory (though not, as yet, enzymically). The dehydrogenation mechanism [equation (l)] on the other hand has been successfully demonstrated enzymically, but no laboratory model for such a reaction step exists up to date.

2. Eliminations from Enol Sulfonates

2.1. Acetylenes from Acylmalonate Enol Sulfonates

In pursuance of a biogenetic analogy, the decarboxylative elimination of enol sulfonates has been examined[28]. A number of enol sulfonates *(16)* were prepared by treatment of acylmalonates *(15)* with sodium ethoxide and arylsulfonyl chlorides. Yields were variable but, in general, were high for those compounds with a sterically unhindered enol group. In homogeneous alkaline aqueous dioxane solution saponification was followed by decarboxylative elimination giving acetylenic acids *(17)* in a number of cases[28,29].

$$R-\overset{O}{\overset{\|}{C}}-\underset{COOC_2H_5}{\overset{COOC_2H_5}{CH}} \xrightarrow[NaOC_2H_5]{ArSO_2Cl} R-\underset{OSO_2Ar}{\overset{COOC_2H_5}{C}}=\underset{COOC_2H_5}{C} \rightarrow R-C\equiv C-COOH$$

(15) *(16)* *(17)*

The product was a mixture of the acetylenic acid *(17)* and the starting acylmalonate *(15)*, the latter arising by hydroxide ion attack on the enol carbon followed by loss of sulfonate ion. This hydrolysis product *(15)*, as opposed to the elimination product *(17)*, was produced in greatest quantity from those enol sulfonates *(16)* which were least hindered for attack on this carbon atom. This tendency, taken in conjunction with the trend in the yield of the enol sulfonates mentioned above, gives rise to an overall yield (based on acylmalonate *(15)*) of acetylenic acid which is much the same (about 20%) for all compounds studied. Recovery of the starting material, however, raises the effective yield considerably (see Table 1).

Table 1. Enol sulfonates *(16)* and acetylenic acids *(17)* obtained from acylmalonates [28, 29, 46].

R	Ar	Yield of *(16)* (%)	Yield of *(17)* (%) [a]
C_6H_5	p-BrC_6H_4	29	73
p-$CH_3OC_6H_4$	p-BrC_6H_4	38	70
2-Furyl	p-BrC_6H_4	12	48
2-Furyl	β-$C_{10}H_7$	51	48
2-Thienyl	p-BrC_6H_4	27	52
$C_6H_5CH=CH$	β-$C_{10}H_7$	68	55
$C_6H_5CH=CH$	p-BrC_6H_4	52	40
$C_6H_5CH=CH$	p-$CH_3C_6H_4$	72	64
$CH_3CH=CH$	p-BrC_6H_4	45	57
$CH_3(CH=CH)_2$	p-BrC_6H_4	61	30
$C_6H_5CH_2$	β-$C_{10}H_7$	21	0
CH_3	p-BrC_6H_4	low	0
CH_3	p-$CH_3C_6H_4$	low	0
Cyclopropyl	p-BrC_6H_4	not isolated	low
Cyclopropyl	p-$CH_3C_6H_4$	not isolated	low
Cyclopropyl	β-$C_{10}H_7$	not isolated	low
CCl_3	p-$CH_3C_6H_4$	low	0
p-$NO_2C_6H_4$	p-BrC_6H_4	60	traces
o-$NO_2C_6H_4$	p-BrC_6H_4	64	traces
o-$NO_2C_6H_4$	β-$C_{10}H_7$	53	traces
m-$NO_2C_6H_4$	p-BrC_6H_4	41	traces
$C_2H_5OCO-CH=CH$	p-$CH_3C_6H_4$	73	0
C_6H_5-CO	p-BrC_6H_4	0.5	0

[a] Yield based on *(16)*.

The chief characteristic of this synthesis of acetylenecarboxylic acids is the mildness of the reaction conditions (room temperature, overnight, about 0.2 N alkali).

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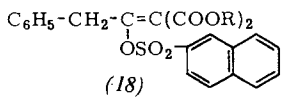
[28] *I. Fleming* and *J. Harley-Mason,* J. chem. Soc. (London) *1963*, 4771.

[28a] *I. Fleming* and *C. R. Owen,* unpublished results.

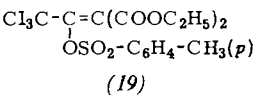
[29] *E. J. D. Brown* and *J. Harley-Mason,* J. chem. Soc. (London) *(C) 1966*, 1390.

The reaction fails when the developing triple bond is not conjugated with a double bond or an aromatic ring.

The diester *(18)*, R = C_2H_5, gave only the diacid *(18)*, R = H, under the usual alkaline conditions. Further treatment under a variety of conditions led only to the hydrolysis products, phenylacetone and phenylacetic acid.

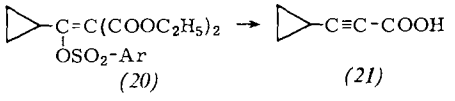


(18)



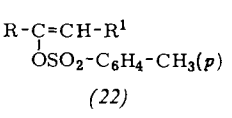
(19)

The enol-*p*-toluenesulfonate *(19)*, with a strongly electron withdrawing trichloromethyl group, gave no acetylenic acid in the crude reaction product. The only exceptions to this rule are the enol sulfonates *(20)*, Ar = p-Br-C_6H_4, *p*-MeC_6H_4, and β-$C_{10}H_7$, treatment of which with alkali gave cyclopropylpropiolic acid *(21)* in low yield [29].



(20) *(21)*

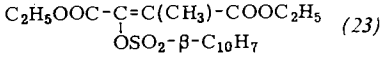
The conversion of the enol *p*-toluenesulfonate *(22a)* (obtained in 38% yield) to ethyl 2-butynoate (ethyl tetrolate) was reported [30] using sodium *tert*-butoxide in benzene. However, the yield of the acetylene was extremely low and the characterization of the product incomplete.



(22)

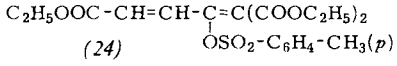
(a), R = CH_3, R^1 = $COOC_2H_5$
(b), R = C_6H_5, R^1 = $COOCH_3$
(c), R = CH_3, R^1 = $COCH_3$

The enol *p*-toluenesulfonates *(22b)* and *(22c)* were prepared [30,48] in low yield, but no acetylenes were obtained from them. The enol naphthalene-2-sulfonate *(23)* from diethyl oxalopropionate similarly failed to give any acetylenic acid on alkaline treatment [29].

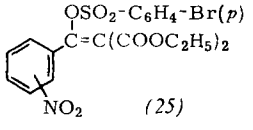


(23)

When the double bond, conjugated with the enol double bond, is further conjugated with a carbonyl group, as in the enol *p*-toluenesulfonate *(24)*, no elimination to give an acetylenic product was observed. Even the nitrobenzoylmalonate enol *p*-bromobenzenesulfonates *(25)*, *o*-, *m*-, and *p*-NO_2, afforded only traces of acetylenic products (detected by



(24)



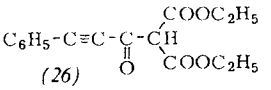
(25)

infrared spectroscopy). Similarly, the enol *p*-bromobenzenesulfonate *(16)*, R = C_6H_4–CO, Ar = *p*-Br–C_6H_4, from diethyl phenylglyoxalylmalonate failed to give any acetylenic product on alkaline treatment [29].

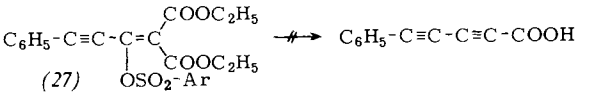
The possibility of extending the enol acylmalonate synthesis to the preparation of diacetylenic acids was examined using the ester *(26)*. However, the presence of a triple bond conjugated with the enol double bond led to the formation of tetronic acids before elimination to the expected diynoic acid could take place.

[30] *G. Nakaminami*, Bull. chem. Soc. Japan *35*, 1629 (1962).

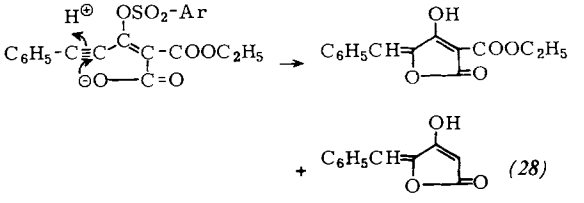
Presumably the reaction proceeds through ester hydrolysis and intramolecular attack by the carboxylate ion on the triple bond or the protonated triple bond [31]



(26)



(27)

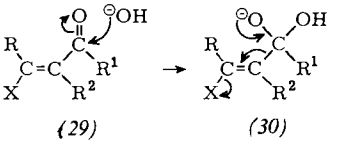


(28)

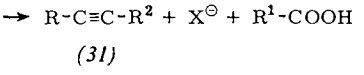
since both the ketoester *(26)* and its enol arenesulfonate *(27)* underwent cyclization to give the same γ-benzylidene tetronic acid *(28)* [47].

2.2. Acetylenes from Enol Sulfonates of α-Acyl-β-diketones and α-Acyl-β-keto Esters

An alternative process to decarboxylation as a source of electrons for the developing triple bond is the attack of hydroxide ion on an acyl group as in *(29)*→*(31)*.

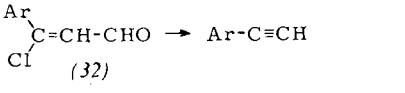


(29) *(30)*

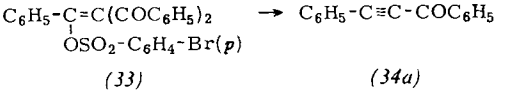


(31)

This fragmentation has been observed, for example, in triple bond formation from β-aryl-β-chloroacroleins *(32)* with alkali [32]. In the enol sulfonate field it has been used for the synthesis of an acetylenic ketone *(33)*→*(34a)* [29].



(32)



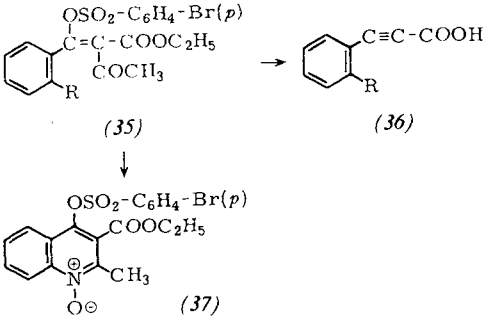
(33) *(34a)*

The enol sulfonates from the α-acylacetoacetates *(35)*, R = H and NO_2, gave the acetylenic acids *(36)*, R = H and NO_2, by loss of acetic acid rather than the ketones by decarboxylation. This was due to the *trans* configuration of the acyl and sulfonate groups about the

[31] *I. Fleming* and *J. Harley-Mason*, J. chem. Soc. (London) *1963*, 4778.

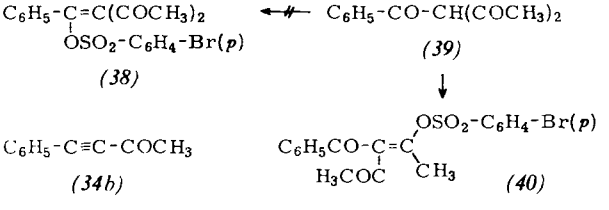
[32] *K. Bodendorff* and *P. Kloss*, Angew. Chem. *75*, 139 (1963); Angew. Chem. internat. Edit. *2*, 98 (1963).

double bond. The configuration was proved in the *o*-nitrophenyl case where reductive cyclization gave the quinaldine *N*-oxide *(37)*. It is interesting that the loss of acetic acid is a better source of electrons for the developing triple bond than decarboxylation: the yield of *o*-nitrophenylpropiolic acid from the enol sulfonate *(35)*, R = NO_2, was 65% compared with a trace from the corresponding malonate derived enol sulfonate *(25)*.



(35) *(36)* *(37)*

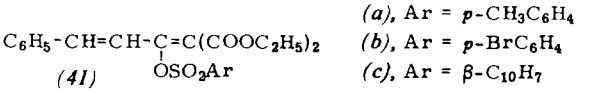
The utility of this fragmentation reaction is probably also limited to those cases where a double bond or aromatic ring is conjugated with the enol double bond. An attempt to prepare 4-phenylbut-3-yn-2-one *(34b)* from the enol sulfonate *(38)* was thwarted when the enol sulfonate actually obtained *(40)* was that in which enolization was not toward the phenyl group. This enol sulfonate *(40)* gave no acetylenic products with alkali [29].



(38) *(39)* *(34b)* *(40)*

2.3. Mechanistic Considerations

An examination of the gross features of both decarboxylative and deacylative eliminations reveals an interesting situation. The reaction rate is very dependent on the leaving group. For example, the three enol sulfonates *(41a)*, *(41b)*, and *(41c)* were treated with alkali under comparable conditions. It was found that the *p*-toluenesulfonate *(41a)* had undergone predominantly carboxylate ester hydrolysis to give the corresponding acid with very little elimination; the *p*-bromobenzenesulfonate *(41b)* had undergone elimination to phenylpropiolic acid; and the β-naphthalenesulfonate *(41c)* was intermediate in reactivity giving some elimination and some ester hydrolysis.

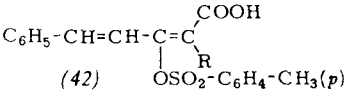


(41) *(a)*, Ar = *p*-$CH_3C_6H_4$; *(b)*, Ar = *p*-BrC_6H_4; *(c)*, Ar = β-$C_{10}H_7$

The group conjugated with the enol double bond has a large influence on the extent to which elimination is observed. In fact the groups which encourage elimination are those which most easily support a carbonium ion at the carbon atom bearing the sulfonate group and those groups which prevent elimination are those which would least tolerate such a carbonium ion.

The reaction also shows a dependence on the nature of the group which is the source of electrons for the developing triple bond. These observations support the expectation of a concerted elimination process (cf. also ref. [28a]). It is interesting to note that, for elimination to occur under the mild conditions cited, the range of groups in the various positions around the enol double bond is fairly narrow.

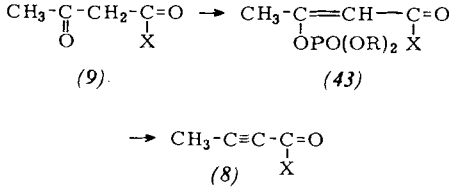
That base catalysis is indeed necessary was shown by examination of the behavior of the *p*-toluenesulfonate of 3-phenylpropenoylmalonic acid enol in a non-basic medium. When the diacid *(42a)* was heated in water for 15 min, decarboxylation *without* elimination occurred, affording the toluene-*p*-sulfonate *(42b)*, without formation of the acetylenic acid *(17)*, R = C_6H_5–CH=CH. On the other hand, treatment of *(42a)* in aqueous base is known [28] to give this acid by concerted elimination-decarboxylation.



(42) *(a)*, R = COOH; *(b)*, R = H

3. Eliminations from Enol Phosphates

Following the biosynthetic analogies discussed in Section 1.2, the conversion of the acylacetates *(9)* to the acetylenes *(8)* was investigated [33,34], using the biologically relevant phosphate leaving group [2,19] in the form of an enol phosphate derivative *(43)*.



(9) *(43)* *(8)*

3.1. Preparation of Enol Phosphates

Vinyl phosphates [35] may be obtained from enolizable ketones by reaction of the sodium enolate with a phosphoryl chloride; this reaction yields the *trans* isomers exclusively (*cis* and *trans* refer, as usual, to the carbon chain). With ketones that enolize little or not at all the interaction of the α-chloroketone with triethyl phosphite by the Perkow reaction [36,37,63] yields predominantly the *cis*-enol phosphate [equation (m)].

The Perkow reaction may also be used to obtain *cis*-enol phosphates from enolizable ketones. Finally, methyl ketones are transformed, through their chloromethyl derivatives, into vinyl phosphates containing a terminal methylene group. In all cases the yields of vinyl phosphates are good to excellent.

---

[33] *J. C. Craig* and *M. Moyle*, Proc. chem. Soc. (London) *1962*, 149.

[34] *J. C. Craig* and *M. Moyle*, J. chem. Soc. (London) *1963*, 3712.

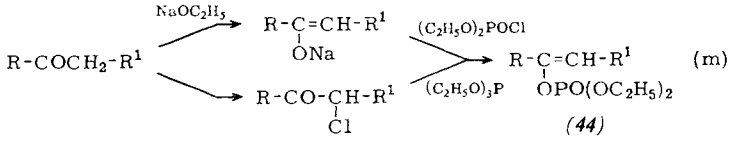
[35] *F. W. Lichtenthaler*, Chem. Reviews *61*, 607 (1961).

[36] *W. Perkow*, *K. Ullerich*, and *F. Meyer*, Naturwissenschaften *39*, 353 (1952); *W. Perkow*, Chem. Ber. *87*, 755 (1954).

[37] *P. A. Chopard*, *V. M. Clark*, *R. F. Hudson*, and *A. J. Kirby*, Tetrahedron *21*, 1961 (1965).

3.2. Acetylenes from Enol Phosphates

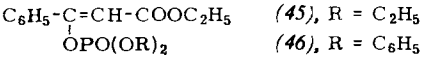
A number of enol phosphates *(44)* were prepared [34] and their base-catalyzed elimination was examined under various conditions [34].



Reaction of dilute aqueous sodium hydroxide on the *trans*-enol phosphate *(45)* in 50% aqueous dioxane or 50% aqueous ethanol at 5 °C or at 25 °C gave only acetophenone. Using potassium hydroxide in refluxing absolute ethanol gave up to 20% of phenylpropiolic acid, with much acetophenone. The findings that elimination was retarded by aqueous media and accelerated by using an alcoholic solution and a stronger base (ethoxide) suggested the characteristics of an E2 elimination in which, owing to the greater charge-dispersal in the E2 transition state, the E2 rate changes faster than the S_N2 rate with decreasing ion-solvating power of the medium [38].

Accordingly, the use of sodamide in liquid ammonia at −70 °C gave phenylpropiolamide smoothly in 72% yield. In agreement with the greater base strength of amide ion than of hydroxyl ion, the absence of acetophenone or of β-ketoester from the product showed that the competing substitution had been suppressed under these conditions. At −33 °C phenylacetylene was the sole product (75%), owing to a fission [40,41] which formally resembles the Haller-Bauer [39] cleavage of non-enolizable ketones by sodamide (see below).

Identical results were obtained when diphenyl *trans*-2-ethoxycarbonyl-1-phenylvinyl phosphate *(46)* was used.



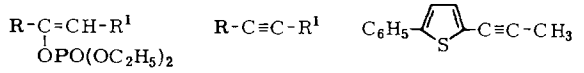
(45), R = C_2H_5
(46), R = C_6H_5

The *cis*-enol phosphate *(45)*, subjected to the previously used conditions (sodamide in liquid ammonia at −33 °C), gave phenylacetylene in almost the same (65%) yield as the *trans*-isomer, and free from ketone or ester. At −70 °C most (80%) of the enol phosphate was recovered, with 12% (spectroscopic) of phenylpropiolamide.

The formation of phenylpropiolamide is in agreement with the known greater ease of conversion of esters into amides in α,β-acetylenic than in α,β-ethylenic systems. For instance, ethyl phenylpropiolate affords phenylpropiolamide with liquid ammonia alone, while both ethyl cinnamate and diethyl 2-ethoxycarbonyl-1-phenyl-vinyl phosphate *(45)* are unchanged by this reagent. It is evident that the elimination of the *trans*-enol phosphate *(45)* at −70 °C is appreciably faster than that of its *cis*-isomer, and that, if the *cis*-enol phosphate had under the conditions of this experiment (−70 °C) suffered isomerization to the *trans*-isomer, then the whole system would have undergone elimination. That this was not the case was shown by the recovery of 80% of the *cis*-enol phosphate.

It is well known that base-promoted *trans*-elimination is fast because the atoms concerned lie in a coplanar arrangement in which the dihedral angle between hydrogen and the departing anion is 180 °. However, in the *cis*-enol phosphate *(45)* in which the dihedral angle is 0 °, the transition state is still flat and coplanar, and a coplanar *cis*-elimination should thus readily take place. It was recently reported [42] that *trans*-2-phenylcyclopentyl toluene-*p*-sulfonate and its *cis*-isomer both underwent base promoted E2 elimination, with a ratio k_{trans}: k_{cis} of only 14:1, while the 2-phenylcyclohexyl ester had $k_{trans}:k_{cis} > 10^4:1$. The reason advanced was that the small dihedral angle in the *cis*-cyclopentyl system (*ca.* 12 °) approaches coplanarity whereas this would not be the case for the *cis*-cyclohexyl compounds in which the dihedral angle will remain at 60 °.

In our cases, the ratio $k_{trans}:k_{cis}$ is at least 6:1, and *cis*- and *trans*-coplanar eliminations both appear relatively easy. In agreement, the *trans*-enol phosphate *(44a)* from deoxyanisoin, and the *cis*-enol phosphate *(44b)* from deoxybenzoin, both gave the expected diphenylacetylenes in >90% yield. The enol phosphates *(44c)* and *(44d)* gave phenyl- and 4-diphenylylacetylene, respectively, in high yield.



(44) *(47)* *(48)*

Table 2. Enol phosphates *(44)* and acetylenes *(47)* obtained from acylacetates [34,43].

	R	R^1	Yield of *(44)* (%)	Yield of *(47)* (%) [a]
	C_6H_5	$CO_2C_2H_5$	*trans*: 75	72 [b]
	C_6H_5	$CO_2C_2H_5$	*trans*	75
	C_6H_5	$CO_2C_2H_5$	*cis*: 88	65
	C_6H_5	$CO_2C_2H_5$	*cis*	12 [b, c]
	C_6H_5	$CO_2C_2H_5$	*trans-(46)*: 80	70
(a)	*p*-$CH_3O-C_6H_4$	*p*-$CH_3O-C_6H_4$	*trans*: 85	94
(b)	C_6H_5	C_6H_5	*cis*: 85	90
(c)	C_6H_5	H	85	75
(d)	*p*-$C_6H_4-C_6H_4$	H	90	92

[a] Yield based on *(44)*.

[b] Experiment at −70 °C; all other experiments in Table at −33 °C. Product was *(47)*, $R^1 = CONH_2$.

[c] 80% of *(44)* was recovered.

[38] *K. A. Cooper, M. L. Dhar, E. D. Hughes, C. K. Ingold, B. J. MacNulty*, and *L. I. Woolf*, J. chem. Soc. (London) *1948*, 2043; *J. Hine*: Physical Organic Chemistry. McGraw-Hill Book Comp., New York 1962, p. 205.

[39] *A. Haller* and *E. Bauer*, C. R. hebd. Séances Acad. Sci. *147*, 824 (1908); *K. E. Hamlin* and *A. W. Weston*, Org. Reactions *9*, 1 (1957).

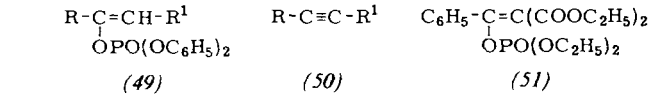
[40] *J. C. Craig* and *M. Moyle*, Proc. chem. Soc. (London) *1962*, 283.

[41] *J. C. Craig* and *M. Moyle*, J. chem. Soc. (London) *1963*, 4402.

[42] *C. H. DePuy, R. D. Thurn*, and *G. F. Morris*, J. Amer. chem. Soc. *84*, 1314 (1962).

Another example is the synthesis[43] of the natural product 2-phenyl-5-(prop-1-ynyl)thiophene *(48)*, isolated from *Coreopsis grandiflora*[44] together with its triacetylenic precursor 1-phenyl-1,3,5-heptatriyne, and illustrating the close biogenetic correspondence between the thiophene and the diacetylenes, which has been so elegantly proved by *K. E. Schulte*[45] by his conversion of the latter into the former.

Nakaminami and his colleagues have prepared[30,48,49] diphenyl *trans*-2-methoxycarbonyl-1-phenylvinyl phosphate *(49b)* and obtained phenylacetylene (28%) by action of sodamide in liquid ammonia, and phenylpropiolic acid in low yield by the use of sodium *tert*-butoxide in benzene. The enol phosphate from dibenzoylmethane *(49a)* was cleaved by sodamide to give phenylacetylene in low yield, but afforded 76% of the acetylenic ketone *(50a)* when sodium *tert*-butoxide in *tert*-butanol was used. No acetylenes were obtained from the enol phosphates of ethyl acetoacetate *(49c)* and acetylacetone *(49d)* (Table 3).



(49) *(50)* *(51)*

Table 3. Acetylenes *(50)* obtained from enol phosphates *(49)* [30, 48, 49].

	R	R^1	Yield of *(49)* (%)	Yield of *(50)* (%) [a]
(a)	C_6H_5	COC_6H_5	59	low [b]
	C_6H_5	COC_6H_5	59	76 [c]
(b)	C_6H_5	$COOCH_3$	62	28 [b, d]
	C_6H_5	$COOCH_3$	62	low [e]
(c)	CH_3	$COOC_2H_5$	64	—
(d)	CH_3	$COCH_3$	69	—

[a] Yield based on *(49)*.

[b] Using sodamide in liquid ammonia.

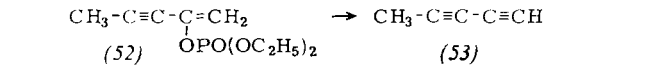
[c] Using sodium *tert*-butoxide in *tert*-butanol.

[d] Together with small amounts of phenylpropiolic acid.

[e] Using sodium *tert*-butoxide in benzene.

The enol phosphate *(51)* was reported[28] to give only hydrolysis products on treatment with alkali under a variety of conditions, with no triple-bond absorption in the infrared spectrum.

Reaction of propyne with chloroacetyl chloride gave 1-chloropent-3-yn-2-one which readily formed the enol phosphate *(52)*. This acetylenic enol phosphate

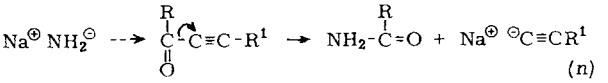


(52) *(53)*

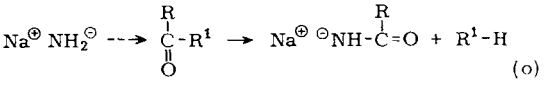
underwent elimination smoothly[34] to give penta-1,3-diyne *(53)*. The method is thus applicable to the transformation of any terminal acetylene into a monosubstituted diacetylene.

The cleavage reaction with sodamide mentioned earlier was found[40,41] to be general for esters and amides derived from α,β-acetylenic acids which do *not* possess a γ-hydrogen atom. The product is the free terminal acetylene in high yield, accompanied by urea. Cinnamide is recovered quantitatively under these conditions.

The reaction [equation (n)] must be analogous to that of the Haller-Bauer reaction [equation (o)] in which sodamide cleaves a non-enolizable ketone to give an amide and a hydrocarbon after prolonged refluxing in toluene[39]. The new fission reaction is useful in a number of ways. It may, for instance, be used to protect a terminal acetylene by carboxylation and then to remove the protecting group at −33 °C converting the acid either to the ester or to the amide.

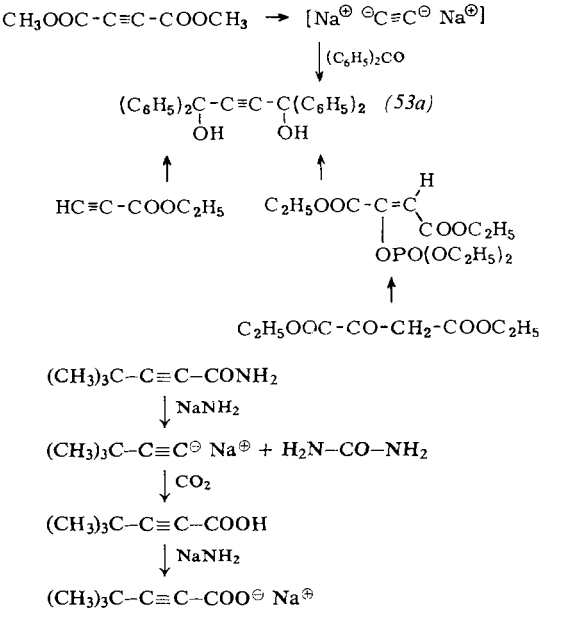


(n)



(o)

Thus, dimethyl acetylenedicarboxylate is cleaved, and on addition of benzophenone gives 1,1,4,4-tetraphenyl-2-butyne-1,4-diol *(53a)*. The same product is obtained from ethyl propiolate, and from oxaloacetic ester, *via* the enol phosphate. The amide of *tert*-butylpropiolic acid was completely cleaved to sodium 3,3-dimethylbut-1-yn-1-ide; no acid was produced. Therefore *no* additional activation of the triple bond is necessary for cleavage to occur. Carboxylation gave back the original acid. The acids themselves were completely stable after the same treatment. showing that the electron-repelling carboxylate ion resists attack by sodamide.



The sodamide-induced cleavage of the enol phosphates *(49a)* and *(49b)* and of the acetylenic ketone *(50a)*, to give phenylacetylene[30,48,49] are clearly further examples of the same reaction.

When the enol phosphate *(54)* contained a methylene group adjacent to the carbon-carbon double bond, allenic products *(55)* were obtained on base-catalyzed elimination[50,51]. The enol phosphates from propio-

[43] *J. C. Craig* and *M. Moyle*, J. chem. Soc. (London) *1963*, 3907.

[44] *J. S. Sörensen* and *N. A. Sörensen*, Acta chem. scand. *12*, 765, 771 (1958).

[45] *K. E. Schulte*, *J. Reisch*, and *L. Hörner*, Chem. Ber. *95*, 1943 (1962); *K. E. Schulte*, *J. Reisch*, *W. Herrmann*, and *G. Bohn*, Arch. Pharmaz. *296*, 456 (1963).

[46] *I. Fleming* and *J. Harley-Mason*, Chem. and Ind. *1962*, 560.

[47] *I. Fleming* and *J. Harley-Mason*, Chem. and Ind. *1962*, 561.

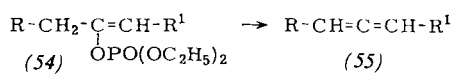
[48] *M. Nakagawa*, *G. Nakaminami*, *F. Ogura*, and *H. Ono*, Bull. chem. Soc. Japan *35*, 1485 (1962).

[49] *M. Nakagawa*, *G. Nakaminami*, *F. Ogura*, and *H. Ono*, Bull. chem. Soc. Japan *35*, 1488 (1962).

[50] *J. C. Craig* and *M. Moyle*, Proc. chem. Soc. (London) *1963*, 56.

[51] *T. L. Jacobs* and *D. Dankner*, J. org. Chemistry *22*, 1424 (1957).

phenone and from pentadecan-2-one gave no acetylene or allene, only hydrolysis to the parent ketone occurring [34] (Table 4).



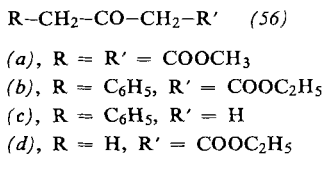
(54) *(55)*

Table 4. Enol phosphates *(54)* giving allenes *(55)* [34].

R	R′	Yield of *(54)* (%)	Yield of *(55)* (%)
C_6H_5	C_6H_5	87; *cis*	77
CH_3	C_6H_5	86; *cis*	75
C_6H_5	H	87;	77
C_6H_5	CH_3	85; *cis*	—
n-$C_{13}H_{27}$	H	not reported	—

The activation for an enol phosphate *(44)* to be transformed into an acetylene thus requires the presence of a double linkage in the group R′ in conjugation with the incipient triple bond; or, if R′ = H, that the group R contains a double bond similarly situated. These findings suggested that a natural β-polyketone, in which each methylene group is doubly activated by a carbonyl group, should be transformed into an acetylene or allene under even milder conditions than those for the enol esters.

The simplest available model for a β-polyketone was acetonedicarboxylic ester *(56a)*. Its enol phosphate was easily transformed [52] into the allene, dimethyl penta-2,3-dienedioate *(55)*, R = R′ = $COOCH_3$, *e.g.*, with dilute aqueous alkali in 10 seconds at 0 °C, or with aqueous sodium carbonate solution in 90 min at room temperature.



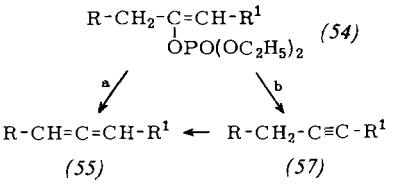
(a), R = R′ = $COOCH_3$
(b), R = C_6H_5, R′ = $COOC_2H_5$
(c), R = C_6H_5, R′ = H
(d), R = H, R′ = $COOC_2H_5$

Some concurrent hydrolysis occurs in each case.

When one of the methoxycarbonyl groups was replaced by phenyl, the resulting γ-phenylacetoacetic ester *(56b)* gave an enol phosphate which required 24 h for complete reaction with alkali, giving a mixture of 66% of the allenic *(59)* and 33% of the 3-ynoic acid *(60)*. None of the 2-ynoic acid was found. Further removal of activating groups from the original ester left either acetoacetic ester *(56d)* or phenylacetone *(56c)*. Their enol phosphates gave neither allene nor acetylene even after 24 h with aqueous alkali.

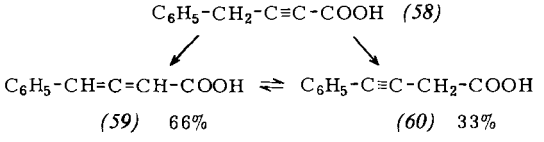
Successful elimination with aqueous base at room temperature therefore requires the presence of activating groups on both sides of the three-carbon system in the enol phosphate, *i.e.*, in both R and R′, in a manner similar to that in a natural β-polyketone. It should be recalled, however, that in the enol phosphate which lacks the methylene group adjacent to the enol double bond, only hydrolysis occurred with aqueous alkali even if both R and R′ were activating groups. Thus the enol phosphate *(44)*, R = R′ = $COOC_2H_5$, undergoes only hydrolysis with aqueous base, while its higher homolog *(54)*, R = R′ = $COOC_2H_5$, is transformed into the allene under the same conditions.

[52] *J. C. Craig* and *M. Moyle*, J. chem. Soc. (London) *1963*, 5356.



(54) *(55)* *(57)*

Formation of the allene *(55)* could take place from the enol phosphate *(54)* either by route a or by route b. Whereas only dimethyl penta-2,3-dienedioate is expected from acetonedicarboxylic ester, in the case of γ-phenylacetoacetic ester the product could be the allene or the acetylene. Since 4-phenyl-2-butynoic acid *(58)* on identical treatment gave a mixture of 66% of the allene *(59)* and 33% of the 3-ynoic acid *(60)*, it is not possible to say whether or not formation of the allene proceeded through the intermediate acetylene [52]. When the elimination reaction was carried out in deuterium oxide [53], the allene *(59)* produced was found to be uniformly deuteriated in both the 1- and 3-positions of the allene moiety, clearly due to intervention of *(60)*.



(59) 66% *(60)* 33%

In an effort to discover a base which might cause elimination of the phosphate from the enol *(54)* without also bringing about the acetylene → allene isomerization, ethyl 4-phenyl-2-butynoate was subjected to a range of bases of decreasing pK_a under otherwise identical conditions (6 h in boiling benzene). With triethylamine (pK_a 10.74), complete disappearance of the acetylenic ester was observed, and the product (which in the infrared spectrum showed only allenic absorption) consisted of 30% of ethyl 4-phenyl-3-butynoate and 70% of the allene ester as determined from the NMR spectrum.

When benzyldimethylamine (pK_a 8.93) and 4-methylmorpholine (pK_a 7.41) were used, the acetylenic absorption in the infrared spectrum was completely replaced by the allene band, while with diethylaniline (pK_a 6.56) the acetylene was recovered quantitatively.

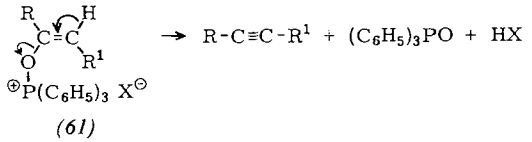
The enol phosphate *(54)*, in which R = C_6H_5, R′ = $COOC_2H_5$, under the same conditions gave 75% elimination when triethylamine was used (complete elimination required 8 h); 4-methylmorpholine afforded only recovered phosphate. It therefore follows that any base of pK_a >7.4 (necessary for the elimination) will also cause the rearrangement to the allene (and subsequently to the 3-ynoic ester), and that the acetylene intermediate, if present, can never be isolated from the reaction.

4. Eliminations from Enol Phosphonium Salts

In view of the successful conversion of enol phosphates and enol sulfonates into acetylenes, the corresponding

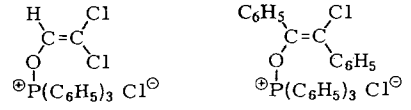
[53] *J. C. Craig* and *M. Moyle*, unpublished.

enol phosphonium ester *(61)* might be expected to react in the same manner.



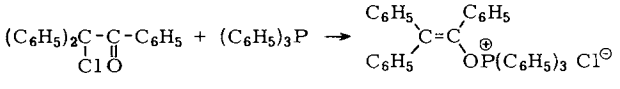
(61)

Such an enol phosphonium salt *(61)*, R = R′ = C_6H_5, is the possible intermediate in the production of diphenylacetylene from the reaction of triphenylphosphine and α-chlorodeoxybenzoin in refluxing benzene [62]. However, although such compounds have been postulated by *Trippett* [54] only two [*(62)* and *(63)*] could be isolated as unstable solids [55].



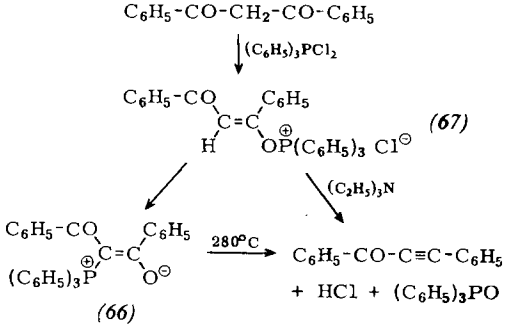
(62) *(63)*

The stable crystalline enol phosphonium salt *(65)* no longer has a hydrogen attached to the double bond [56].



(64) *(65)*

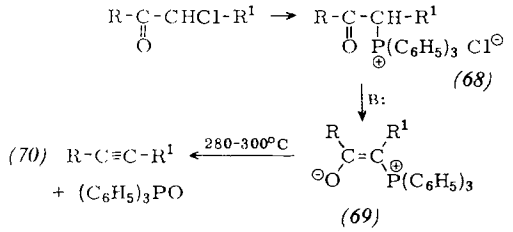
Enol phosphonium salts *(61)* are probable intermediates in the reaction of dihalotriphenylphosphoranes with β-keto esters and β-diketones [57] in the presence of base. However, in some cases [58] phosphoranes *(66)* are isolated which then require pyrolysis at 280 °C to give acetylenes, yet in other instances [55] the method gives enol phosphonium salts *(67)* which undergo elimination to form acetylenes merely by the action of triethylamine.



(66) *(67)*

In most other cases examined, a "normal" phosphonium salt *(68)* is formed in which phosphorus is attached to carbon, and which is converted into a phosphorane *(69)* by aqueous alkali. These phosphoranes are analogous to the *cis*-enol phosphates mentioned above, and have been successfully converted into the acetylenes *(70)* [58–60] by pyrolysis at 280–300 °C for 1 h.

The reaction requires that either R or R′ must be a phenyl or carbonyl group or the equivalent, but not hydrogen. The requirements for activation adjacent to the incipient triple bond are thus similar to those found in the other elimination reactions (Table 5).

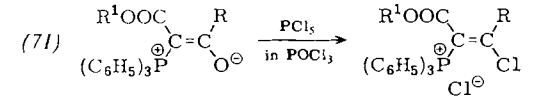


(68) *(69)* *(70)*

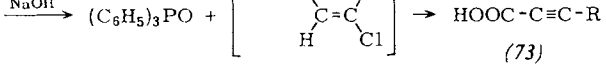
Table 5. Acetylenes *(70)* from phosphoranes *(69)*.

R	R′	Yield of *(70)* (%)	Ref.
C_6H_5	C_6H_5	–	[59]
CH_3–CH_2–CH_2	COO C_2H_5	–	[58]
CH_3	C_6H_5	58	[58]
CH_3–CH=CH	COO C_2H_5	87	[58]
C_6H_5	COO C_2H_5	91	[58]
C_6H_5	COOH	73	[60]
C_6H_5–CH=CH	COOH	65	[60]
m-NO_2–C_6H_4	COOH	66.5	[60]
p-Cl–C_6H_4	COOH	81.1	[60]
o-Cl–C_6H_4	COOH	66.2	[60]
$CH_3(CH=CH)_2$	COO Et	21	[58]
C_6H_5	CN	84	[58]
CH_3–CH_2–CH_2	CN	60	[58]
CH_3	COO Et	91	[58, 60]
p-CH_3–C_6H_4	COOH	81	[60]
α-naphthyl	COOH	81.5	[60]
o-CH_3O–C_6H_4	COOH	74.6	[60]
m-CH_3O–C_6H_4	COOH	29	[60]
2-furyl	COOH	75.5	[60]

The preparation of the phosphoranes from α-chloro ketones is however not a general method, and the phosphoranes *(69)* have usually to be synthesized by the action of acid chlorides on Wittig reagents [54,60]. The method has been markedly improved by conversion of the phosphoranes *(71)* to the chlorinated



(71) *(72)*



(73)

Table 6. Acetylenic acids *(73)* prepared from phosphoranes *(71)* [61].

R′	Yield of *(73)* (%)	R′	Yield of *(73)* (%)
C_6H_5	73	CH_3	17
p-CH_3–C_6H_4	100	*m*-CH_3O–C_6H_4	100
p-Cl–C_6H_4	90	α-naphthyl	87
m-NO_2–C_6H_4	94	2-furyl	56

ylids *(72)* [61], which then split to give the corresponding acetylenic acids *(73)* after 20 minutes' boiling with dilute alkali (Table 6).

Received: July 22, 1968 [A 700 IE]
German version: Angew. Chem. *81*, 437 (1969)

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[56] *A. J. Speziale* and *R. D. Partos*, J. Amer. chem. Soc. *85*, 3312 (1963).
[57] *L. Horner* and *H. Oediger*, Chem. Ber. *91*, 437 (1958).
[58] *S. T. D. Gough* and *S. Trippett*, J. chem. Soc. (London) *1962*, 2333.
[59] *S. Tripett* and *D. M. Walker*, J. chem. Soc. (London) *1959*, 3874.
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[62] *S. Trippett* and *D. M. Walker*, J. chem. Soc. (London) *1960*, 2976.
[63] *H. Hoffmann* and *H. J. Diehr*, Angew. Chem. *76*, 944 (1964); Angew. Chem. internat. Edit. *3*, 737 (1964).

The Meaning and Use of the Arrhenius Activation Energy

By M. Menzinger and R. Wolfgang[*]

The nature of the Arrhenius activation energy and frequency factor is reexamined in terms of information now becoming available on the microscopic aspects of collisional reactions. It is pointed out that the activation energy is not generally equal to the threshold for reaction, and its correct conceptual meaning is discussed. The temperature dependence of this quantity and its relation to the threshold energy is developed for a number of representative forms of the energy dependence of the reaction cross-section (excitation function). The uses and limitations of the activation energy as a means of evaluating thresholds, excitation functions, and the presence of tunneling processes are discussed.

1. Introduction

The Arrhenius equation, now eighty years old, continues to play a dominant role in classical studies of chemical kinetics. It enables the experimentalist to express the dependence of the rate constant over a wide range of temperatures in terms of only two empirical parameters:

$$k(T) = A\exp(-E_{exp}/kT) \qquad (1)$$

These are the "experimental activation energy" (E_{exp}) and the "pre-exponential factor" (A). The meaning of these parameters has been the subject of much debate. While the Arrhenius equation deals with macroscopic aspects of chemical reactions, the field has recently been revolutionized by newer, non-classical techniques (molecular beams[1], photochemical[2–4], hot atom[5], mass spectrometric[6], trajectory calculations[7]) which emphasize the more fundamental microscopic nature of chemical collisions. These methods can give direct information on the dependence of the reaction rate on energy. Such data are usually presented as energy or velocity dependent cross-sections, ($\sigma(E)$ or $\sigma(v)$), also known as "excitation functions". It seems appropriate at this time to review our understanding of the meaning of the Arrhenius parameters in terms of this new knowledge.

The Arrhenius equation was first discovered by *Hood*[8] as a purely empirical relationship. Subsequently *van't Hoff*[9] and *Arrhenius*[10,11] showed that it was theoretically consistent with thermodynamical theory. They interpreted the activation energy as the height of the energy barrier which has to be overcome by the relative translational motion of the reactants in order for reaction to occur. This concept is basically correct but oversimplified since, as we now know, the probability of reaction is a complex function of internal as well as translational energy and also of geometrical configuration.

Various attempts[12–15] to theoretically justify the Arrhenius equation all lead to equations of the type

$$k(T) = B(T)\exp(-E_0/kT) \qquad (2)$$

Here E_0 is the threshold, the lowest relative translational energy at which reaction can occur. No single one of these forms has, however, been particularly successful. The reason for this is not hard to understand, for each presupposes a specific assumption as to which part of the total energy of the system is available to drive such reaction[15]. Every such model implies a specific excitation function – the translational energy dependence of the microscopic reaction

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[1] *M. Menzinger* and *R. Wolfgang*, J. Amer. chem. Soc. *89*, 5992 (1967); J. chem. Physics *50*, 2991 (1969).

[2] *A. Kuppermann* and *J. M. White*, J. chem. Physics *44*, 4352 (1966).

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[9] *J. H. van't Hoff*: Etudes de Thermodynamique Chimique. F. Muller and Co., Amsterdam 1884.

[10] *S. Arrhenius*, Z. physik. Chem. *4*, 226 (1889).

[11] Cf. *K. Laidler*: Chemical Kinetics. McGraw-Hill, New York 1965.

[12] For approaches to Equation (2) using collision theory, see [7a] and [13]. Ref. [14] gives the Equilibrium Transition State Theory.

[13] *M. Eliason* and *J. O. Hirschfelder*, J. chem. Physics *30*, 1426 (1959).

[14] *S. Glasstone, K. Laidler*, and *H. Eyring*: The Theory of Rate Processes. McGraw-Hill, New York 1941.

[15] Transition State Theory attempts to approximate the information contained in $\sigma(E)$ by estimates of partition functions and the transmission coefficient $\varkappa$. However, there exists to date no reliable method to compute these functions on an *a priori* basis. On the other hand, there is considerable promise that $\sigma(E)$ for many gas phase processes will be directly accessible through theory as well as experiment. This should in the future tend to favor an approach to gas phase kinetics based on microscopic collision dynamics.

cross-section $\sigma(E)$. For instance, the well-known "line-of-centers" model [13,16] implies a cross-section dependence of the form

$$\sigma = \sigma_{AB}\left(1 - \frac{E_0}{E}\right) \tag{3}$$

where E is the translational energy of the reactants, and σ_{AB} the hard sphere collision cross-section. But it seems reasonable that the excitation function $\sigma(E)$ can have many forms [7,17,18] depending on the nature of the reaction. Thus, no single version of Equation (2) is likely to be very widely applicable.

For this reason as well as for its simplicity, the original Arrhenius equation still provides by far the most useful format within which to summarize the data of classical kinetics. As a practical matter, it nearly always yields values of E_{exp} and A which are constant within the experimental temperature range and limits of accuracy.

If it is futile to search for a "better" equation than that of Arrhenius, it becomes all the more necessary to understand the precise meaning of the Arrhenius parameters. In particular, it should be a matter of practical importance to chemists to understand the difference between the activation energy and the threshold – two quantities which are commonly and erroneously assumed to be identical.

1.1. Arrhenius Parameters and Microscopic Reaction Cross-Section

The activation step of any chemical reaction always involves a collisional process. The Arrhenius activation energy reflects that collision step which is rate determining [19]. This is true even for unimolecular reactions since the decaying entity is always formed by some kind of bimolecular interaction.

The fundamental measure of the probability of any collisional reaction is the cross-section $\sigma(v)$, defined for collisions at relative velocity v by

$$\text{Rate} = -\left(\frac{dn_A}{dt}\right)_v = \sigma(v)v n_A n_B \tag{4}$$

Here n_A and n_B are the concentrations (molecules/cc) of reactants A and B. In order to interpret the Arrhenius parameters, they must be related to this cross-section. (At this point, we should note that the cross-section is defined for bimolecular reactions only, and that which follows is therefore inapplicable to higher order collisions. It should be meaningful for solution reactions, however, at least to the extent that effects of the medium can be included in the cross-section.)

The bimolecular rate constant k_v, for reaction between reactants A and B moving at relative velocity v, is defined by

$$\text{Rate} = -\left(\frac{dn_A}{dt}\right)_v = k_v n_A n_B \text{ (molecules/cc)} \tag{5}$$

Comparison of (4) and (5) gives

$$k_v = \sigma(v)v \tag{6}$$

If the reacting species possesses a distribution of velocities $f(T,v)$, then the rate constant (6) has to be weighted by this function to give the average rate constant

$$k(T) = \int_0^\infty f(T,v)\sigma(v)v\,dv \tag{7}$$

Note that the integrand of this equation gives the relative number of reactive collisions at velocity v. For a system at thermal equilibrium where $f(T,v)$ is given by the Maxwell Boltzmann distribution, the general relationship between the temperature dependent rate constant and the energy dependent cross-section [20] can be easily derived [7a,13]:

$$k(T) = \left[\left(\frac{2}{kT}\right)^{3/2}\left(\frac{1}{\mu\pi}\right)^{1/2}\int_0^\infty E\,\sigma(E)\exp(E_0-E)/kT)dE\right]\exp(-E_0/kT) \tag{8}$$

1.2. Activation Energy

The activation energy is in practice taken to be the slope of an Arrhenius plot of $(\ln k)$ vs. $(1/T)$. This means that its experimental definition is given by the following differential form of Equation (1) [21]:

$$E_{exp} = kT^2\frac{d\ln k(T)}{dT} = -k\frac{d\ln k(T)}{d(1/T)} \tag{9}$$

[16] *E. A. Moelwyn-Hughes*: Physical Chemistry. Pergamon Press, London 1957.

[17] *E. P. Wigner*, Physic. Rev. *73*, 1002 (1948).

[18] *M. E. Riley* and *A. Kuppermann*, Chem. Physics Letters *1*, 537 (1968).

[19] If a chemical reaction involves two or more bimolecular steps, the overall activation energy will be principally determined by the rate-limiting process. If different steps are limiting over different temperature ranges, the measured activation energy will, of course, change with temperature. This type of temperature dependence associated with a complex reaction sequence, or a change in mechanism, is obvious and will not be further discussed here.

[20] For simplicity, Equation 8 does not take internal degrees of freedom into account. The reaction cross-section is assumed to already represent a suitable average over the distribution of internal states of reactants, as obtained for instance from beam experiments without internal state selection. However, the distribution of internal states is a function of temperature, and the reaction cross-section for each vibrational-rotational state is in general different. Consequently, the averaged cross-section $\sigma(E,T)$ becomes temperature dependent. Over a limited temperature range, as accessible in classical thermal experiments, this effect will be small and has been neglected in the present calculation. For the more general formula, which assumes a separate excitation function $\sigma(E,i,j)$ for each internal state and finally sums up the distribution of final states, see Ref. [7a].

[21] The full differential form of Equation (1), allowing both A and E_{exp} to be temperature dependent, is

$$k\frac{d\ln k(T)}{d(1/T)} = k\frac{d\ln A}{d(1/T)} + E_{exp} - T\frac{dE_{exp}}{dT} \tag{9a}$$

In view of the experimental definition of E_{exp} as given in Equation (9), the temperature dependences of A and E_{exp} are related as follows:

$$\frac{d\ln A(T)}{dT} = \frac{1}{kT}\frac{dE_{exp}(T)}{dT} \tag{9b}$$

Differentiating the logarithmic form of Equation (8), we then have, as first derived by *Tolman* nearly 50 years ago [7a,22,23]

$$E_{exp} = \frac{\int_0^\infty \sigma(E)\, E^2 \exp(-E/kT)\mathrm{d}E}{\int_0^\infty \sigma(E) E \exp(-E/kT)\mathrm{d}E} - \frac{3}{2} kT \qquad (10)$$

Note that the integrand in the denominator is proportional to the energy distribution of reactive collisions $f(T,E)\sigma(E)v$ [Equation (7)]. Now the average value $\bar{g}(x)$ of a function $g(x)$, where $h(x)$ is the distribution of x, is given by

$$\bar{g}(x) = \frac{\int g(x)h(x)\mathrm{d}x}{\int h(x)\mathrm{d}x} \qquad (11)$$

Hence, the first term on the right-hand side of Equation (10) is identified as the average energy ($<E^*>$) of collisions in which reaction takes place. $\frac{3}{2} kT$ is, of course, the mean energy $<E>$ of all collisions (reactive and non-reactive) in the system. The activation energy is then simply [7a,22,23]

$$E_{exp} = <E^*> - <E> \qquad (12)$$

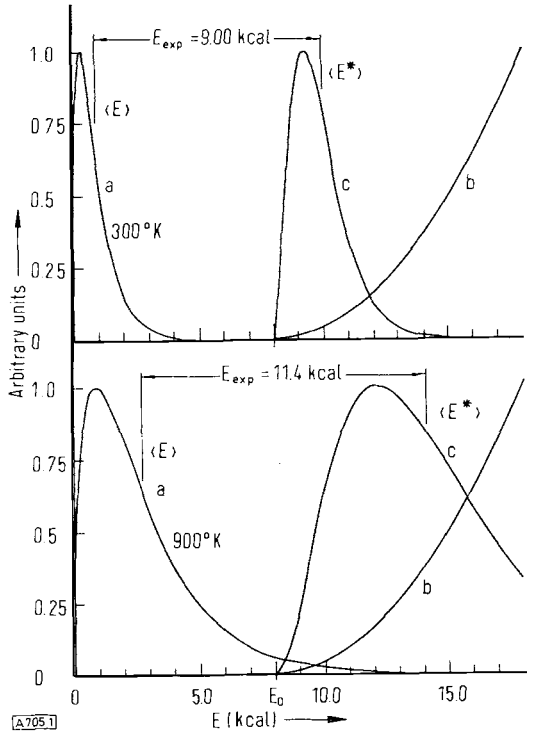


Fig. 1. Illustration of the temperature dependence of the activation energy, E_{exp}, using as an example the excitation function $\sigma(E) \propto (E-E_0)^2$, where E_0 is the threshold energy. The Maxwell-Boltzmann distribution of all collisions is shown at two temperatures together with the corresponding distribution of collisions which result in reaction. All three functions are arbitrarily normalized. The activation energy, given by the difference between the mean energy of reactive collisions $<E^*>$ and all collisions $<E>$, is seen to increase significantly with temperature. (For purposes of illustration, the ratio kT/E_0 has been chosen to be rather unrealistically high in the second part of the figure. Resulting non-equilibrium effects (see text) have been neglected but would result in some reduction of the actual $<E^*>$ and E_{exp}. Note that in Figs. 1 and 4, the energy is expressed in terms of kilocalories per mole, while the equations in the text refer to energy per molecule.

This can be visualized using Figure 1. This shows the equilibrium Maxwell Boltzmann distribution function of relative energies $f(T,E)$ of pairs of reactant molecules. Using the same energy scale, a typical cross-section function, $\sigma(E)$, is also given. The product $f(T,E)\,\sigma(E)\,v$ (see Equation 7) is then identified as the energy distribution of collisions resulting in reaction, a quantity which may be called the *reaction function.* Note that the average value of this function, $<E^*>$, will not in general coincide with its maximum, just as the average energy $<E> = \frac{3}{2}kT$ of all collisions does not coincide with the maximum of the Maxwell Boltzmann distribution function.

Several facts are qualitatively apparent from Figure 1. (1) Because of heavy damping by the Maxwell Boltzmann distribution, only reactions near threshold tend to be important in thermal systems. It is evident that knowledge of $\sigma(E)$ a few kilocalories beyond threshold allows the determination of the rate constant to high accuracy [24]. (2) As the temperature increases, the change in $<E^*>$ will not in general equal the increment in $<E>$. Hence, E_{exp} is temperature dependent. However, (3) this temperature dependence will be relatively small if E_0 or $<E^*>$ is large compared to kT, as is normally the case.

Point (3) thus accounts for the success of the Arrhenius equation, while Point (2) shows why it is not perfect.

1.3. Frequency Factor

Combining Equations (1) and (8), we obtain an expression for the pre-exponential factor in terms of the cross-section.

$$A = \left[\left(\frac{2}{kT}\right)^{3/2} (\pi\mu)^{-1/2} \int_{E_0}^\infty E\sigma(E) \exp\left(\frac{E_{exp}-E}{kT}\right) \mathrm{d}E\right] \qquad (13)$$

This expression basically consists of the product $\sigma(E)\,v$ weighted by a Maxwell Boltzmann distribution and multiplied by $\exp(E_{exp}/kT)$. It does not lend itself to as ready a conceptual interpretation as does the expression for E_{exp}. However, it is important to recognize that while the activation energy depends only on the shape of $\sigma(E)$, the frequency factor depends also on its magnitude.

1.4. Non-Equilibrium Effects

The derived relationships between the activation energy, frequency factor and the cross-section assume an equilibrium distribution of reactants. However, as reaction proceeds, the more energetic molecules will be removed. This leads to a perturbation of the Maxwell Boltzmann distribution which is counteracted by energy-exchange collisions tending to re-establish equilibrium. The net depletion of energetic molecules will tend to lower $k(T)$. This effect can be included

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into the present treatment by introducing the steady state (non-equilibrium) distribution into Equation (7) instead of the Maxwell Boltzmann distribution (Figure 2a, b).

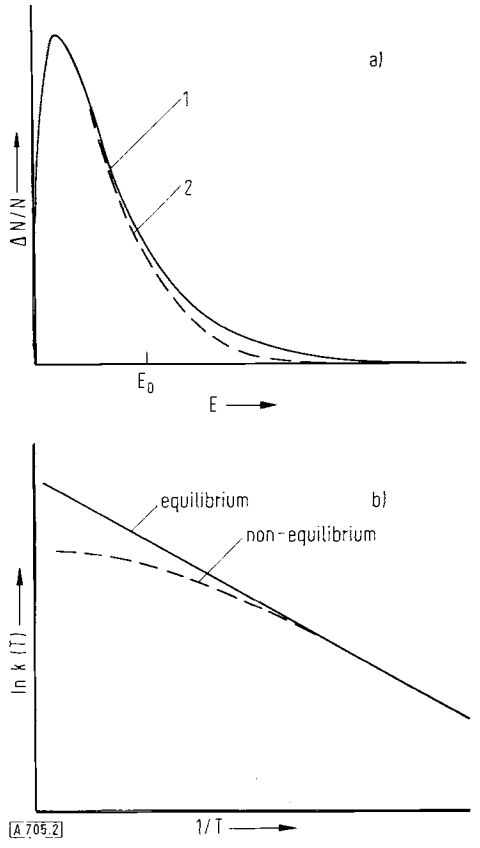


Fig. 2. a) Non-equilibrium effects for a reaction occurring at high thermal energies relative to threshold or activation energy ($E_{exp}/kT \gtrsim 5$) are schematically illustrated. Reaction depletes the number of higher energy collisions (even below E_0), so that the stationary state distribution lies below the Maxwell-Boltzmann distribution. The effect on the reaction function would be similar.
b) Schematic representation of non-equilibrium effects on the form of an Arrhenius plot.

Because of lack of detailed information on thermal relaxation mechanisms and rates, there has been relatively little work[25–35] on the exact magnitude of non-equilibrium effects. However, making reasonable assumptions, the conclusion has been reached[27] that for $(E_{exp}/kT) = 5$ the rate constant lies only about 8% below that calculated for equilibrium conditions. This deviation decreases rapidly as (E_{exp}/kT) increases. Thus, non-equilibrium effects are a limitation on the present treatment only for reactions having a very low activation energy occurring at high temperatures.

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2. Calculations

We now examine the temperature dependence of the activation energy and its relation to the threshold for a variety of plausible forms of the excitation function $\sigma(E)$. This will permit us to develop more quantitatively our notions of the significance and limitations of the Arrhenius activation energy.

As accelerator[1], photochemical[2–4], and theoretical[7] methods for the study of hot reactions are developed, we can expect a great deal of information on the shape of $\sigma(E)$ for various reactions[17,18]. At this time, however, very little is known about these functions for processes having appreciable thresholds. We shall therefore assume various forms of $\sigma(E)$, some of which appear reasonable from studies of analogous nuclear processes. Only the low energy portion of the excitation function is of concern here, since as mentioned earlier, it is its behavior in the vicinity of the threshold that governs the reaction rate constant.

Calculations have been made for excitation functions having the general form

$$\begin{aligned} \sigma(E) &= C(E-E_0)^n \qquad E > E_0 \\ \sigma(E) &= 0 \qquad\qquad\quad E \leqslant E_0 \end{aligned} \tag{14}$$

where n has the values 0, 1, 2 and 3. Results on the excitation function

$$\begin{aligned} \sigma(E) &= C\,\frac{(E-E_0)}{E} \qquad E > E_0 \\ \sigma(E) &= 0 \qquad\qquad\quad E \leqslant E_0 \end{aligned} \tag{15}$$

are also presented. This corresponds to the frequently used assumption of elementary collision theory that only the relative energy along the line-of-centers of colliding hard spheres is available to drive the reaction[13,16]. In addition, calculations on the function

$$\begin{aligned} \sigma(E) &= C\,\frac{(E-E_0)^{1/2}}{E} \qquad E > E_0 \\ &= 0 \qquad\qquad\quad E \leqslant E_0 \end{aligned} \tag{16}$$

have been made. This dependence has been shown earlier[7a] to be the only one yielding temperature-independent Arrhenius parameters.

For each of the excitation functions (14), (15), and (16), the temperature dependences of the activation energies have been evaluated using equation (8) and (9). This can be done numerically but analytical forms (due to *LeRoy* and *Blakley*[36]) are preferred. These are

$$\frac{E_{exp}}{E_0} = 1 + \frac{kT}{E_0}\left[\left(n-\frac{1}{2}\right)+\left(1+\frac{E_0}{(n+1)kT}\right)^{-1}\right]; \qquad \text{where } \sigma(E) = C(E-E_0)^n \tag{17}$$

$$\frac{E_{exp}}{E_0} = 1 + \frac{kT}{2E_0}; \qquad \text{where } \sigma(E) = C\left(\frac{E-E_0}{E}\right) \tag{18}$$

$$\frac{E_{exp}}{E_0} = 1; \qquad \text{where } \sigma(E) = C\,\frac{(E-E_0)^{1/2}}{E} \tag{19}$$

[36] *R. LeRoy* and *C. Blakley*, private communication.

Results are shown in Figure 3, where the reduced activation energy E_{exp}/E_0 is plotted against the reduced temperature kT/E_0.

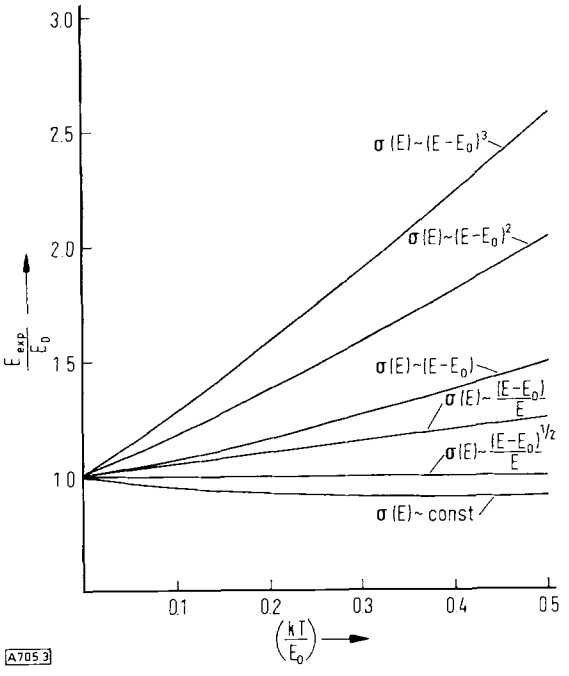


Fig. 3. Dependence of the reduced Arrhenius activation energy E_{exp}/E_0 on the reduced temperature kT/E_0 for various forms of the onset of the excitation function E_0. (Non-equilibrium effects are neglected and would become significant when $kT/E_0 \lesssim 0.2$.)

3. Discussion

Inspection of Figure 3 shows that the activation energy normally equals the threshold energy only when the mean thermal energy is extremely small compared to reaction energies. As the temperature increases, so does the difference between the activation and threshold energies. Only in the very improbable situation where the excitation function is given by Equation (16) will E_{exp} be constant and equal E_0. This is the only case in which the Arrhenius equation is "true" in the sense that its parameters are temperature invariant. Figure 4b shows that this is a result of the Maxwell Boltzmann distribution $f(T,E)$ and the reaction function $f(T,E)\sigma(E)v$ having the same temperature dependence.

If $\sigma(E)$ rises more rapidly than the function $(E-E_0)^{1/2}/E$ then E_{exp} will be less than E_0 and will show a negative temperature dependence. Figure 4a illustrates the basic reason for this, using the step function $\sigma(E)$ = constant as an example. It is seen that the reaction function is narrower than the Maxwell Boltzmann distribution, which means that the difference $<E^*>-<E>$ = E_{exp} is less than E_0. Furthermore, as the temperature rises, $<E^*>$ increases less rapidly than $<E>$, resulting in a decline in E_{exp}.

A more likely situation is one in which the excitation function rises less rapidly than $(E-E_0)^{1/2}/E$. This will

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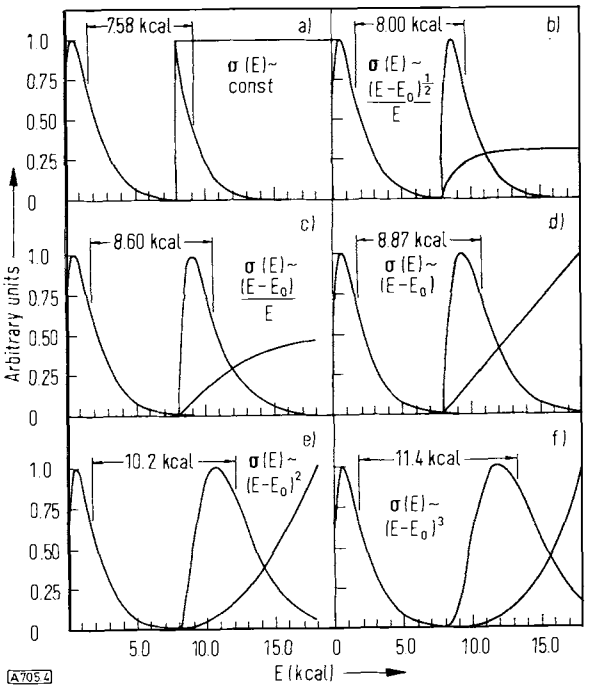


Fig. 4. Effect of the shape of the excitation function $\sigma(E)$ on E_{exp}. (For the temperature 600 °K and threshold, 8 kcal — chosen for clarity of illustration — non-equilibrium effects will have some importance, but are neglected.)

result in E_{exp} being greater than E_0 and having a positive dependence on temperature. Cases of this type are illustrated in Figures 1 and 4(c–f). The reaction function is wider than the Maxwell Boltzmann distribution resulting in the trends in E_{exp} which are shown in Figure 3.

3.1. Information on the Excitation Function from Thermal Data

Figure 4 demonstrates that knowledge of the temperature dependence of the Arrhenius activation energy can in principle be used to estimate the shape of the onset of the excitation function[38]. Such information is obtained from deviations from linearity of an Arrhenius plot of ln k vs. $1/T$. However, the temperature range over which accurate thermal rate data can be obtained is rarely great enough to make the deviations detectable. Hence, while rate constants can readily be estimated from data on the microscopic cross-section, there is generally little chance of doing the reverse.

The potential barrier for certain reactions (internal rotation) can, however, be measured directly, for instance, by microwave techniques. Information on the activation energy could then be used to estimate the low energy portion of the excitation function. This may be conveniently done by use of Figure 3. No such studies appear to have been made as yet, but such a procedure could lead to some interesting results.

[38] It has been shown [13] that $\sigma(E)$ is proportional to the Fourier transform of $k(T)$. The inversion of Equation (7) is mathematically quite feasible; however, practically it is almost hopeless.

3.2. Tunneling

As deviations from linearity of Arrhenius plots have been sought as evidence for possible tunneling [39,40], a discussion of this phenomenon in the present context is relevant. In principle, tunneling can take place through any energy level of the barrier [41–43]. Strictly speaking, this means that the threshold will be zero for an exoergic reaction and correspond to the energy of reaction for an endoergic process. In actuality, however, there is unlikely to be significant reaction until considerably higher energies are reached.

Tunneling will thus provide additional cross-section for reaction below the classical threshold for surmounting the barrier [37]. This is shown in Figure 5. The shape of this tunneling excitation function and the effective "threshold" for tunneling is a complex function of the shape of the barrier and the nature of the transmitted particle. However, the net effect of tunneling will be to make the total excitation function at very low energies be quite concave. It will resemble a function of the type $\sigma(E) \propto E^n$ where n is fairly large. As has been seen from Figure 4, this means that E_{exp} will decrease makedly at low temperatures. The present formulation can easily be made to include tunneling, by requiring $\sigma(E)$ in Equation (7) to include barrier penetration effects. In fact, every experiment which directly measures $\sigma(E)$ yields this compound excitation function.

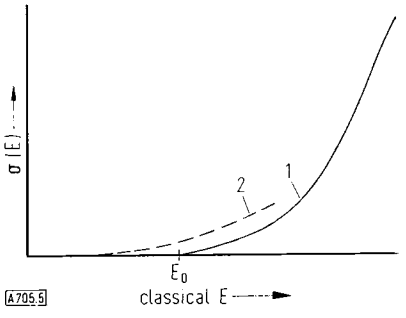


Fig. 5. Schematic illustration of the effect of quantum mechanical tunneling on the excitation function $\sigma(E)$.

A non-linearity of the Arrhenius plot showing a negative dependence of the Arrhenius activation energy on the temperature can thus be caused by tunneling [39,40,44,45]. However, such behavior can also occur if there is no tunneling but if the low energy portion of the cross-section for over-the-barrier reaction rises very slowly. Such behavior of the normal excitation function is by no means implausible, and has in fact been indicated by classical calculations [7] on potential barrier crossing in the system H + H_2. This implies that it is risky to draw firm conclusions as to the extent of tunneling on the sole basis of non-linearities in Arrhenius plots.

3.3. Activation Energy as a Measure of Threshold Energy

Figure 3 shows that for reactions having a high threshold compared to thermal energies, the activation energy will generally provide an accurate estimate of the threshold. Thus for a reaction with E_0 = 20 kcal/mole and $\sigma(E) \sim E^2$, the activation energy measured at room temperature will be E_{exp} = 21 kcal/mole.

However, the activation energy can differ quite significantly from the threshold and barrier [46] for low energy reactions. This has presented no real problem until recently, since truly fast reactions were not accessible by the more classical methods of chemical kinetics. Now, however, very rapid processes can be measured by thermal relaxation of systems following shock wave passage [47,48], flash photolysis [49,50] or temperature jump [51–53]. Line broadening techniques [54] also offer effective means of following fast reactions. With all these methods, the ratio kT/E_0 can be sufficiently large to make the activation energy an inaccurate measure of the threshold. Simple examples are atomic reactions [55–57], such as

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[46] It should be noted that the lowest pass across a potential energy surface, called the barrier or saddle point, is not necessarily equal to the threshold or lowest energy at which reaction can occur. Such a pass may not be kinematically accessible for a normal reaction trajectory across the multidimensional surface. Since the reaction paths usually show considerable curvature around the saddle point [14], the resulting centrifugal potential will cause the trajectory to follow a path of higher energy than the saddle point. This effect has only recently been given detailed consideration [58–60]. The results of *Karplus*, *Porter*, and *Sharma* [7a] show dramatically the extent of the effect of a curved reaction path. While their effective barrier height (the barrier height minus the zero point energy of the reactant molecule) for the hydrogen exchange reaction is 2.93 kcal, the reaction threshold, as obtained by classical trajectory calculations, lies at 5.69 kcal and above, depending on the rotational state of the reactant. Their Arrhenius Activation Energy is 7.435 kcal, in good agreement with experiment [40].

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$H^{\bullet} + Br_2 \rightarrow HBr + Br^{\bullet}$ $E_{exp} = 900$ cal/mole [55]

$O^{\bullet} + H_2 \rightarrow OH^{\bullet} + H^{\bullet}$ $= 6000$ cal/mole [57]

$F^{\bullet} + H_2 \rightarrow HF + H^{\bullet}$ $= 1710$ cal/mole [56]

Theoretical calculations of the corresponding potential energy surfaces have been performed for a number of simple reactions[39] leading to the height of the energy barrier. Great care has to be taken, however, in comparing E_{exp} and the calculated barrier heights, and conversely in fitting an empirical surface to the activation energy of a kinetic experiment. Yet one frequently finds examples[39,61] in the literature where activation energies are erroneously equated to the barrier height or threshold.

This work was supported by the U.S. Atomic Energy Commission. We are grateful to R. LeRoy and C. Blakley for permitting us to use results of their calculations prior to publication and to Dr. D. R. Davis for pointing out several numerical errors in the original draft of this paper.

Received: May 10, 1968 [A 705 IE]
German version: Angew. Chem. *81*, 446 (1969)

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COMMUNICATIONS

Reaction of Silver Cyanate with Cyanogen Chloride

By *E. Mayer* and *K. Kleboth*[*]

Silver cyanate reacts quantitatively with an excess of cyanogen chloride at room temperature in a bomb tube to yield silver chloride and a yellow polymeric compound.

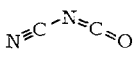
$$AgNCO + ClCN \rightarrow AgCl + (C_2N_2O)_x$$

The reaction proceeds very slowly at room temperature, and requires several weeks for completion; its course can readily be followed by IR spectroscopy. After the excess of ClCN has been pumped off the product, $(C_2N_2O)_x$, which is involatile at room temperature, remains behind together with AgCl.

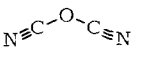
The yellow product is highly sensitive to hydrolysis; on reaction with water evolution of gas occurs and cyanate is formed. The IR spectrum of the polymer contains bands at 2275 and 1770 cm^{-1} that are characteristic for the stretching vibrations of $C \equiv N$ and $C=O$.

When heated to about 140 °C at a pressure of 10^{-2} torr, about 80% of the polymer undergoes depolymerization. At low pressure, the gaseous degradation product can be fed through a vacuum apparatus and condensed in a cold trap with liquid nitrogen. If the condensate is warmed, polymerization sets in even at a low temperature and a yellow, involatile substance is again formed whose IR spectrum is identical with that of $(C_2N_2O)_x$.

The mass spectrum of the gas formed on depolymerization contains peaks corresponding to $C_2N_2O^+$ (m/e = 68, 100%; molecular ion) and CN_2^+ (m/e = 40, 75%). The structures most likely for a molecule having the composition C_2N_2O are *(1)* (cyanogen isocyanate) and *(2)* (dicyanogen oxide),



(1)



(2)

neither of which has previously been reported. The mass spectrum provides no conclusive evidence in favor of either one of these structures. However, the high intensity of the peak m/e = 40 (CN_2^+) is more consistent with structure *(1)*.

Owing to the high polymerizability of the gas no IR spectrum could be recorded at room temperature. The low-temperature IR spectrum (condensation of the gas onto KBr at −196 °C) contains bands at 2340 s, 2250 vs, 2208 s (sh), 1458 m, 1080 w, 869 m, 608 s, 561 s, 487 m, 470 w (sh), and 462 s cm^{-1}. Both the very strong band at 2250 cm^{-1} (ν_{as} NCO)[1] and the absence of intense bands in the C–O stretching region[2] indicate the presence of cyanogen isocyanate.

Comparison with chlorine isocyanate[3] shows that replacement of chlorine by cyanogen strongly increases the polymerizability of the system.

Received: March 4, 1969 [Z 972 IE]
German version: Angew. Chem. *81*, 423 (1969)

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Selective Oxidative Coupling of Phenols by Silver Carbonate/Celite

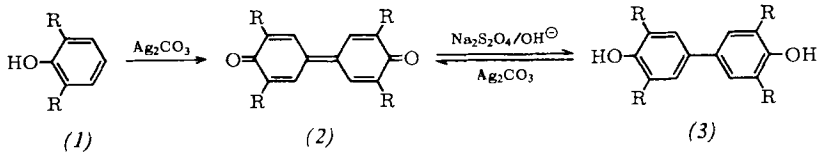
By *V. Balogh*, *M. Fetizon*, and *M. Golfier*[*]

The reaction of phenols with most oxidizing agents[1] gives a complicated mixture of quinones, dimers, and polymers and therefore the yield of a desired product is frequently poor. In the case of 2.6-dimethylphenol, where coupling between the *para* positions is enhanced, the best yields of the tetramethyl-*p*-diphenoquinone are 55–75% when such oxidizing agents as chromium trioxide, peroxides, and ferric chloride[2] are used.

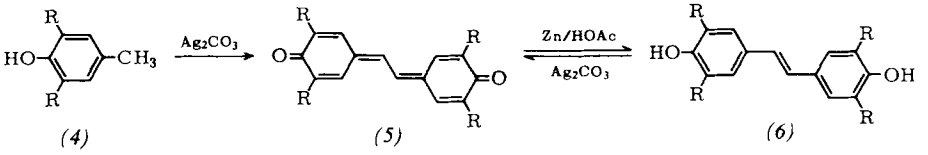
Silver carbonate precipitated on Celite is known to be a suitable reagent for selective oxidation, in a neutral medium, of very sensitive alcohols to aldehydes or ketones[3]; quantitative oxidation of hydroquinone to quinone has been carried out in the same manner.

We have now found that silver carbonate on a Celite support in refluxing benzene is also a very efficient reagent for the oxidative coupling of phenols *(1)* and *(4)* to give the *p*-diphenoquinones *(2)* and stilbenequinones *(5)*, respectively, in high yield (see Table).

The quinones *(2)* and *(5)* are easily reduced either by sodium hydrosulfite in dilute alkaline solution [*(2)*] or by zinc dust in acetic acid medium [*(5)*]. The resulting diphenols *(3)* and *(6)* can also be oxidized in high yield to *(2)* and *(5)*, respectively, by silver carbonate on celite. Attempts to oxidize the *pp'*-biphenyldiol to *p*-diphenoquinone were unsuccesful owing to the limited solubility of the starting material.

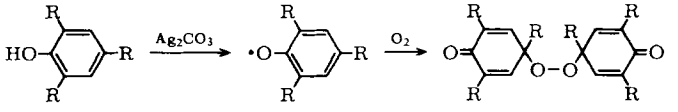


(1) (2) (3)



(4) (5) (6)

(a), R = CH_3 (b), R = $(CH_3)_3C$



(7b) (8b) (9b)

R = $(CH_3)_3C$

Phenol	Product [a]	M. p. (°C) found	M. p. (°C) values [b]	Yield (%)
(1a)	(2a)	217–218	215 [2]	98
(1b)	(2b)	248	245–247 [5]	99
(4a)	(5a)	227–228	220–230 [6]	93
(4b)	(5b)	313–314	316 [7]	90
(7b)	(9b)	147–148 (dec.)	148–149 (dec.) [4]	90
(2a)	(3a)	228–229	226 [2]	85
(2b)	(3b)	184–185	185 [8]	95
(5a)	(6a)	237–240	239–240 [6]	81
(5b)	(6b)	244–246	240–241 [4]	80

[a] The structure of the products is confirmed by satisfactory elemental analysis, IR, UV, and NMR measurements.

[b] These values are the highest ones reported in the literature.

Oxidation of 2,4,6-*tert*-butylphenol *(7b)* by silver carbonate/Celite in benzene under nitrogen gives a deep blue solution of the stable radical *(8b)*. In the presence of oxygen, *(8b)* affords the peroxide *(9b)* in high yield.

It is expected that the easy preparation of the reagent[3], the simplicity of the oxidizing procedure, and the high purity of the final products will lead to further applications of the silver carbonate/Celite reagent in oxidative coupling of phenols.

3,3',5,5'-Tetramethyldiphenoquinone (2a)

30 g of purified celite[**] is added to a mechanically stirred solution of 34 g (200 mmoles) of silver nitrate in 200 ml distilled water.

A solution of 30 g (105 mmoles) $Na_2CO_3 \cdot 10\,H_2O$ [or 21 g (210 mmoles) of $KHCO_3$] in 300 ml distilled water is then added slowly to the resulting homogeneous suspension. When the addition is complete, stirring is continued for a further 10 minutes. The yellow-green precipitate which is formed is then filtered off, washed with distilled water until neutral, and finally dried in a rotary evaporator over a period of several hours. The silver carbonate/celite reagent contains about 1 mmole Ag_2CO_3/0.57 g.

2,6-Dimethylphenol (1.2 g) was refluxed for 30 minutes in benzene (150 ml) with silver carbonate/Celite reagent (25.1 g). Removal of the solid phase and evaporation of benzene leaves 1.16 g (98%) of practically pure *(2a)* (m.p.217–218 °C). Recrystallization does not raise the melting point.

Received: March 24, 1969 [Z 974 IE]
German version: Angew. Chem. *81*, 423 (1969)

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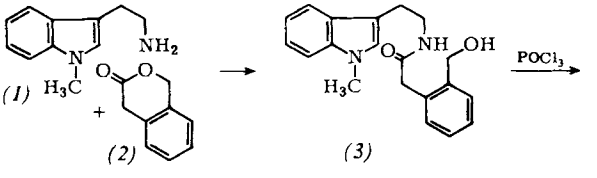
[**] The celite was purified by washing it successively with methanol containing 10% Conc. HCl and then with distilled water until neutral; it was finally dried at 120° C.

New Two-stage Synthesis of the Yohimbane Ring System[1]

By *W. Meise* and *F. Zymalkowski*[*]

We recently prepared a Berberis alkaloid, (±)-xylopinine, in a simple two-stage synthesis from homoveratrylamine and 6,7-dimethoxyisochroman-3-one[2]. The ring system of yohimbane can be built up in the same way.

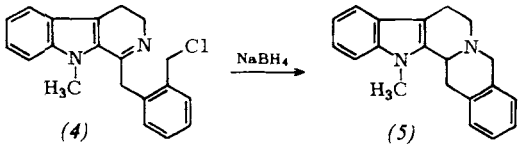
N_b-Methyltryptamine *(1)* and isochroman-3-one *(2)* give a 92% yield of *N*-[2-(1-methyl-3-indolyl)ethyl]-*o*-(hydroxymethyl)phenylacetamide *(3)*, which affords 1-[2-(chloromethyl)benzyl]-3,4-dihydro-9-methyl-β-carboline *(4)* by a Bischler-Napieralski reaction with phosphorus oxychloride. If *(4)* is isolated by the usual methods, by-products are formed whose separation is difficult and involves losses. These



(1) (2) (3)

side reactions are, however, avoided if crude *(4)* is dissolved in methanol and treated directly with $NaBH_4$; under these conditions reduction of the C=N double bond and ring-closure to the benz[*g*]indolo[2,3-*a*]quinolizine derivative *(5)*

occur. The melting point of the base and its picrate, as well as the UV, IR, and NMR spectra, accord with expectation; distillation and purification by way of the picrate are unnecessary in this process [3,4].



(4) (5)

The synthesis can be applied also to tryptamine and to its derivatives with substituents in the benzene ring; use of substituted isochromanones gives a simple method of preparing alkaloids of yohimbane type.

15,16,17,18,19,20-Hexadehydro-1-methylyohimbane (5)

8.7 g (50 mmoles) of *(1)* and 8.9 g (60 mmoles) of *(2)* are boiled under reflux in 50 ml of ethanol for 18 h. 14.2 g of *(3)*, having m.p. 151–153 °C, crystallizes from the solution and a further 0.65 g (total yield 92%) is obtained on concentration of the mother-liquors. The product is recrystallized from ethanol, giving colorless needles of m.p. 153–154 °C.

3.22 g (10 mmoles) of *(3)* is boiled under reflux with 30 g of phosphorus oxychloride for 2 h, then cooled and treated with 50 ml of light petroleum; *(4)* separates as an oil. The upper layer is decanted and the crude *(4)* is digested five times with light petroleum (50-ml batches) and taken up at once in methanol (50 ml). This solution is treated with 5 g of $NaBH_4$ during 1.5 h, with stirring and cooling in ice, and then boiled for 0.5 h under reflux. Next the methanol is removed in a vacuum and the residue is suspended in 50 ml of water and shaken out with five portions, each 50 ml, of chloroform. Material recovered on evaporation of the organic phase solidified when kept. Rubbing this with 5 ml of methanol, collecting it, and washing it with a total of 10 ml of methanol gave 2.00 g of *(5)*, m.p. 133–135 °C; adding water to the filtrate gives an additional 0.25 g (total 78%). NMR ($CDCl_3$; TMS as internal standard): τ = 5.95 (2H on C-21, s); 6.30 ($N-CH_3$, s).

Received: March 31, 1969 [Z 977 IE]
German version: Angew. Chem. *81*, 425 (1969)

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

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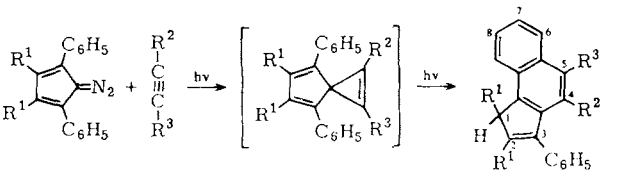
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Formation of Benzindenes on Photolysis of Phenyl-substituted Diazocyclopentadienes in Alkynes[1]

By *H. Dürr* and *L. Schrader* [*]

Photolysis of substituted diazocyclopentadienes *(1)* in benzene [2] to give benzocycloheptenes or cyclopentacyclooctenes made it of interest to study the photolysis of *(1)* in alkynes. If phenyl-substituted diazo-compounds *(1)* are photolyzed in ethyl propiolate *(2a')* or in dimethyl acetylenedicarboxylate *(2b')*, the carbenes formed from *(1)* react in participation with the phenyl substituents. The benzindenes *(4)* are thus formed in moderate yield from 5-diazo-1,4-diphenyl-*(1a)* and 5-diazo-1,2,3,4-tetraphenyl-cyclopentadiene *(1b)* [3]. The structure of the benzindenes *(4)* is shown in particular by the spectra. For instance, the NMR spectrum of *(4aa')* shows the signals of the aromatic protons at δ = 7.4–9.3 ppm; the olefinic proton at C-2 appears as a triplet (δ = 6.79 ppm,



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

Reactants		Products	R^1	R^2	R^3	M.p. (°C)	Yield (%)
(1a)	*(2a')*	*(4aa')*	H	H	$CO_2C_2H_5$	155–156	47
(1a)	*(2b')*	*(4ab')*	H	CO_2CH_3	CO_2CH_3	208–210	21
(1b)	*(2a')*	*(4ba')*	C_6H_5	H	$CO_2C_2H_5$	[a]	7
(1b)	*(2b')*	*(4bb')*	C_6H_5	CO_2CH_3	CO_2CH_3	204–206	40

[a] M.p. of an inseparable mixture of *(4ba')* (70%) and an unknown substance (30%) is 81–99 °C (proportions determined by NMR spectroscopy).

^3J = 2.0 Hz), the methylene protons on C-1 as a doublet (δ = 3.86 ppm) with the coupling constant ^3J = 2.0 Hz typical of indenes; the ester protons appear at 4.59 ppm (q, ^3J = 7.5 Hz) and at 1.46 ppm (t, ^3J = 7.5 Hz) in the ratio 10:1:2:2:3. The structure is further proved by degradation of *(4aa')* by hydrogenation, hydrolysis, and decarboxylation to the known 3-phenylbenz[*e*]indane [4].

On photolysis (Philips HPK 125-W high-pressure lamp) of *(1b)* in *(2b')*, the dimethyl 2,3,4,5-tetraphenyl-2,4-cyclopentadienespiro-2'-cyclopropene-2',3'-dicarboxylate *(3bb')* postulated as intermediate could be isolated by chromatography in $CHCl_3$ on silica gel as red crystals, m.p. 143–144 °C, in 31% yield. Typical for *(3bb')* was the NMR spectrum which indicated a highly symmetrical molecule with δ = 3.78 ppm (6H, s) and 6.9–7.3 ppm (20H, m) also the cyclopropene bands at 1865 cm^{-1} and the molecular ion at *m/e* = 510.

Ethyl 3-phenylbenz[e]*indene-5-carboxylate (4aa')*

2.00 g (8.2 mmoles) of *(1a)* [3] in 150 ml of *(2a')* were irradiated with a Philips HPK 125 Hg high-pressure lamp (Pyrex filter; 18–20 °C) until the theoretical amount of N_2 had been evolved (~1.5 h). When the ester *(2a)* was removed under vacuum, yellowish-brown crystals were precipitated. The whole residue was taken up in benzene and chromatographed on silica gel with benzene/light petroleum (1:1; b.p. 40–80 °C). 1.20 g (47%) of *(4aa')*, m.p. 155–156 °C, were obtained from the eluate after recrystallization from CH_2Cl_2/methanol IR spectrum (KBr): 1715 cm^{-1} (s, C=O), 1585 (m), 1495 (m), 1465 (m).

Received: March 31, 1969 [Z 978 IE]
German version Angew. Chem. *81*, 426 (1969)

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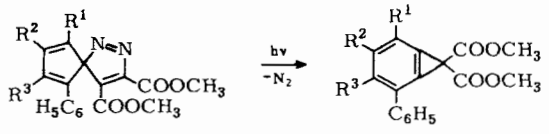
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A New Benzocyclopropene Synthesis[1]

By *H. Dürr* and *L. Schrader* [*]

The photolysis of phenyl-substituted diazocyclopentadienes in dimethyl acetylenedicarboxylate affords benzindenes [2] *via* the corresponding spirocyclopropenes. Our interest lay in establishing whether photolysis of the spiro-3*H*-pyrazoles *(1a)–(1c)* [3], which are formed by 1,3-dipolar addition of

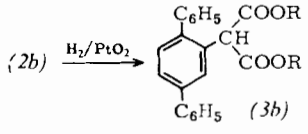
the diazo compound to acetylenedicarboxylate, also yields spirocyclopropenes (in analogy to the findings of *Ege*[4]) or their subsequent reaction products. We found, however, that irradiation of *(1a)–(1c)* in benzene leads to benzocyclopropenes *(2a)–(2c)*.



(1a)-(1c) *(2a)-(2c)*

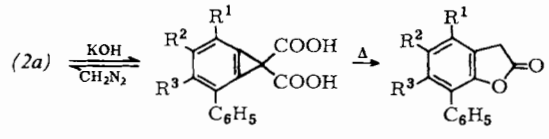
	R^1	R^2	R^3	M.p. (°C)	Yield (%)
(a)	C_6H_5	C_6H_5	C_6H_5	175	85
(b)	C_6H_5	H	H	187	86
(c)	*o*-phenylene		C_6H_5	158	30

The NMR and IR spectra of *(2a)–(2c)* show few signals and bands respectively, and demonstrate the high degree of symmetry of the molecules. Thus the two methoxycarbonyl groups appear as a singlet at $\delta = 3.81$ ppm (6H) in the NMR spectrum of *(2a)*, and a multiplet due to the aromatic protons is observed at 6.8–7.4 ppm (20 H) (in $CDCl_3$ with TMS as internal reference). Catalytic hydrogenation of *(2b)* in acetic ester with PtO_2 as catalyst affords the terphenylylmalonic ester *(3b)* [$\delta = 3.37$ ppm (6H, s); 4.98 ppm (1H, s); 7.2–7.8 (12H, m); 7.94 (1H, d)]. This finding is in accord with observations by *Vogel et al.*[5], who obtained benzene derivatives in addition to cycloheptanes on catalytic hydrogenation of benzocyclopropene.

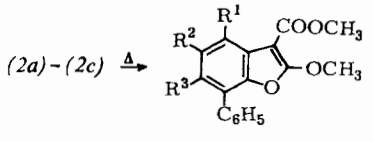


(2b) *(3b)*

Hydrolysis of the diesters *(2a)* proceeds without rearrangement to give the dicarboxylic acid *(4a)*, which can be esterified by treatment with diazomethane to *(2a)*. In quinoline, *(4a)* undergoes rearrangement, with decarboxylation, to tetraphenylcoumaranone *(5a)* (IR: ν(CO) 1820 cm^{-1}).



(4a) *(5a)*



(6a)-(6c)

If *(2a)–(2c)* are heated above their melting points, they isomerize to the substituted benzofurans *(6a)–(6c)* (cf. ref.[6]). All these reactions are typical of benzocyclopropenes.

Dimethyl 2,3,4,5-tetraphenylbenzocyclopropene-1,1-dicarboxylate (2a) and methyl 2-methoxy-4,5,6,7-tetraphenylbenzo[b]furan-3-carboxylate (6a)

Compound *(1a)* (1.40 g, 2.6 mmole) is dissolved in anhydrous benzene (150 ml). After passage of N_2 for 15 min, the solution is irradiated for 90 min (Philips HPK 125 W, $\lambda \geq 280$ nm, Pyrex filter). Removal of the solvent leaves a reddish oil which is taken up in methylene chloride and treated with methanol, whereupon colorless needles of *(2a)* (m.p. 175 °C, yield 1.13 g, 85%) are precipitated [ν(CO) = 1755 cm^{-1}; M^+ = 510, *m/e* = 479 ($M-OCH_3$), 451 ($M-COOCH_3$)][7].

If *(2a)* (1.00 g) is heated at a temperature slightly above its melting point the melt soon solidifies. Colorless needles of *(6a)* (m.p. 227 °C, yield 0.92 g, 92%) are precipitated from a methylene chloride/methanol solution of the solidified melt[7].

Received: April 10, 1969 [Z 980 IE]
German version: Angew. Chem. *81*, 426 (1969)

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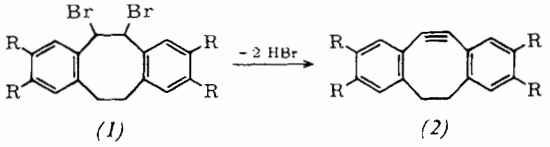
[7] Correct analyses were obtained for all compounds.

5,6-Didehydro-11,12-dihydrodibenzo[*a*,*e*]-cyclooctene

By *G. Seitz, L. Pohl*, and *R. Pohlke*[*]

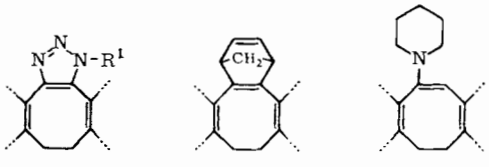
It was to be expected that, because of its greater classical ring strain, 5,6-didehydro-11,12-dihydrodibenzo[*a*,*e*]cyclooctene *(2a)* would be less stable and more reactive than cyclooctyne[1]. We have prepared *(2a)* and its 2,3,8,9-tetramethoxy derivative *(2b)* and have found that *(2b)* in particular is very stable. Whereas *(2a)* decomposes within a few days at room temperature, *(2b)* has been stored unchanged for three years. This compound *(2b)* is also not unusually reactive, in contrast to cyclooctyne which can be stored for only a short time. Azides, cyclopentadiene, and piperidine add as expected to afford *(3)*, *(4)*, and *(5)*, respectively, but heating is usually required to effect these reactions, whereas cyclooctyne reacts spontaneously with phenyl azide. Also, *(2a)* reacts only very slowly with phenyl azide at room temperature.

For preparation of *(2a)* and *(2b)* the 5,6-dibromo derivatives *(1a)* and *(1b)* were dehydrobrominated with a mixture of potassium *tert*-butoxide and 1-methylpiperazine. On hydrogenation of *(2b)* over a palladium catalyst, two moles of



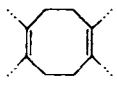
(1) *(2)*

(a), R = H; *(b)*, R = OCH_3

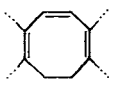


(3), R^1 = C_6H_5, CH_3, $COOC_2H_5$, CH_2-$COOC_2H_5$ *(4)* *(5)*

hydrogen were absorbed with formation of the known 5,6,11,12-tetrahydro-2,3,8,9-tetramethoxydibenzo[*a*,*e*]cyclooctene *(6)*[2]. If the reaction is interrupted after absorption of one mole of hydrogen, one obtains 5,6-dihydro-2,3,8,9-tetramethoxydibenzo[*a*,*e*]cyclooctene *(7)*, which has also been prepared previously[2].



(6)



(7)

The triple bond in *(2)* has a bond angle that deviates from 180° and thus causes severe ring strain. As a result, the $-C\equiv C-$ stretching vibration that is strictly forbidden on symmetry grounds appears in the IR region, so that, *e.g.*, *(2b)* gives a weak band at 2155 cm^{-1}; that this is really the vibration of the triple bond is shown by a very strong band at 2153 cm^{-1} in the Raman spectrum; this is comparatively broad and lies at longer wavelengths than for tolane (2220 cm^{-1}), which again is an indication of the increase in ring strain due to the angled substituents [**].

The UV spectrum of diphenylacetylene type [3] [*(2b)*: λ_{max} = 332 nm, ε = 28000], which is much shifted to longer wave lengths, can be explained only on similar grounds.

Further proofs of the structure of *(2)* are provided by the NMR (Varian HA-100) and mass spectra (LKB 9000). The methylene protons of *(6)* and *(7)* give a singlet at δ = 2.95 and 3.09 ppm, respectively, and are thus magnetically equivalent, but for *(2b)* there are two multiplets at δ = 2.35 and 3.20 ppm with J_{gem} = 11 Hz. The reason for the large chemical shift between the geminal methylene protons is the molecular distortion on conversion of *(7)* into *(2b)*, whereby one proton is caused to lie in the plane of the neighboring benzene ring while the other is transferred to above the $-C\equiv C-$ bond.

The mass spectrum of *(2b)*, measured at 70 eV, indicates, in analogy to the chemical findings, an unusual stability of this compound, for it consists of only three groups of lines: M^+ at *m/e* = 324 with $\%\sum_{30}$ = 57, (M-15) with $\%\sum_{30}$ = 10, and M^{2+} with $\%\sum_{30}$ = 7. The molecular mass and the fragmentation support the structure proposed.

5,6-Didehydro-11,12-dihydrodibenzo[a,e]cyclooctene (2b)

Bromine (16 g, 0.1 mole) is added dropwise, with stirring, to 5,6-dihydro-2,3,8,9-tetramethoxydibenzo[*a,e*]cyclooctene *(7)* (32.6 g, 0.1 mole) [2] in benzene (325 ml). The solution becomes almost colorless within a short time. The benzene is distilled off in a vacuum, the residue is dissolved in ethyl acetate, and the solution is filtered from a small amount of a red decomposition product. Crystallization in the cold affords *(1b)* (42.7 g, 88%), m.p. 173 °C.

A solution of potassium (15.6 g, 0.4 mole) in *tert*-butyl alcohol (400 ml) is treated with 1-methylpiperazine (150 g) and then diluted with anhydrous ether (250 ml). Compound *(1b)* (48.6 g, 0.1 mole) is then added and the whole is stirred for 3 days at room temperature. The mixture is then evaporated to dryness without removal of the precipitate and the residue is freed from potassium bromide by repeated treatment with water and filtration. The residue is dried in a vacuum and on recrystallization from acetonitrile affords colorless crystals of *(2b)* 21.2 g, 65%), m.p. 221 °C.

Received March 21, 1969 [Z 979 IE]
German version: Angew. Chem. *81*, 427 (1969)

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[**] We thank Dr. *B. Schrader*, Dortmund, for measuring the Raman spectrum with a He–Ne laser Raman spectrograph.

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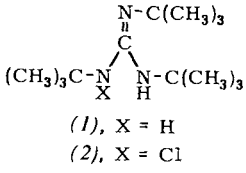
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A Diaziridine Imine

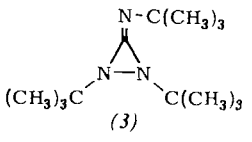
By *H. Quast* and *Edeltraud Schmitt* [*]

Although increasing attention [2, 3] has been paid to aziridinones and diaziridinones since the first discovery of an α-lactam [1], the analogous imines have so far been unknown [4]. Compounds of this type would be interesting in respect of their behavior on thermolysis [2, 5] and as possible intermediates in the rearrangement of *N*-haloguanidines to semicarbazide derivatives [6, 6a]. We now report the first synthesis of a diaziridine imine and some of its properties.

In the few cases studied, the action of hypochlorite on *N,N',N''*-trisubstituted guanidines has given only very unstable *N*-haloguanidines [7]. However, from two moles of *N,N',N''*-tri-*tert*-butylguanidine *(1)* [8] and one mole of *tert*-butyl hypochlorite in carbon tetrachloride or *n*-pentane we obtained smoothly (80–85% yield) the diaziridine imine *(3)* alongside one mole of *(1)* · HCl.



(1), X = H
(2), X = Cl



(3)

The *N*-chloroguanidine *(2)* must be assumed to be an intermediate, undergoing ring closure in an intramolecular S_N reaction under the influence of a second molecule of the strong base *(1)* [9]. A corresponding mode of reaction has been proved for the formation of 1,2-di-*tert*-butyldiaziridinone [3]. The imine *(3)* can be prepared even more conveniently from *N,N',N''*-tri-*tert*-butylguanidinium perchlorate, *(1)* · $HClO_4$ and *tert*-butyl hypochlorite in *tert*-butyl alcohol/carbon tetrachloride in the presence of an excess of potassium *tert*-butoxide.

The structure of *(3)* is proved by elemental analysis and molecular-weight determination (calc. 225.4; found 229, osmometrically in benzene) and also by the IR and NMR spectra. The IR spectrum in CCl_4 contains no trace of NH bands [*(1)*: 3465 cm^{-1} (NH)]; the C=N vibration [*(1)*: 1650 cm^{-1}] is, as expected [2, 3], at very high frequency (1790 cm^{-1}). The UV spectrum shows no maximum above 200 nm, only a slightly developed shoulder at 226 nm (log ε = 2.95, in *n*-hexane).

The NMR spectrum contains three singlets of equal intensity (+10 °C, CCl_4, δ = 1.09, 1.17, 1.25 ppm). The two upfield signals are temperature-dependent; they broaden as the temperature is raised and coalesce at 50 °C ($\Delta\nu$ = 5.0 Hz, $\Delta G_c^{\ddagger}$ = 17.4 kcal/mole); at 100 °C there are two sharp singlets in the intensity ratio 2:1. This behavior can be ascribed to inversion at the imino-nitrogen atom [10].

The imine *(3)* is thermally less stable than the corresponding carbonyl compound; whereas the latter survives for 2 h at 175 °C, *(3)* decomposes wholly within one hour at 150 °C, giving 2,2'-azoisobutane and *tert*-butyl isocyanide which can be isolated in more than 80% yield. This reaction strongly supports structure *(3)*; it is paralleled by the decomposition of imino α-lactones into carbonyl compounds and isocyanides [2], and by the thermolysis of several three-membered ring compounds [11] in which an olefin and CO, N_2, N_2O, or SO_2 are formed.

N-(1,2-Di-tert-butyldiaziridin-3-ylidene)-tert-butylamine (3)

tert-Butyl hypochlorite (7.6 g, 70 mmoles) is added to a solution of potassium (4.1 g, 0.105 mole) and *(1)* · $HClO_4$ (11.5 g, 35 mmoles) in 1:1 *tert*-butyl alcohol/CCl_4 (240 ml) at −30 °C under nitrogen. After being stirred for 4 h at −30 ° to −8 °C with exclusion of light, the solution is washed with ice-water, dried over K_2CO_3, and evaporated under reduced

pressure; vacuum distillation of the residue gives a colorless oil, b.p. 29–31 °C/0.005 torr, in 77–79% yield (6.07–6.24 g).

Received: August 10, 1968; revised: April 2, 1969 [Z 981a IE]
German version: Angew. Chem. *81*, 428 (1969)

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[8] *(1)* · $HClO_4$ (m.p. 170–171 °C), obtained in 69–77% yield from di-*tert*-butylcarbodiimide and *tert*-butylammonium perchlorate in hot ethanol, was converted into *(1)* (b.p. 93–94 °C/11 torr, $n_D^{20} = 1.440$; 86% yield) by sodium hydride in tetrahydrofuran.

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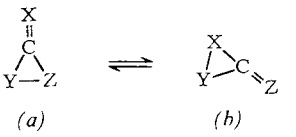
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Reversible Valence Isomerization of Diaziridine Imines

By *H. Quast* and *Edeltraud Schmitt* [*]

The reversible thermal isomerization of the methylenecyclopropane system *(1a)*⇄*(1b)* [1] has been thoroughly studied in respect of its kinetics [2] and stereochemistry [3] because of the theoretically interesting diradical intermediates involved. An analogous irreversible rearrangement in the heterocyclic series was postulated [4] as one step *(2a)* → *(2b)* in the complex reaction of *cis*-3-chloro-3-methyl-1,2-diphenylaziridine with potassium *tert*-butoxide in boiling *tert*-butyl alcohol and as an explanation for the formation of carbonyl compounds and isocyanides in the pyrolysis of α-lactams *(4a)* [5]. However, isomerization of *(3a)* (at 190 °C) [4] or *(6a)* (at 175 °C) [6] could not be observed. The valence isomerization of allene oxides to cyclopropanones, *(5a)* → *(5b)*, repeatedly discussed, has only recently been proved [7].

The first proof has now been found for the equilibrium *(a)* ⇄ *(b)* of a diaziridine compound [7a]. The diaziridine imine *(7)* is, however, not suitable for this purpose, since



(a) *(b)*

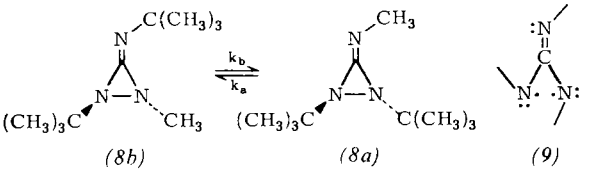
	X	Y	Z
(1)	CR_2	CR_2	CR_2
(2)	CH_2	CHC_6H_5	$N\text{-}C_6H_5$
(3)	CH_2	CH_2	$N\text{-}C_2H_5$
(4)	O	CR_2	N-R
(5)	CR_2	CR_2	O
(6)	O	$N\text{-}C(CH_3)_3$	$N\text{-}C(CH_3)_3$
(7)	$N\text{-}C(CH_3)_3$	$N\text{-}C(CH_3)_3$	$N\text{-}C(CH_3)_3$

there is no line broadening in the NMR spectrum at 150 °C (signal width < 1 Hz, $k < 3$ sec^{-1}, $\Delta G^{\ddagger} > 24.1$ kcal/mole) and because thermal decomposition [8] prevents use of higher temperatures. To demonstrate a slow rearrangement we synthesized diaziridine imines in which one nitrogen atom was substituted differently from the others.

From *N,N'*-di-*tert*-butyl-*N''*-methylguanidine and *tert*-butyl hypochlorite we obtained (cf. ref. [8]) an 83% yield of a mixture of the isomeric diaziridine imines *(8a)* and *(8b)* in the ratio 3:2, and at −20 °C part of the *(8a)* crystallized (yield 31%). The structures were assigned on the basis of the differing IR and NMR spectra (neat liquids). *(8a)*: colorless crystals, m.p. 18–19.5 °C (from *n*-pentane), which according to the NMR spectrum contain 0.3% of *(8b)*; NMR, 1.10 (9H, s), 1.13 (9H, s), 3.03 (3H, s); IR, 1810 cm^{-1} with a shoulder at 1835 and a weak side band at 1925 cm^{-1} (C=N), and a band at 1403 cm^{-1}, but no absorption at 1070–1190 cm^{-1} in contrast to *(8b)*.

Repeated distillation of the residual oil at 0.2 torr through a 75-cm Normag spinning-band column enriched the *(8b)* content to 82%. *(8b)*: colorless oil, b.p. 14–15 °C/0.2 torr; NMR, 1.09 (9H, s), 1.24 (9H, s), 2.76 (3H, s), and signals corresponding to the presence of 18% of *(8a)*; IR, 1805 cm^{-1} with weak side bands at 1778, 1890, and 1920 cm^{-1} (C=N), bands at 928, 1130, and 1158 cm^{-1}, but no absorption at 1390–1440 cm^{-1} in contrast to *(8a)*.

Whereas *(8a)* and *(8b)* remain unchanged at −20 °C, at 60–90 °C use of either *(8a)* or *(8b)* leads to an equilibrium mixture of the two in which the IR and NMR spectra show less than 2% of isocyanide (produced by thermal decomposition [8]) to be present. The rate of equilibration was followed by NMR spectroscopy of undiluted, degassed samples.



(8b) *(8a)* *(9)*

Table 1. Equilibrium and rate constants for the isomerization *(8a)* ⇄ *(8b)*.

Starting cpd.	Temp. (±0.1 °C)	$K = \frac{k_b}{k_a}$ (±0.1)	$10^5 \times (k_a + k_b)$ (sec^{-1})
(8b)	60.0	9.75	1.335 ± 0.005
(8a)	70.0	8.35	4.65 ± 0.12
(8b)	70.0	8.35	4.685 ± 0.028
(8b)	80.0	7.85	15.08 ± 0.06
(8b)	90.0	7.20	44.03 ± 0.07

From Table 1 can be calculated: $\Delta H = -2.3 \pm 0.3$ kcal/mole; $\Delta S = -1.1 \pm 0.4$ cal degree^{-1} mole^{-1}; and the activation parameters $\Delta H_a^{\ddagger} = 29.4 \pm 0.4$ kcal/mole, $\Delta S_a^{\ddagger} = 2.6 \pm 1.2$ cal degree^{-1} mole^{-1}, and $\Delta H_b^{\ddagger} = 27.1 \pm 0.2$ kcal/mole, $\Delta S_b^{\ddagger} = 0.1 \pm 0.5$ cal degree^{-1} mole^{-1}.

A possible intermediate in the rearrangement is the planar molecule *(9)*, which is comparable with trimethylenemethane[2,3,9] and would be formed by disrotatory opening of the three-membered ring[10] if the two substituents in the ring are *trans* to one another[11]. We are currently investigating some of the preparative and mechanistic consequences of this first reversible valence isomerization of a hetero analog of methylenecyclopropane.

Received: April 2, 1969 [Z 981b IE]
German version: Angew. Chem. *81*, 429 (1969)

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Bis(trimethylsilyl) Monoperoxosulfate[1]

By *A. Blaschette, B. Bressel*, and *U. Wannagat*[*]

The only derivatives of Caro's acid (monoperoxosulfuric acid) described so far are the alkali-metal salts M^IHSO_5. Attempts to prepare other derivatives from the free acid failed because of its tendency to decompose and its marked oxidizing action.

We have obtained the first ester of monoperoxosulfuric acid, namely, bis(trimethylsilyl) monoperoxosulfate *(2)*, by a quantitative, exothermic insertion reaction[2] of bis(trimethylsilyl) peroxide *(1)* with an equimolar amount of sulfur trioxide:

$$\underset{(1)}{(CH_3)_3Si\text{-}O\text{-}O\text{-}Si(CH_3)_3} + SO_3 \xrightarrow{CH_2Cl_2,\ -30^\circ C}$$

$$(CH_3)_3Si\text{-}\overset{SO_3}{\overset{\uparrow}{O}}\text{-}O\text{-}Si(CH_3)_3 \rightarrow (CH_3)_3Si\text{-}O\text{-}\overset{O}{\overset{\|}{S}}\text{-}O\text{-}O\text{-}Si(CH_3)_3$$
$$\underset{(2a)}{\qquad\qquad} \qquad\qquad \underset{O}{\qquad\qquad} \underset{(2)}{\qquad}$$

The ester *(2)* (M.wt. 258; cryoscopic in CCl_4: 243) is a water-clear liquid that is very viscous at −30 °C, solidifies to a glass below −80 °C, and distills only with decomposition. It is readily soluble in CH_2Cl_2, CCl_4, and diethyl ether, sparingly soluble in light petroleum, and reacts with benzene and cyclohexane with development of a brown color. Warming pure *(2)* to room temperature soon leads to violent deflagration with evolution of clouds of SO_3. In dilute CH_2Cl_2 solution the ester decomposes at 20 °C in 1–2 days with rearrangement of the $(CH_3)_3SiOO$ to a $(CH_3)_2(CH_3O)SiO$ group[3].

The ^{1}H-NMR spectrum of *(2)* at 32 °C consists of a single signal at $\tau = 9.60$, which is split below −20 °C into two lines of approximately equal intensity at $\tau = 9.58$ and 9.72 (at −50 °C) (measured in and against CH_2Cl_2, τ values converted to TMS as standard). This behavior indicates a rapid exchange between the two trimethylsilyl groups above −20 °C. *(2)* is a very strong oxidizing agent. When it is dropped on to paper or on to cotton soaked in light petroleum it causes inflammation. It reacts violently with solid NaCl or KI with liberation of Cl_2 or I_2 and formation of hexamethyldisiloxane *(3)* and alkali-metal sulfate. It is reduced by gaseous HCl in CH_2Cl_2 at −20 °C with formation of Cl_2, *(3)*, and H_2SO_4. Pyridine is oxidized instantaneously and quantitatively to its *N*-oxide by *(2)* in CH_2Cl_2 at −30 °C; pyridine · SO_3, which would be expected to be formed if the adduct *(2a)* were present, is not formed in this reaction. *(1)* reacts under the above conditions neither with solid NaCl nor with pyridine, and with gaseous HCl gives Cl_2, *(3)*, and H_2O only slowly. On cautious hydrolysis of *(2)* with a little water there is formed, together with *(3)*, an aqueous phase that gives the specific reactions of Caro's acid (instantaneous oxidation of I^- to I_2, oxidation of aniline to nitroso- and nitro-benzene and of acetone to 3,3,6,6-tetramethyl-1,2,4,5-tetroxane[4]). Gaseous NH_3 ammonolyzes *(2)* in CH_2Cl_2 at −30 °C instaneously and exothermally to hexamethyldisilazane and unstable NH_4HSO_5.

Experimental:

SO_3 (1.601 g, 20.0 mmoles) in CH_2Cl_2 (20 ml) is added very slowly with continuous stirring and rigid exclusion of moisture to the peroxide *(1)* (3.568 g, 20.0 mmoles) in very pure CH_2Cl_2 (30 ml) at −30 °C. The mixture is then stirred for a further 30 min at the same temperature, whereafter the solvent is removed cautiously by means of an oil-pump. *(2)* remains quantitatively as residue.

Received: March 31, 1969 [Z 983 IE]
German version: Angew. Chem. *81*, 430 (1969)

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Mono-, Bis-, and Tris(phenylseleno)methyllithium (Selenium-Stabilized Carbanions)

By *D. Seebach* and *N. Peleties*[*]

Unlike anisole[1], thioanisole is metalated in the side chain by butyl lithium[2] whereas selenoanisole is cleaved by this reagent to phenyllithium and methyl butyl selenide [eq.

(a)][2a]. The reaction does not throw any light on the stability of the hitherto unknown α-seleno carbanions[3].

$$C_6H_5\text{–}Se\text{–}CH_3 + C_4H_9Li \rightarrow C_6H_5Li + CH_3\text{–}Se\text{–}C_4H_9 \quad (a)$$

We have found that the lability of the Se–C bond can be exploited for the preparation of lithium derivatives of such anions. According to eq. (b), reaction of bis(phenylseleno)methane *(1)* (prepared in the same manner as the sulfur compound[2b]) and *n*-butyllithium in THF affords phenylselenomethyllithium *(2)*[5]. This was established by reaction with D_2O (according to NMR analysis > 95% $C_6H_5SeCH_2D$), isolation of the butyl phenyl selenide[6], and preparation of the benzophenone adduct *(3)*.

$$(C_6H_5Se)_2CH_2 \;(1) + C_4H_9Li \xrightarrow[-78\,^\circ C]{1.5\ h}$$

$$C_6H_5\text{-}Se\text{-}CH_2Li \;(2) + C_6H_5\text{-}Se\text{-}C_4H_9 \quad (b)$$

$$\downarrow$$

$$C_6H_5\text{-}Se\text{-}CH_2\text{-}C(OH)(C_6H_5)_2 \;(3)$$

Reaction of tris(phenylseleno)methane *(6)* (prepared in a similar way to the sulfur compound[4a]) with butyllithium (−40 to −100 °C), however, always leads to a mixture of the lithium derivatives *(4)* and *(7)*. The pure compounds *(4)* and *(7)* are formed by metalation of bis- and tris(phenylseleno)-methane, *(1)* and *(6)* respectively, with lithium diisobutylamide according to equations (c) and (d).

$$(1)\ (C_6H_5Se)_2CH_2 + LiN[CH_2\text{-}CH(CH_3)_2]_2 \xrightarrow[-78\,^\circ C]{1\ h} (C_6H_5Se)_2CHLi\ (4) \quad (c)$$

$$(4) \xrightarrow[(C_6H_5)_2C=O]{14\ h,\ -20\,^\circ C} (5)\ (C_6H_5Se)_2CH\text{-}C(OH)(C_6H_5)_2$$

$$(C_6H_5Se)_3CH\ (6) + LiN[CH_2\text{-}CH(CH_3)_2]_2 \quad (d)$$

$$\xrightarrow[-78\,^\circ C]{1\ h} (C_6H_5Se)_3CLi\ (7) \xrightarrow[-78\,^\circ C]{1\ h} (8)\ (C_6H_5Se)_4C + C_4H_9Li \quad (e)$$

As shown in eq. (e) loss of a C_6H_5Se group[5] from the orthocarbonic acid derivative *(8)* [prepared from *(7)* and $(C_6H_5Se)_2$] yields amine-free solutions of the metalated triselenoorthoformic ester *(7)*. The presence of the lithium compounds *(4)* and *(7)* is proved, not only by hydrolysis with D_2O (> 95% deuteration in each case), but also by the formation of the derivatives *(5)* and *(8)–(12)*. Yields and characteristic data for the new selenium compounds are given in the Table.

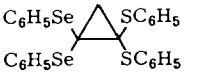
The colorless solutions of mono- *(2)* and bis(phenylseleno)-methyllithium *(4)* are stable at temperatures up to 0 °C, whereas the greenish-yellow solutions of tris(phenylseleno)-methyllithium *(7)* gradually become discolored at temperatures in excess of −20 °C.

Preparation of 1,1-diphenyl-2-phenylselenoethanol (3) via phenylselenomethyllithium (2):

A solution of butyllithium (5.0 mmole, 2.3 M in *n*-hexane) is added to a stirred solution of *(1)* (1.63 g, 5.0 mmole) in THF (30 ml) at −78 °C. After 1.5 h, a solution of benzophenone (0.90 g, 5.0 mmole) in *n*-hexane (15 ml) is added all at once. The reaction vessel is sealed under argon and kept at −35 °C for 14 h and then at +20 °C for 1 h. The contents are poured into water and the resulting product taken up in $CHCl_3$. Drying over K_2CO_3 and removing the solvent leaves an oil, which on treatment with pentane and on cooling to 0 °C affords colorless crystals of *(3)* (yield 1.50 g, 85%; m.p. 88.9–89.1 °C, needles precipitated from $CHCl_3$ with pentane).

$(C_6H_5Se)_2C{=}P(C_6H_5)_3$ *(9)* $\qquad$ $(C_6H_5Se)_3C\text{-}CH_3$ *(10)*

$(C_6H_5Se)_3C\text{-}CHOH\text{-}C_6H_5$ *(11)*



(12)

Cpd.	Yield (%)	M.p. (°C)	Chemical shifts of the non-aromatic protons (τ) [a]
(1)	95	b.p. 138/0.1 torr	CH_2: 5.98 [b]
(3)	85	88.9–89.1	CH_2: 6.33 [b]
(5)	60	99.0–99.4	CH: 4.95 [b]
(6)	64	90.5–91.5	CH: 4.58 [c]
(8)	89	131–132	[c]
(9) [d]	65	148–149	[c]
(10) [e]	93	150–152	CH_3: 8.22 [b]
(11) [f]	86	150–151	CH: 4.96 [c]
(12) [g]	65	102.6–103.4 [h]	CH_2: 8.17 [c]

[a] Measured against TMS as internal standard; all signals are singlets; α-selenium proton signals show satellites at a separation of 5–6 Hz owing to ^{77}Se–^1H coupling. [b] in CCl_4; [c] in $CDCl_3$; [d] from *(7)*, $(C_6H_5)_3P$, and 1,2-Epoxy-cyclohexane (cf. [4]); [e] from *(7)* and CH_3I; [f] from *(7)* and C_6H_5–CHO; [g] from *(7)*, $(C_6H_5S)_2C{-}CH_2$, and 1,2-Epoxy-cyclohexane (cf. [4]); [h] A second crystal modification melts at 67.4–68.2 °C.

Received: April 8, 1969 [Z 988 IE]
German version: Angew. Chem. *81*, 465 (1969)

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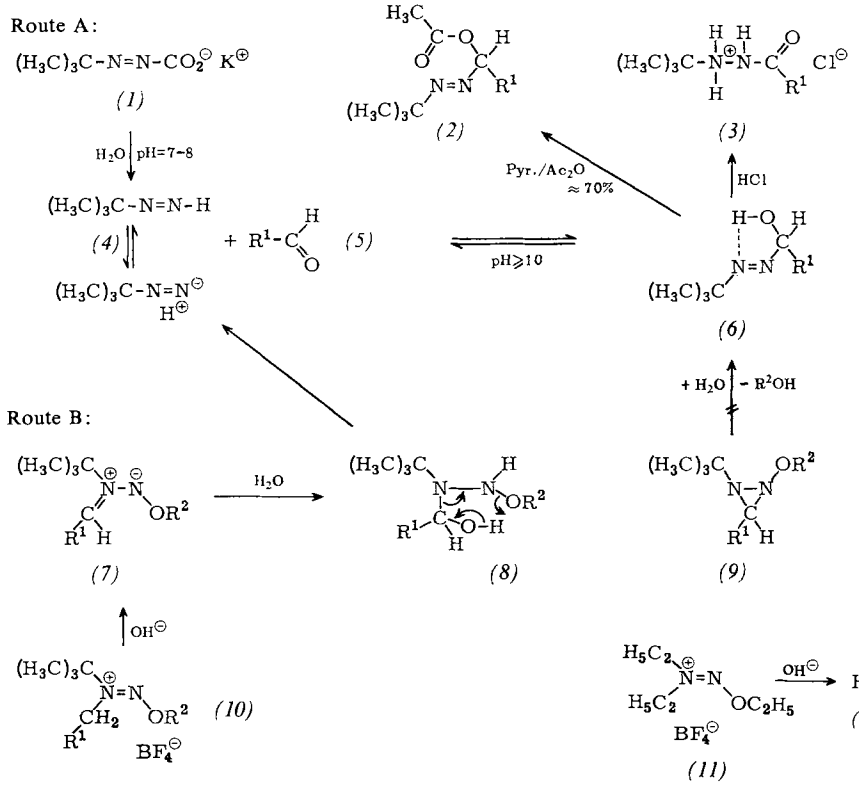
tert-Butyl-α-hydroxyalkyldiazenes from *tert*-Butyldiazenes

By *S. Hünig* and *G. Büttner*[*]

Although phenyldiazene[1,3], a compound characterized by its extreme oxygen-sensitivity, and *tert*-butyldiazene *(4)*[2] can be prepared as short-lived species in highly dilute solutions, attempts to intercept them in a manner such that the original diazene structure is retained[1c] have hitherto been unsuccessful. We have now found that *tert*-butyldiazene *(4)*,

formed according to routes A or B, can be intercepted in high yields by aliphatic aldehydes *(5)* in aqueous-alkaline media without any need for exclusion of oxygen.

The resulting *tert*-butyl-α-hydroxyalkyldiazenes *(6)* [4–6] are distillable, yellow liquids [7] which can be stored, but which slowly rearrange to the isomeric hydrazides [*(3)*-HCl] [5] and partly decompose to give polymeric products. This rearrangement is proton-catalyzed and on addition of HCl gas in ether leads quantitatively to the hydrochlorides *(3)*. Reaction with acetic anhydride in pyridine gives the esters *(2)* (cf. ref. [5]). The trans configuration of *(2)* and *(6)* follows from the low intensity of the n-π* band [8]. The OH band at 3390–3370 cm^{-1} (CS_2), which remains unchanged when the sample is diluted, confirms the presence of the intramolecular hydrogen bond in *(6)*.



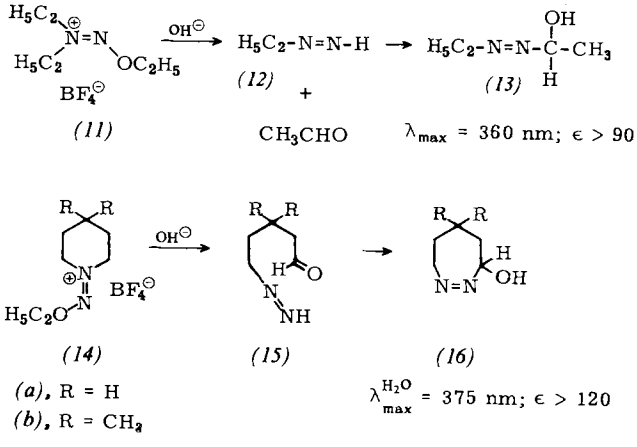
	R^1	*(6)* λ_{max} (nm)	ε	*(2)* λ_{max} (nm)	ε
		[a]		[a]	
(a)	H	340	18.8	359	16.3
(b)	CH_3	345	18.9	360	16.3
(c)	$CH_2CH_2CH_3$	343	19.6	363	17.2
(d)	$CH(CH_3)_2$	346	20.8	360	19.3

[a] In cyclohexane.

Route A: The characteristic absorption band of *(1)* at 373 nm disappears at pH 7–8. Subsequent addition of formaldehyde *(5a)* brings about no change since the *tert*-butyldiazene *(4)* formed transiently has already decomposed. However, if *(1)* is decomposed in the presence of *(5a)*, the spectrum of *(6a)* is immediately established. The adducts *(6a)*–*(6d)* are isolable on a preparative scale.

Route B: The alkoxydiazenium salts *(10)* [7,9] prepared from the nitrosamines [7] and trialkyloxonium fluoroborates (R^2 = CH_3, C_2H_5) are deprotonated by bases to the zwitterions *(7)* [10] which decompose with addition of water (or hydroxide ions), probably *via (8)*, to give *(4)* and *(5)* (as well as HOR^2). *(4)* and *(5)* combine immediately to give the adduct *(6)*. UV-spectroscopic measurements during the reaction of, *e.g.*, *(10a)* at pH 10 show that the band due to *(6a)* does not appear until ≈15% of *(10a)* has decomposed. This oxygen-independent induction period disappears completely if the solution contains an excess of formaldehyde right from the outset. It may thus be seen that the R^1–CH group in *(7)* does not migrate intramolecularly, *e.g. via (9)*, but that *(6)* results from a bimolecular reaction of *(4)* and *(5)*. Formation of *(6)* is reversible. If *(6c)* is treated for 1 h with 1.2 equivalents of formaldehyde at pH 10, then 20% of *(6a)* is formed (determined by gas chromatography). It would therefore appear that formation of *(6)* proceeds *via* the anion of *(4)*, *i.e.* in a manner analogous to the cyanohydrin reaction. The presence of formaldehyde during the reaction *(10c)* → *(6c)* also leads to the formation of *(6a)*.

The compounds *(13)* and *(16)* have been detected in solution (UV, NMR) as products of the reaction of *(11)* [11], *(14a)* [5], and *(14b)* [7,12] with bases, thus showing that both alkyldiazenes having an α-methylene group and those having the *cis* configuration can be intercepted by aldehydes. *(16)* is, however, much less stable than 3,5,5-trimethyl-1-pyrazolin-3-ol (described in ref. [6]) which carries no hydrogen atoms in the immediate vicinity of the functional group.



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

tert-Butylazo-2-methyl-1-propanol (tert-butyl-α-hydroxypropyldiazene) (6d)

Route A:

Methyl *tert*-butyldiazenecarboxylate (2.16 g, 15 mmole) is hydrolyzed with KOH (1.23 g, 22 mmole) in H_2O (10 ml), first at room temperature and then at 50–60 °C. The homogeneous solution is concentrated by evaporation under reduced pressure and the voluminous yellow precipitate *(1)* is added portionwise to *(5d)* (2.16 g, 30 mmole) in phosphate buffer solution (20 ml). During the ensuing reaction (evolution of CO_2), the pH is kept at 7–8 by addition of more

phosphate buffer. The reaction mixture is then extracted with three 25-ml portions of ether. Distillation of the residue left by the dried ether solution at 20–22 °C/0.05 torr gives 0.900 g (38%) of *(6d)* as a pale yellow liquid.

Route B:

5.2 g (20 mmole) of *(10d)* ($R^2 = CH_3$) in 50 ml H_2O is added dropwise with stirring to 2.07 g (15 mmol) of K_2CO_3 in 10 ml of H_2O at 40–45 °C. After one hour the filtered solution is extracted with four 40-ml portions of ether. Working up as for route A gives 1.722 g (55%) of a yellow liquid that is identical with *(6d)* prepared *via* route A.

Received: April 22, 1969 [Z 990 IE]
German version: Angew. Chem. *81*, 465 (1969)

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New Stationary Phase for Chromatography

By *I. Halász* and *I. Sebestian* [*]

The esterification of polysilicic acids with alcohols has already been described [1]. *Rossi et al.* [2] resolved C_1 to C_4 hydrocarbons in gas chromatographic columns packed with silica esterified with benzyl or lauryl alcohol. This separation, however, was not faster than those on other stationary phases.

We have esterified the porous glass "Porasil C" [2a] (having silanol groups on its surface, specific surface area 50 m^2/g, pore radius 100–200 Å) with 3-hydroxypropionitrile at 180 °C. The esterified product was extracted with methylene chloride and dried.

The gas and liquid chromatographic equipment used in these experiments was similar to that used in previous studies [3]. The rapid gas chromatographic separation of C_1 to C_3 hydrocarbons is shown in Fig. 1a. The vapor pressure of the stationary phase is extremely small; the noise level of the baseline could be neglected although the sample weighed only 10^{-8} g. This is of considerable importance if quantitative analysis is desired. The rate of separation achieved in this packed column is extremely high: 42 theoretical (n) or 23 effective plates (N), are generated per second. Values of only 0.1 to 2 effective plates per second are obtained with conventional packed columns [4].

Other hydrocarbons were resolved in the same column as shown in Fig. 1b. The peak due to the polar ether is symmetrical although the partition ratio is unusually high ($k' = 12.4$).

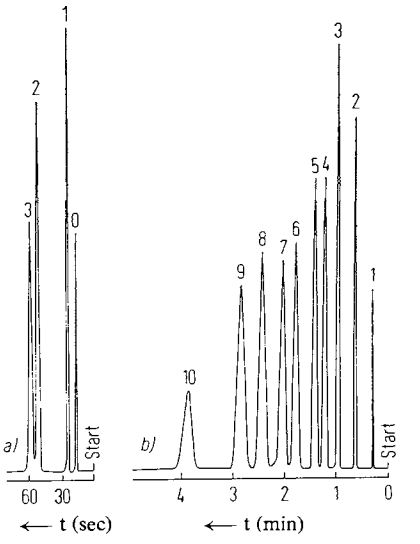


Fig. 1a) Gas chromatographic separation in a packed column. Stationary phase: Porasil C/3-hydroxypropionitrile (conditions not optimized). 0 = methane, 1 = ethane, 2 = propane, 3 = propene. T = 28 °C. Internal diameter of the column (i.d.): 2 mm; column length (L): 1 m; sieve fraction (d_p): 75–100 μm; carrier gas: N_2; time averaged linear velocity of the carrier gas ($\bar{u}$): 6.3 cm/sec; sample weight (s): 1–100 μg.

Fig. 1. b) 1 = methane, 2 = *n*-pentane, 3 = cyclohexane, 4 = 2,4-dimethylpentane, 5 = methylcyclohexane, 6 = 2,2,4-trimethylpentane, 7 = 2,3,4-trimethylpentane, 8 = *n*-octane, 9 = 2,2,5-trimethylhexane, 10 = diethylether.

Column and carrier gas as in Fig. 1a. Δp = 5.5 atm; $\bar{u}$ = 5.7 cm/sec; T = 121 °C.

Characteristic data for propene (Fig. 1a), cyclohexane, and ether (Fig. 1b).

partition ratio k'	2.9	2.27	12.4
number of theoretical plates n	2500	1950	2350
number of effective plates N	1380	950	2020
n/t (sec^{-1})	42	34	10.2
N/t (sec^{-1})	23	16.5	8.8

A liquid chromatographic separation on the same stationary phase with a narrower sieve fraction is illustrated in Fig. 2. Almost one effective plate per second was generated for *N,N*-dimethylaniline, this rate being comparable with values achieved in routine gas chromatographic separations.

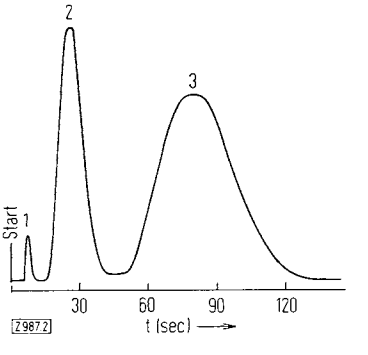


Fig. 2. Liquid chromatographic separation at 20 °C. Stationary phase: Porasil C/3-hydroxypropionitrile (conditions not optimized). 1 = toluene ($k' = 0$); 2 = *N,N*-dimethylaniline ($k' = 2.5$); 3 = 2,6-xylidine ($k' = 9.6$).

i.d. = 3 mm; L = 40 cm; d_p = 60–75 μm; mobile phase: *n*-heptane (liquid); Δp = 29 atm; u = 5 cm/sec; s = 40 μg; UV detector (cell volume 1 μl).

Characteristic data for *N,N*-dimethylaniline and 2,6-xylidine.

height equivalent to an theoretical plate h (mm)	12	13
hight equivalent to an effective plate H (mm)	6.2	11
n/t (sec^{-1})	1.2	0.36
N/t (sec^{-1})	0.9	0.32

The organic compounds of the stationary phase described above are orientated like bristles on the surface of the inorganic compounds[1,5]. Consequently the speed of the mass transfer is considerably higher here than in liquid stationary phases.

Further gas chromatographic experiments with columns packed with such "brushes" have shown, that the height equivalent to a theoretical plate (h) is independent of: (i) the nature of the sample (paraffins, aromatics, ether, esters, chlorinated hydrocarbons have been injected); (ii) the temperature of analysis (70–140 °C); (iii) the partition ratio ($k' = 1$–140); and (iv) the sample size (10^{-8} to 10^{-3} g in a column with internal diameter of 2 mm).

Received: April 8, 1969 [Z 987 IE]
German version: Angew. Chem. *81*, 464 (1969)

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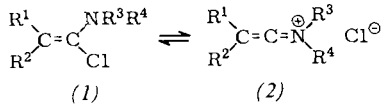
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Alkyl and Aryl α-Chloro Enamines

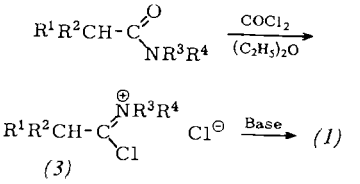
By *L. Ghosez, B. Haveaux*, and *H. G. Viehe*[*][1]

To the best of our knowledge α-chloroenamines *(1)* without stabilizing electronegative β-substituents[2] such as fluorine, chlorine, or carbonyl are hardly known. A brief report[3] on two representatives of this class has remained unconfirmed since 1929.



(1) *(2)*

(1) or *(2)* have been postulated as intermediates in the synthesis of ynamines from α-halogeno iminium salts[4] and in the reaction of ynamines with protonic acids[5], alkylating agents[5], or ketenes[6]. We have now prepared alkyl- or aryl-substituted α-chloro enamines by controlled dehydrochlorination of the readily available α-chloro iminium chlorides[7] *(3)*.



(3)

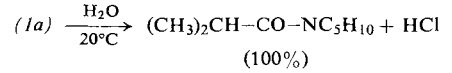
(1)	R^1	R^2	R^3	R^4	Base [a]	Temp. (°C)	Yield (%)	B.p. (°C/torr)
(a)	CH_3	CH_3	$-(CH_2)_5-$		A	20	70	95–100/15
(a)	CH_3	CH_3	$-(CH_2)_5-$		B	20	62	95–100/15
(b)	CH_3	H	$-(CH_2)_5-$		A	20	57	85–90/14
(c)	C_2H_5	H	$-(CH_2)_5-$		A	20	57	98/8
(d)	C_6H_5	H	C_2H_5	C_2H_5	A	−20	60–70 [b]	– [c]
(d)	C_6H_5	H	C_2H_5	C_2H_5	B	20	60–70 [b]	– [c]
(e)	C_6H_5	H	$-(CH_2)_5-$		A	−20	60–70 [b]	– [c]
(f)	C_6H_5	H	$-(CH_2)_2O(CH_2)_2-$		A	−20	60–70 [b]	– [c]

[a] A = triethylamine, B = pyridine.
[b] Yields 60–70%; determined by titration with bromine or with NaOH after hydrolysis.
[c] Distillation of *(1d)*–*(1f)* gave the corresponding cyclobutenecyanines *(5)*, possibly *via* the ynamines.

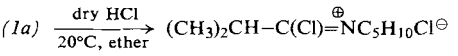
Physical and spectroscopic data for the α-chloro enamines exclude the presence of a substantial amount of the polar form at equilibrium. However, the compounds show the expected versatile behavior as exemplified in the following reactions:

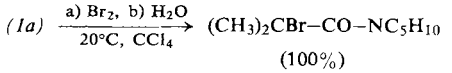
1. Addition

1.1. Hydrolysis:

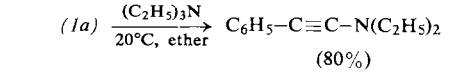


1.2. Formation of α-chloro iminium salts:

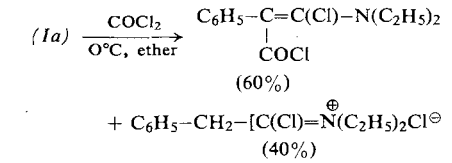




2. Eliminations yielding ynamines. α-Chloro enamines *(1)* may produce ynamines as well as their corresponding α-chloro iminium chlorides by elimination of hydrogen chloride. The stepwise formation of phenylynamine with triethylamine at room temperature shows the unusually mild conditions of this acetylene synthesis:



3. Acylation. α-Chloro enamines are less readily acylated than enamines or ynamines; even the relatively more reactive β-monosubstituted α-chloro enamines condense only with the most powerful acylating agents. This indicates that the α-chlorine substituent effectively reduces the nucleophilicity of the β-carbon atom.



4. Nucleophilic chlorine substitution. One outstanding chemical characteristic of α-chloro enamines is their exceptional reactivity in nucleophilic substitution reactions.

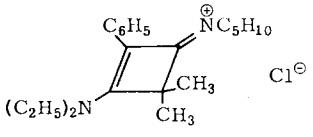
For example, *(1a)* affords enamines and *S,N-*, *O,N*, and *N,N*-ketene acetals of the type *(4)*.

$(CH_3)_2C{=}C(R)NC_5H_{10}$ *(4)*

R	Reagent	Conditions	Yield (%)	B.p. (°C/torr)
CH_3	CH_3Li	20 °C, 3 h, Ether	70	
C_6H_5	C_6H_5MgBr	20 °C, 3 h, Ether	65	90/0.4
SC_2H_5	C_2H_5SNa	20 °C, THF	90	76/0.3
OC_2H_5	C_2H_5ONa	20 °C, THF	80	80/8
$N(C_6H_{11})_2$	$LiN(C_6H_{11})_2$	0 °C, Ether	80	155/0.9

5. Cycloadditions. The reaction of α-chloro enamines with ynamines yields cyclobutenecyanines:

(1a) + $C_6H_5{-}C{\equiv}C{-}N(C_2H_5)_2$ $\xrightarrow[(C_2H_5)_2O]{20°C,\ 30\ min}$



(5) (70%)

It is of preparative value that diaryl derivatives of *(5)*, *e.g.* diethyl(3-diethylamino-2,4,4-triphenyl-2-cyclobutenylidene)-ammonium chloride, are obtained in high yields from α-chloro iminium salts with stoichiometrical amounts of tertiary amines or simply by thermal HCl elimination (in example: 55% yield, $(C_2H_5)_3N$, 20 °C, in ether).

N-(1-Chloro-2-methylpropyl)piperidine (1a)

Phosgene (17 g, 0.17 mole) was passed slowly into a cooled (0 °C) solution of *N*-piperidinoisobutyramide (21 g, 0.135 mole) in dry ether (150 ml). After 5 h the excess of phosgene was removed at water pump vacuum and the resulting mixture was treated with triethylamine (14 g, 0.138 mole) at room temperature. Complete precipitation of the triethylamine hydrochloride was effected by addition of 60 ml of pentane. After filtration of the reaction mixture in the absence of moisture, the solution was concentrated *in vacuo*. Distillation through a short Vigreux column yielded 16.3 g (70%) of *(1a)*, b.p. 95–100 °C/15 torr.

Received: April 28, 1969 [Z 991 IE]
German version: Angew. Chem. *81*, 468 (1969)

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[1] We thank Mrs. *A. Dekoker* for experimental assistance.

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Crystal Structure of $PCl_4(NCH_3)_2CCl$, a Four-Membered Ring System containing Hexavalent Phosphorus[1]

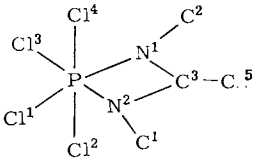
By *M. L. Ziegler* and *J. Weiss* [*]

By reaction of *N,N'*-dimethylchloroformamidine hydrochloride with PCl_5, *Latsche* and *Hormuth*[2] recently obtained a compound with the composition $C_3H_6Cl_5N_2P$ which they formulated as a four-membered ring compound with six-fold coordinated phosphorus, $Cl_4P^{\ominus}(NCH_3)_2C^{\oplus}Cl$ *(1)* on account of the ^1H- and ^{31}P-NMR spectra.

We have established the structure of this unusual compound by X-ray analysis. Because of its extreme sensitivity to moisture the crystal used for measurement was sealed in three Lindemann-glass tubes placed one inside the other, the outermost tube being filled with P_4O_{10} at each end; in spite of this, it was not possible to prevent gradual hydrolysis during the photography.

Crystallographic data: monoclinic, space group $C_{2h}^5-P2_1/c$; $a = 12.813$, $b = 6.915$, $c = 13.215$ Å, $\beta = 114.6°$; $N = 4$; $d_{X\text{-ray}} = 1.72$ g/cm³.

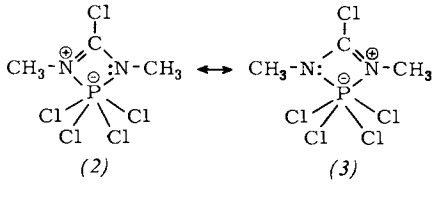
Weissenberg photographs (Cu–K_α radiation) about the c^*-axis ($l = 0$–7) gave 451 independent reflections, whose intensities were estimated visually and corrected in the usual way. The structure determined by three-dimensional Patterson and Fourier syntheses was refined by the method of least squares with isotropic temperature factors to give an *R* factor of 0.13.



Bond lengths (Å; with standard deviations) and bond angles (degrees).

P–Cl^1	2.15 (2)	N^2–P–N^1	70.7	Cl^2–P–N^1	88.8
P–Cl^2	2.09 (1)	P–N^1–C^3	81.4	Cl^2–P–N^2	90.2
P–Cl^3	2.07 (2)	N^1–C^3–N^2	119.3	Cl^3–P–N^1	97.2
P–Cl^4	2.10 (1)	C^3–N^2–P	88.6	Cl^3–P–N^2	167.7
P–N^1	1.91 (4)	Cl^1–P–Cl^2	88.4	Cl^4–P–N^1	88.8
P–N^2	1.85 (6)	Cl^1–P–Cl^3	95.5	Cl^4–P–N^2	90.2
N^1–C^2	1.45 (6)	Cl^1–P–Cl^4	91.8	P–N^1–C^2	133.8
N^1–C^3	1.34 (5)	Cl^2–P–Cl^3	92.0	P–N^2–C^1	131.0
N^2–C^1	1.48 (6)	Cl^2–P–Cl^4	178.5	C^3–N^1–C^2	143.2
N^2–C^3	1.19 (6)	Cl^3–P–Cl^4	89.6	C^3–N^2–C^1	138.4
C^3–Cl^5	1.84 (4)	Cl^1–P–N^1	167.1	N^1–C^3–Cl^5	111.0
		Cl^1–P–N^2	96.7	N^2–C^3–Cl^5	129.7

The four-membered ring is planar. In the ring plane there lie also two of the chlorine atoms bound to the phosphorus, the chlorine atom bound to carbon, and the carbon atoms of the two methyl groups. The phosphorus atom is in an approximately octahedral environment. The P–Cl distances are normal, with a mean of 2.10 Å. The P–N distances are distinctly greater than the P–N single-bond distance (1.77 Å) and the C–N bond lengths in the ring appear to be shorter than for a C–N single bond (1.48 Å). This shows that the



(2) *(3)*

positive charge is not localized on the carbon atom (cf. *(1)* [2]) but on the nitrogen atoms with formation of a partial double bond; thus one comes to the mesomeric limiting structures *(2)* and *(3)*. The bond lengths between the methyl

carbon atoms and the nitrogen atoms are within the limits for a C–N single bond.

Received: March 17, 1969 [Z 982 IE]
German version: Angew. Chem. *81*, 430 (1969)

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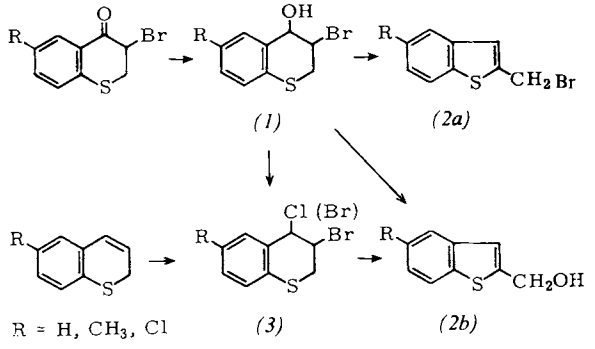
[1] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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Ring Contraction of 1-Thiochromans to Benzo[*b*]thiophenes

By *H. Hofmann* and *G. Salbeck* [*]

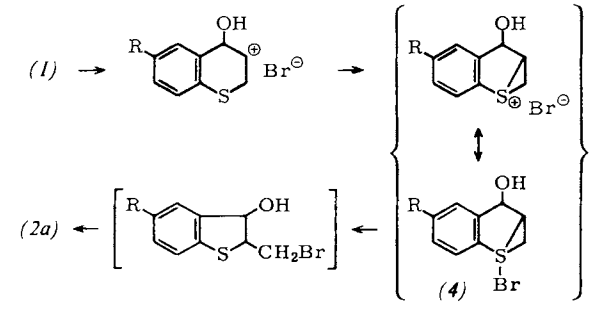
Reduction of 3-bromo-1-thio-4-chromanone (R = H) with $NaBH_4$ or $LiAlH_4$ leads to the formation of *trans*-3-bromo-1-thio-4-chromanol *(1)*, R = H, in high yields [1]. On heating in dioxane under reflux, compound *(1)* rearranges with loss of water to 2-bromomethylbenzo[*b*]thiophene *(2a)*, R = H. The same rearrangement takes place when *(1)* is distilled with potassium hydrogen sulfate at 0.1 torr. If the rearrangement is carried out in aqueous dioxane (2-benzo[b]thienyl)-methanol *(2b)*, R = H, is formed. *trans*-3,4-Dihalogeno-1-thiochromans *(3)*, R = H, which can easily be prepared from the hydroxy compound *(1)* or from the known 1-thio-2*H*-chromene, also rearranges to *(2b)* with loss of halogen hydride on heating in dioxane/water.



The structure of the rearrangement products *(2a)* and *(2b)* follows from their UV-, IR-, and ^{1}H-NMR spectra as well as from independent syntheses from the correspondingly substituted benzo[*b*]thiophene-2-carboxylic acid [2].

3-Bromo-2-methyl-1-thiochroman-4-ol, prepared in a similar manner, likewise rearranges on heating in dioxane to 2-(α-bromoethyl)benzo[*b*]thiophene; however, in aqueous dioxane further elimination of hydrogen bromide takes place and 2-vinylbenzo[*b*]thiophene [3], m.p. 55–58 °C, is formed.

We assume that in the case of *(1)* and *(3)* loss of bromide ion is facilitated and the carbonium ion already formed is stabilized by neighboring group participation of the thioether group. We cannot as yet decide how the rearrangement itself is initiated.



An indication of the participation of *(4)* is reflected in the stability of the acetate of *(1)*, which does not undergo rearrangement; the acetoxy group on C-4 evidently stabilizes the carbonium ion on C-3. The same argument can be used for the stability of the 3,3-dibromo-1-thio-4-chromanols and of 3-bromo-3-methyl-1-thio-4-chromanol.

2-Bromomethylbenzo[b]thiophene (2a), R = H

A solution of 3-bromo-1-thio-4-chromanol *(1)*, R = H [1] (2.8 g; 11.4 mmoles) in anhydrous dioxane (40 ml) is heated under reflux for 3 h and then evaporated under vacuum. After crystallization of the residue from 25 ml of petroleum ether at −20 °C, 2.3 g (89%) of *(2a)*, R = H, was obtained (m.p. 48–52 °C, which on recrystallization from petroleum ether increased to 58–59 °C). UV (ethanol): λ_{max} = 206 nm (ε = 2.5 × 10⁴); 229 (2.5 × 10⁴); 273 (1.5 × 10⁴); 300 (0.5 × 10⁴). IR (KBr): benzo[*b*]thiophene skeletal vibration 1530 cm^{-1}; ν-CH_2– 1428 cm^{-1}. ^{1}H-NMR ($CDCl_3$): τ = 5.35 (CH_2, s).

(5-Methyl-2-benzo[b]thienyl)methanol (2b) R = CH_3

A solution of 3-bromo-6-methyl-1-thio-4-chromanol *(1)*, R = CH_3, (1.5 g; 6 mmoles) in dioxane (20 ml) and water (5 ml) is heated under reflux for 10 h and then poured into 0.4 l of water with stirring. The colorless precipitate, 1.0 g, is then recrystallized from 15 ml of ligroin. 0.87 g (83% yield) of *(2b)* (R = CH_3; m.p. = 92–93 °C) is obtained. UV (ethanol): λ_{max} = 206 nm (ε = 3 × 10⁴); 233 (3.7 × 10⁴); 265 (1.3 × 10⁴); 295 (0.4 × 10⁴); 305 (0.4 × 10⁴). IR (KBr): νOH 3400 cm^{-1}; benzo[*b*]thiophene skeletal vibration 1500 cm^{-1}; νCH_2 1450 cm^{-1}. ^{1}H-NMR ($CDCl_3$): τ = 5.2 (CH_2, s); 7.2 (OH, s); 7.6 (CH_3, s).

Received: March 24, 1969 [Z 976 IE]
German version: Angew. Chem. *81*, 424 (1969)

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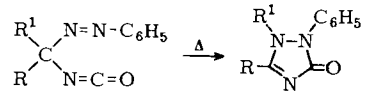
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Thermal Rearrangement of Phenylazomethyl Isocyanates

By *H. Schildknecht* and *G. Hatzmann* [*]

Oxidation of semicarbazones usually leads to the formation of 1,2,4-triazolones or 1,3,4-oxadiazoles. In the case of 2-phenylsemicarbazones of ketones, however, a direct oxidative cyclization is not possible. With chromyl acetate or lead tetraacetate they are oxidized to phenylazomethyl isocyanates *(1)* [1,2], which subsequently can be cyclized to 1,2,4-triazolones *(2)*. For example, if *(1a)* is heated in the absence of solvent for a few minutes at 140 °C migration of the ethyl group and ring closure take place resulting in the formation of *(2a)*, m.p. 113–114 °C; λ_{max} ($CHCl_3$) = 263 nm (log ε = 3.94).

The structure of the rearrangement product can be deduced from the results of elemental analysis and from IR and NMR spectra. The IR spectrum of *(2a)* does not show the isocyanate band at 2220 cm^{-1}. Instead, a new band appears at 1678 cm^{-1}; NH-bands are absent. The ^{1}H-NMR spectrum ($CDCl_3$) of *(2a)* indicates migration of the ethyl group to a N-atom or O-atom. The spectrum shows, in addition to the multiplet of the aromatic protons (τ = 2.62; 5H) and the singlet for the protons of the C-methyl group (τ = 7.60; 3H),

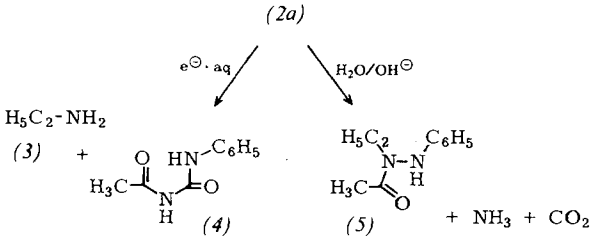


(1) (2)

(2)	R	R^1	M.p. (°C)	Yield (%)
(a)	CH_3	C_2H_5	113–114	96
(b)	CH_3	CH_3	174–176	94
(c)		$-(CH_2)_5-$	150–152	92
(d)	CH_3	$CH_2-C_6H_5$	142–144	94
(e)	C_6H_5	C_6H_5	236–238	90

a quadruplet (τ = 6.17; 2H) and a triplet (τ = 8.98; 3H) due to an ethyl group that is bound to a N- or O-atom.

The structure of *(2a)* can be proved unequivocally to be 2-ethyl-3-methyl-1-phenyl-1,2,4-triazol-5-one by electron pyrolysis[3], which furnishes ethylamine *(3)* and *N*-acetyl-*N'*-phenylurea *(4)* as main fragmentation products.



(2a)

Like *(1a)*, compounds *(1b)–(1e)* can also be converted into the corresponding triazolones *(2)*. Yields are almost quantitative. Reaction of *(1b)* does not start until a temperature of 170 °C is reached; in the case of the other compounds, however, a temperature of 140 °C suffices.

1,2,3-Substituted triazolones are very soluble in water and, unlike the 1,2,4-substituted triazolones, are stable toward acid hydrolysis. However, they dissociate on treatment with aqueous alkalis with formation of the corresponding acyl hydrazines; *e.g.*, *(2a)* yields *(5)*.

Received: May 2, 1969 [Z 993 IE]
German version: Angew. Chem. *81*, 469 (1969)

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[2] The compound obtained by oxidation of acetone-2-phenylsemicarbazone with iodine may likewise be a phenylazomethyl isocyanate; cf. *D. J. Blackstock* and *D. A. R. Happer*, Chem. Commun. *1968*, 63.

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Preparation of Cyclic Amidines by Reduction of Dinitriles with $LiAlH_4$

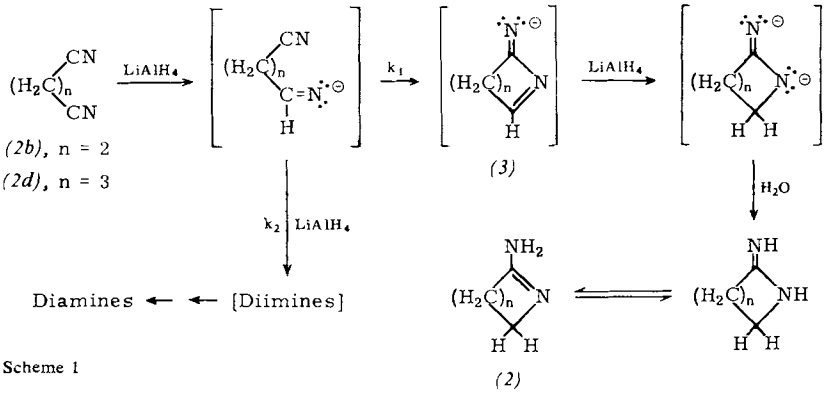
By *H. U. Sieveking* and *W. Lüttke*[*]

In an attempt to prepare 1,2-bis(aminomethyl)cyclobutane from a mixture (40:60) of *cis*- *(1a)* and *trans*-cyclobutanedicarbonitrile by reduction with an excess of $LiAlH_4$ we obtained only 35% of the expected product instead of the 65% reported in ref.[1]. Instead, we isolated the cyclic amidine *(2a)*, which was formed only from the *cis*-dinitrile as shown by treatment of the pure isomer with $LiAlH_4$; the *trans*-form gave mainly the diamine.

To test the generality of application of this ring-closure reaction the dinitriles *(1a)–(1d)* were treated with $LiAlH_4$ (see Table).

	Dinitrile *(1)*	Amidine *(2)*	Yield (%)	B.p. (°C/torr)	M.p. (°C)	M.p of picrate (°C)
(a)	*cis*-		22	88/0.5	41–49	202–204
(b)			30	65/0.1	77–79 78–80 [2]	190–192
(c)			45	125/1.0	110–112	232–233
(d)			8	82/0.1	95–97	200–201 207 [3]

In agreement with previous results[4,5] we consider the most probable mode of reaction to be that in Scheme 1.



Scheme 1

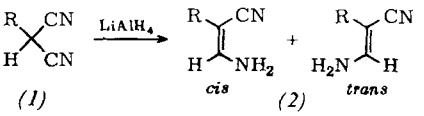
Because of its negative charge the imino group formed in the first step is protected against further nucleophilic attack by the tetrahydroaluminate; if it stands close to the second nitrile group it protects the latter from reduction and with its favorable steric orientation attacks that group itself in a nucleophilic reaction that leads to ring closure. As a Schiff base the intermediate amidine anion *(3)* is readily reduced further, so that the more stable amidine *(2)* can be isolated.

Reduction of *(1b)* and *(1c)*, where $n = 2$ can give a strain-free five-membered ring; here $k_1 \gg k_2$, so that the cyclic amidines *(2b)* and *(2c)* are the only monomeric products.

When the nitrile groups are further apart ($n \geqq 3$), k_2 is greater, since the negatively charged imino group can protect the nitrile group only to a smaller extent, whilst k_1 decreases owing to the sterically less favorable position of the reacting groups; thus reduction of *(1d)* gives comparable amounts of diamine and amidine *(2d)* ($k_1 \approx k_2$) with a little piperidine.

That open-chain amidine can be formed analogously from mononitriles (where $n = \infty$) is shown by the reaction of benzonitrile with an excess of $LiAlH_4$; we were able to isolate

N^1-benzylbenzamidine [b.p. 170 °C/0.8 torr, m.p. 77 °C (77–78 °C in ref.[6]) as well as the products obtained by *Soffer*[7] (benzylamine, benzylidenebenzylamine, triphenyltriazine); however, since $k_1 < k_2$ the yield of the amidine is only 2.5%.



(1) *cis* *(2)* *trans*

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

	M.p. (°C)	B.p. (°C/0.4 torr)	IR (cm^{-1}) (N–H)	(C≡N)	(C=C)	NMR (H)	(R)	J_{R-H}(Hz)
cis-(2a)	8	67–68	3470, 3360	2180	1595	6.79	3.88	8.3
trans-(2a)						7.03	4.20	13.5
cis-(2b)	70–71	70	3470, 3350	2170	1600	6.79	1.66	1
trans-(2b)						6.95	1.73	1

The reaction of dinitriles with $LiAlH_4$ gives open-chain and cyclic anions that can undergo intramolecular condensation with unattacked nitrile groups[4,8]. More than 50% of oligomers and polymers are formed, but this can be reduced by dilution, use of an excess of $LiAlH_4$, and short reaction times.

The amidines were characterized by their IR, NMR, and mass spectra as well as by analysis. In the monomeric state the cyclic amidines of the type studied appear to exist primarily in the tautomeric form *(2)* containing an endocyclic double bond, since, in all the C_2Cl_4 solution spectra, increasing dilution increases only the intensity of the bands at 3500 and 3400 cm^{-1} which, according to *Moritz*[9], can be assigned to the stretching vibrations of the NH_2 group.

2-Amino-1-pyrroline (2b)

A solution of *(1b)* (26 g, 0.325 mole) in ether/THF (4:1, 250 ml) is added dropwise to a suspension of $LiAlH_4$ (26 g, 0.72 mole) in ether/THF (6:1, 1.6 l). The mixture is stirred for 2 h at room temperature, washed with, successively, H_2O (25 ml), 20% NaOH solution (25 ml), and H_2O (75 ml), filtered, and dried over K_2CO_3. Crude *(2b)* (12 g) crystallized on concentration and could be purified by distillation in a vacuum; the yield of pure product was 30% (8 g).

Received: April 1, 1969 [Z 986a IE]
German version: Angew. Chem. *81*, 431 (1969)

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Preparation of Enamino Dinitriles and Pyridines by Reduction of Geminal Dinitriles with $LiAlH_4$

By *H. U. Sieveking* and *W. Lüttke*[*]

In contrast to longer-chain α,ω-dinitriles, malonodinitrile *(1a)* and methylmalonodinitrile *(1b)* do not give cyclic amidines on reduction by $LiAlH_4$[1]. Instead, the imino nitrile first formed stabilizes itself by tautomerization, which leads to the new enamino nitriles *(2a)* and *(2b)* as sole monomeric products in about 40% yield.

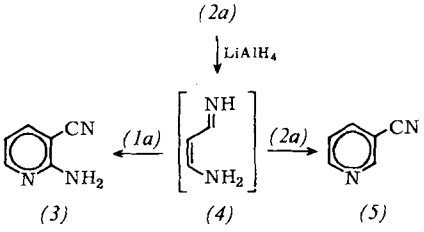
Metalation of all the acidic protons of *(2)* gives an anion that is relatively stable toward further attack by hydride[2] because of its negative charge and, in particular, because a sparingly soluble complex is formed.

The initial products formed from *(1a)* and *(1b)* are *cis-trans*-mixtures; however, only the more stable *cis*-enamino nitriles can be isolated since the *trans*-form rearranges to the *cis*-form on distillation[3,4].

The structures of *(2a)* and *(2b)* were elucidated primarily by their NMR spectra, the H–R coupling constants and the chemical shifts permitting assignment of the tautomeric forms; as in the case of the 3-aminoacrylic esters[4], coupling with the NH_2 group (J_{H-NH_2} = 10 Hz) was observed. *(2a)* and *(2b)*, which are very useful starting materials for the synthesis of substituted heterocycles, behave in many respects like 3-aminocrotononitrile[5]. Thus, thiocytosine and methylthiocytosine can be prepared by reaction with thiourea, in analogy to *Polonowski*'s work[6]; unlike 3-aminocrotononitrile, however, *(2a)* reacts with the less nucleophilic urea giving cytosine, which is thus now available in two steps. By reaction of phenylhydrazine with *(2a)* we obtained 5-amino-1-phenylpyrazole by way of the phenylhydrazone, in analogy to *Mohr*'s work[7].

On reduction of *(1a)* with $LiAlH_4$ we isolated, not only *(2a)*, but also a 10% yield of 2-aminonicotinonitrile *(3)* (m.p. 132.5–134 °C), which is otherwise more difficulty accessible[8]; on slow reduction by an excess of $LiAlH_4$, 2% of nicotinonitrile[5] was also formed, being recognizable by its typical NMR spectrum and its molecular ion in the mass spectrum. The formation of this product can be described formally by condensation of *(1a)* or *(2a)* with 3-imino-1-propenylamine *(4)*, which can arise by further reduction of the enamine *(2a)*[2,5,9].

No pyridine derivative could be obtained from *(1b)*, since the latter contains no mobile hydrogen that is necessary for aromatization.



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

β-Aminoacrylonitrile (2a) and 2-aminonicotinonitrile (3)

A solution of *(1a)* (20 g, 0.30 mole) in ether/THF (1:2; 100 ml) is added to $LiAlH_4$ (10 g, 0.26 mole) in ether/THF (4:1; 1.2 l), and the mixture is treated as in ref.[1]. *(3)* (1.8 g) crystallizes from the crude product (13.2 g); recrystallization from ether (charcoal) gives 7% (1.2 g) of pure *(3)*. The mother liquors, containing an approximately 90% yield of 1:1 *cis-trans*-mixture *(2a)*, is fractionated through a 10-cm Vigreux column, whereupon 40% (8 g) of *cis-trans-(2a)* (5:1) is obtained; a second distillation gives 5 g of the pure *cis*-isomer.

Received: April 1, 1969 [Z 986b IE]
German version: Angew. Chem. *81*, 432 (1969)

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[1] Cf. *H. U. Sieveking* and *W. Lüttke*, Angew. Chem. *81*, 431 (1969); Angew. Chem. internat. Edit. *8*, 457 (1969).

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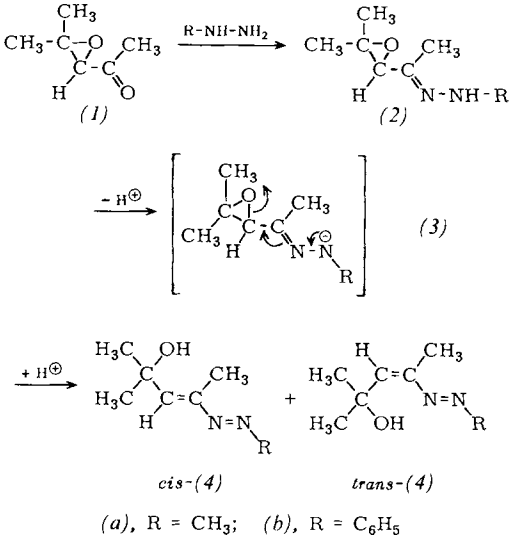
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A New Method for the Preparation of α,β-Unsaturated Azo Compounds

By *E. Gründemann* [*]

During attempts to prepare the hydrazones *(2a)* and *(2b)* by reaction of equimolar amounts of 4-methyl-3,4-epoxy-2-pentanone *(1)* [1] with methyl- and phenylhydrazine α,β-unsaturated azo compounds were obtained as deep yellow and red compounds, respectively, whose spectra and analytical data are consistent with structures *(4a)* and *(4b)*.



cis-(4) *trans-(4)*

(a), R = CH_3; *(b)*, R = C_6H_5

The electron shift to give *(3)*, which is induced by deprotonation of the hydrazone intermediate *(2)* by unreacted hydrazine [2], leads to epoxide ring cleavage; re-addition of a proton then gives α,β-unsaturated azo compounds *(4)*. Compounds of this type may also be prepared by reaction of α-halogeno ketones with methylhydrazine [3] or by oxidation of α,β-unsaturated monoalkyl hydrazones with lead(IV) acetate [4].

Reaction of *(1)* with 2,4-dinitrophenylhydrazone does not proceed beyond the hydrazone *(2)*. Although the presence of the two nitro groups considerably enhances formation of the hydrazone anion, the nucleophilic character of the anion is nevertheless reduced at the same time. An electron shift, which can be brought about by the use of high temperatures or prolonged reaction times, leads to complete decomposition. *Eschenmoser et al.* [5] have suggested that fragmentation of the *p*-toluenesulfonylhydrazone of an epoxy ketone proceeds, *inter alia*, by way of α,β-unsaturated azo compounds as intermediates.

According to their NMR and IR spectra, the azo compounds *(4)* exist as a mixture of the *cis* and *trans* isomers. Investigation of the undistilled reaction product shows that it contains 90% of the *trans* isomer, whereas after distillation the *cis* isomer can predominate. Since intramolecular hydrogen bonding can only take place in the cis form, measurement of the ν-OH vibrations and the resonance of the hydroxyl group permit assignment of the configuration. *cis-* and *trans-(4a)* can even be separated by distillation. As expected, *cis-(4a)* has a lower boiling point than *trans-(4a)* and the resonance of its hydroxyl group appears downfield from that of *trans-(4a)*. In the OH stretching region, the IR spectrum of *trans-(4a)* (5×10^{-3} N in CCl_4) contains only a sharp band at 3600 cm^{-1}, and at higher concentrations also a broad band at 3400 cm^{-1}, whereas the spectrum of *cis-(4a)* shows only a broad band at 3400 cm^{-1}, which is also observed in dilute solution and which is assigned to an associated OH stretching vibration.

2-Methyl-4-methylazo-3-penten-2-ol (4a) and 2-methyl-4-phenylazo-3-penten-2-ol (4b)

Methylhydrazine (4.6 g, 0.1 mole) or phenylhydrazine (10.8 g, 0.1 mole) is added to compound *(1)* (11.4 g, 0.1 mole). The heat evolved during reaction is removed by cooling with water. After 20 hours' standing at room temperature, the reaction mixture is treated with ether (25 ml), water evolved during the reaction is separated off, and the ethereal phase is dried over calcium chloride and distilled under vacuum.

The reaction with methylhydrazine affords 12.7 g (89%) of a yellow liquid containing 75% of *trans-(4a)* and 25% of *cis-(4a)*, b.p. 78–93 °C/12 torr. *cis-* and *trans-(4a)* can easily be separated by fractional distillation over a Widmer spiral.

trans-(4a), b.p. 92–93 °C/12 torr; UV: λ_{max} = 394.6 nm (log ε = 1.907); NMR: (C_6D_6, TMS as internal standard) τ = 8.65 (6H, s); 7.91 (3H, d, *J* = 1.1 Hz); 7.50 (1H, s, –OH); 6.28 (3H, d, *J* = 0.5 Hz); 3.28 (1H, m).

cis-(4a), b.p. 77–78 °C/12 torr; UV: λ_{max} = 389.1 nm (log ε = 2.072); NMR: (C_6D_6) 8.53 (6H, s); 8.30 (3H, d, *J* = 1.1 Hz); 6.49 (3H, d, *J* = 0.7 Hz); 4.13 (1H, s, –OH); 4.05 (1H, m).

The reaction with phenylhydrazine yields 16.2 g (80%) of a red liquid containing 40% of *trans-(4b)* and 60% of *cis-(4b)*, b.p. 102–108 °C/0.1 torr.

Received: April 18, 1969 [Z 989 IE]
German version: Angew. Chem. *81*, 467 (1969)

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The Scope of NMR Studies on Paramagnetic Compounds

By *K. E. Schwarzhans*[*]

NMR techniques were originally assumed to be suitable only for the study of diamagnetic substances, in the same way that ESR methods are only applicable to paramagnetic compounds. About 10 years ago *McConnell*[1] developed a model showing that paramagnetic compounds also give NMR spectra in almost all cases in which the electron relaxation times are shorter than 10^{-6} seconds. The most striking feature of the NMR spectrum of a paramagnetic compound is the exceptionally large shift of the resonance signals compared to those in the spectra of comparable diamagnetic substances. According to *McConnell*, these shifts arise from the delocalization of unpaired electrons over the whole molecule.

Contradictions between the McConnell model and experiment became apparent during NMR studies on the paramagnetic representatives of the bis(cyclopentadienyl)metal complexes of the 3d elements. The ^{1}H-NMR spectra of this class of substances becomes readily interpretable, however, if direct transfer of unpaired electrons from partly occupied d orbitals of the central metal atom to s orbitals of the ligand hydrogen atoms is assumed to occur in addition to electron delocalization.

This postulate was tested by means of the ^{1}H- and ^{14}N-NMR spectra of a large number of substituted bis(cyclopentadienyl)metal complexes and bis(salicylaldehydato) and bis(salicylideneiminato) complexes of cobalt(II) and nickel(II) containing pyridine and picolines as axial ligands. In every case the sign and magnitude of the shift showed a strong dependence on the position of the relevant nucleus in the molecule. Shifts of up to 1% of the resonance frequency were observed. In extreme terms, a strong direct electron transfer, *e.g.* in the bis(cyclopentadienyl)metal complexes studied, can be regarded as leading to a metal-hydrogen-carbon bond. Results obtained by *I. A. Ronova*[2] from electron diffraction studies on bis(cyclopentadienyl)metal complexes, which show the cyclopentadienyl protons to be deflected out of the plane of the ring in the direction of the metal atoms, lend support to this concept.

Lecture at Berlin on February 17, 1969 [VB 198 IE]
German version: Angew. Chem. *81*, 433 (1969)

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The Structure of Molten Alloys in Relation to their Properties

By *S. Steeb*[*]

Results of wide-angle X-ray studies on molten metals and alloys were used for the plotting of electron distribution curves from which four pieces of information could be obtained: Classification of the melt; partial and total coordination numbers; the Cowley short range order parameter; and finally, as the most recent development, the quantitative resolution of certain alloys into their structural components. We employed our new technique for measurement of the small-angle scattering of melts at temperatures up to 800 °C. For molten aluminum, the isothermal compressibility calculated from small-angle scattering agrees well with that obtained from measurements on the velocity of sound (2.387×10^{-6} bar^{-1}). Small-angle studies on molten Al–Sn alloys evidence the presence of Sn clusters.

According to recent theories, the compressibility[1] and electrical resistance[2] of alloys can also be calculated from X-ray diffraction data.

Lecture at Berlin on February 11, 1969 [VB 199 IE]
German version: Angew. Chem. *81*, 433 (1969)

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Chemical Applications of Electron Microscopy: Topotactic Reactions

By *H. R. Oswald*[*]

In 1919 *V. Kohlschütter* introduced the term "Topochemical Reaction" for chemical processes in which the properties of the solid reaction products are determined by reactions which take place on or in a solid substance, *i.e.* locally. "Topochemistry" ought to include all influences of structure and morphology of the starting materials and end products on the course of reactions between solids and solids, solids and liquids, and solids and gases.

Modern electron microscopy has proved itself an invaluable tool for investigations in this field of chemistry. In addition to the direct picture method – often carried out with the aid of heating, cooling, and goniometer accessories – various reproduction methods have been successfully introduced. In the investigation of topochemical processes, electron microscopical (*i.e.* morphological) findings must always be combined with the results obtained by structural methods, usually X-ray methods. Fine-range electron diffraction is an important method in this connection; also of importance are thermal analysis and specific surface area measurements.

In recent times, the term "topotaxy" or "topotactic reaction" has developed within the broad field of topochemistry; it is used to describe "reactions in which a product is formed that has a crystalline orientation related to that of the starting material". The mutual structure relations and course of the topotactic rearrangement have been studied in detail on the basis of the following three reactions:

1. Conversion of solid copper hydroxide salts (fluoride, nitrate, nitrite, perchlorate, sulfate) into copper hydroxide in sodium hydroxide solutions.

2. Oxidation of manganese(II) hydroxide with molecular oxygen (*e.g.* for a solid/gaseous system; influence of topotaxy on the reaction kinetics).

3. Conversion in cobalt chloride solutions of zinc hydroxide nitrate crystals, into zinc-cobalt hydroxide chlorides, which can be prepared only by a topotactic route.

The definition of topotaxy as crystal structure nucleation and growth relation of two or more solid phases has been discussed on the basis of these studies. The three dimensional structure analogy of the topotactic partner claimed by several authors can be dispensed with, for one- and two-dimensional structure relations obviously also suffice. To delineate it from epitaxy the topotactic reaction must embrace the whole starting lattice.

Topotactic reactions occur in all processes involving participation of solids; they occur much more frequently than has hitherto been assumed and must always be taken into consideration in investigations on the interelation of structure, appearance and chemical reactivity. Thus, topotaxy plays an important role in numerous branches of applied chemistry such as sintering processes and corrosion in aqueous solutions or in hot gases. The interesting biological process of bone formation also involves topotactic reactions.

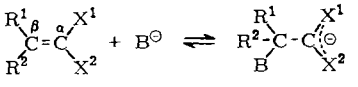
Lecture at Bonn, February 4, 1969 [VB 201 IE]
German version: Angew. Chem. *81*, 470 (1969)

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Stable Organic Lewis Acids

By *O. E. Polansky* [*]

Olefins of structure L (in which X^1 and X^2 are strongly electron accepting groups that are fully conjugated with the C=C double bond and R^1 and R^2 are groups that have little or no acceptor or donor properties) usually behave as electrically neutral, reversibly titratable organic Lewis acids. They combine with bases *via* the β-carbon atom with polarization of the C=C double bond, the negative charge being distributed over the site of the X^1 and X^2 groups so that only a relatively slight partial charge results on the β-carbon atom in the anion $A^{\ominus}$.



L $\qquad$ $A^{\ominus}$

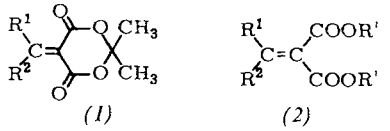
The apparent pK'_L values of the Lewis acids L can be determined, *inter alia*, by potentiometric titration with the base conjugated to the solvent

$$pK'_L = pK_L + pK_{HB}$$

(pK_L = true pK of Lewis acid, K_{HB} = ionic product of the solvent).

The substituents R affect the pK'_L of the Lewis acids to a greater extent than they do the pK values of the corresponding carboxylic- or ammonium acids; increasing acceptor strength of the substituent X^1 and X^2 lowers the pK'_L value.

The relatively low pK'_L values of *(1)* compared with those of *(2)* are due to the positive entropy of reaction in the reaction of bases with *(1)*. In *(1)* the two COO groups are coplanar; in *(2)* repulsive forces between the two COOR' groups presumably lead to coplanarity of only one COOR' group and to decoupling of the other. Accordingly, the K band of *(1a)* ($\nu' = 31600\ cm^{-1}$) lies bathochromic to that of *(2a)* ($\nu' = 36000\ cm^{-1}$), which actually corresponds more to the K band of methyl cinnamate ($\nu' = 36500\ cm^{-1}$).



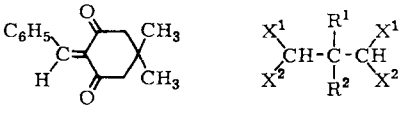
(1) $\qquad$ *(2)*

(a), $R^1 = C_6H_5$, $R^2 = H$

The structure of the anion $A^{\ominus}$ has been established by synthesis and by UV- and NMR spectroscopy.

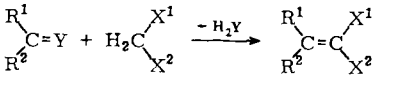
The stability of the Lewis acids under discussion is limited by hydrolytic cleavage of the C=C double bond (retro Knoevenagel reaction). This reaction follows a complicated multistep mechanism according to an overall first order rate law; the rate constant of the overall reaction is dependent on pH and has a maximum when $pH \approx pK'_L$. In the pK'_L determination the retro Knoevenagel reaction is taken into consideration by extrapolation to time $t = 0$.

The Lewis acid character of the olefins L is occasionally adversely affected by acid H atoms or by acidification of H atoms in the R^1 and R^2 groups.



(3) $\qquad$ *(4)*

The synthesis of the above Lewis acids can be achieved either by direct condensation in a water extractor (in the case where Y = O) or by reaction of the corresponding *N*-alkylamine (Y = NR^1) in a glass autoclave.



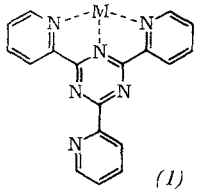
The synthesis is limited: 1. Aldehydes of the constitution RCH_2CHO have hitherto always afforded resinous products; 2. strong Lewis acids (such as *(3)*) obviously immediately react with $X^1CH_2X^2$ to form Michael-addition products *(4)*.

In accord with their Lewis acid character the olefins L catalyze the etherification of alcohols by diazo compounds as well as the rearrangement of epoxides to carbonyl compounds. They react with diazoalkanes at low temperature to give, among other things, thermally labile pyrazol-1-ines. At room temperature, on the other hand, the reaction is usually characterized by spontaneous evolution of N_2; depending on the substitution the reaction products that can be isolated are, cyclopropanes, dihydrofurans, alkylation- or rearrangement products.

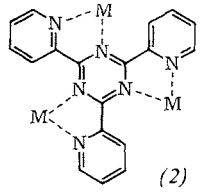
Lecture at Basel on January 23, 1969 [VB 200 IE]
German version: Angew. Chem. *81*, 469 (1969)

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The lanthanide complexes of 2,4,6-tri-α-pyridyl-1,3,5-triazine (L) have been studied by *D. A. Durham, G. H. Frost,* and *F. A. Hart.* L was found to form complexes having metal: ligand ratios of 1:1 *(1)* and 3:1 *(2)*. $M(NO_3)_3LOH_2$ crystallizes from alcoholic lanthanide nitrate solutions (M = La–Nd, Sm–Lu, and Y), and loses water at 100 °C/0.1 torr to form the yellow compounds $M(NO_3)_3$. (The cerium(III) complex is orange.) These complexes are stable even at



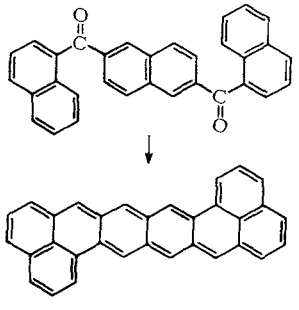
(1)



(2)

300 °C. The chlorides behave similarly. The IR spectra show that the complexes are in the form of *(1)*. As expected, complexes of the type $Eu(C_{18}H_{12}N_6)_3(ClO_4)_3$ are formed with the poorly coordinating perchlorate anion. / J. inorg. nuclear Chem. *31*, 571 (1969) / –Kr. [Rd 5 IE]

Dibenzo[*lm,yz*]hexacene (octazethrene) *(2)*, an aromatic hydrocarbon with six formally fixed double bonds (in the "middle" four rings), has been obtained by *R. Kemalettin Erünlü* from 2,6-dinaphthoylnaphthalene *(1)* by ring closure to form the quinone, reduction, and dehydrogenation. *(2)* is very reactive and was therefore not prepared in large quantities; the color of its hot solution in trichlorobenzene fades on cooling. The absorption spectrum of *(2)* (λ_{max} = 623 and

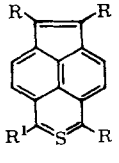


(1)

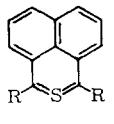
(2)

403 nm) may be compared with the spectra of zethrene (dibenzo[*hi,qr*]naphthacene) and heptazethrene (dibenzo[*jk,uv*]-pentacene). Octazethrene fits perfectly into *Clar*'s ring fusion series for aromatic compounds. / Liebigs Ann. Chem. *721*, 43 (1969) / –Kr. [Rd 6 IE]

New aromatic heterocycles containing tetravalent sulfur have been described by *R. H. Schlesinger, J. M. Hoffman jun.,* and *I. S. Ponticello.* The compounds are obtained by dehydration of cyclic sulfoxides, or by reaction of 1,5-diketones with phosphorus sulfides. The compounds *(1)–(4)*, which contain 14 (4n + 2, n = 3) peripheral π electrons, are stable, whereas *(5)* and *(6)*, having 12 peripheral π electrons, occur only as intermediates. / 157th Meeting Amer. chem. Soc. 1969, ORG N 21 / –Ma. [Rd 14 IE]

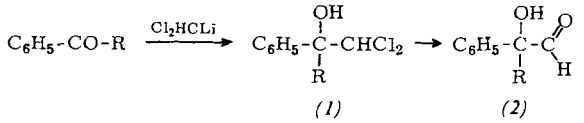


(1), R = Br, $R^1 = C_6H_5$
(2), $R = R^1 = H$
(3), R = H, $R^1 = C_6H_5$
(4), $R = R^1 = C_6H_5$



(5), R = H
(6), $R = C_6H_5$

The synthesis of α-hydroxy aldehydes *(2)* from ketones and dichloromethyllithium is reported by *P. Blumbergs* and *M. P. LaMontagne.* Alkyldichloromethylphenylmethanols *(1)* are prepared by addition of dichloromethyllithium to alkyl phenyl ketones in THF at –100 °C (yield 75–80%). Hydrolysis of *(1)* by K_2CO_3 in aqueous isopropanol affords α-hydroxy aldehydes *(2)* in yields between 33 and 44%. Alkyl-

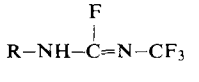


(1) *(2)*

R = cyclopropyl, cyclobutyl, cyclopentyl, isopropyl

phenyltrichloromethylmethanols can be prepared from ketone and trichloromethyllithium in a similar manner but they are not hydrolyzed in acid or in weakly alkaline solutions, and treatment with strong alkali yields the starting ketone. / 157th Meeting Amer. chem. Soc. 1969, ORG N 40 / –Ma. [Rd 15 IE]

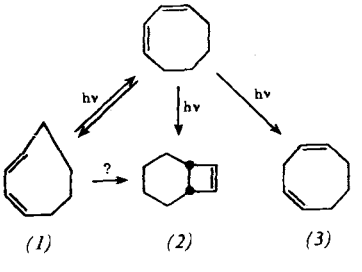
Derivatives of N^2-(trifluoromethyl)fluoroformamidine have been obtained by *K. O. Alt* and *C. D. Weis* by reaction of cyanogen chloride in liquid HF at –60 °C with fluoroalkanes. For example, reaction of fluorocyclohexane with 2 mol. equiv. of ClCN in the presence of catalytic amounts of KF gives N^1-cyclohexyl-N^2-trifluoromethylfluoroformamidine *(1)* (m.p. 68–70 °C, yield 84%). Similarly, 2-fluoronorbornane gives compound *(2)*. Compounds *(1)* and *(2)* are probably formed by way of a fluorinated linear dimerization



(1), R = cyclohexyl
(2), R = 2-norbornyl

product of ClCN. Only secondary fluoro compounds react in the manner described. / Helv. chim. Acta *52*, 812 (1969) / –Ma. [Rd 16 IE]

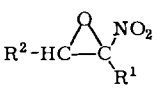
Photolysis of *cis,cis*-1,3-cyclooctadiene (25 °C, λ = 248 ± 4 nm, in hexane) has been reinvestigated by *W. J. Nebe* and *G. J. Fonken.* The authors found three photoproducts in proportions that varied with the reaction time. Formation of the known bicyclo[4.2.0]oct-7-ene *(2)* proceeds alongside



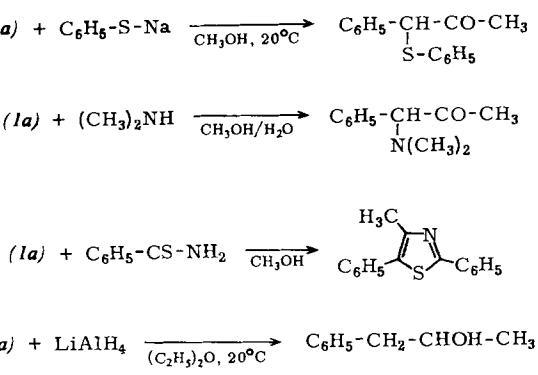
(1) *(2)* *(3)*

geometrical isomerization to *cis,trans*-1,3-cyclooctadiene *(1)*. A small amount of *cis,cis*-1,4-cyclooctadiene *(3)* is also formed. / J. Amer. chem. Soc. *91*, 1249 (1969) / –Ma. [Rd 17 IE]

Nitrooxiranes (α-nitro epoxides), a new class of compounds, form the subject of a report by *H. Newman* and *R. B. Angier*. The compounds are produced by the action of H_2O_2/dilute NaOH on nitroolefins in methanol, provided that the C atom attached to the NO_2 group also carries a further substituent. The nitrooxiranes behave similarly to the electronegatively substituted epoxides toward nucleophilic reagents (see formulas). Examples: *(1a)*, b.p. 77–78 °C/0.1 torr, pale yellow liquid, from β-methyl-β-nitrostyrene, yield 67%; *(1b)*: m.p. 108–110 °C, from α-nitrostilbene,



(1a), $R^1 = CH_3$, $R^2 = C_6H_5$
(1b), $R^1 = R^2 = CH_3$
(1c), $R^1 = CH_3$, $R^2 = c\text{-}C_6H_{11}$



85%; *(1c)*, b.p. 68–71 °C/0.1 torr, from 2-cyclohexyl-1-methyl-1-nitroethylene, 91%. / Chem. Commun. *1969*, 369 / –Ma. [Rd 18 IE]

Repression of RNA synthesis by actinomycin D is reversible, as has been reported by *I. J. Lorch* and *K. W. Jeon* on the basis of transplantation studies on amoebas. Since actinomycin D is used in the chemotherapy of cancer and in the investigation of cell metabolism, it is important to know whether the cell nuclei suffer irreversible damage. Amoebas were chosen for the studies because their cell nuclei are transplanted particularly readily. After treatment of normal amoebas with actinomycin D, this substance can be detected in the nucleus and in the cytoplasm. When nuclei that had received a lethal dose of actinomycin D were transplanted into normal cytoplasm, the cells became viable again and resumed synthesis of RNA. Conversely, cytoplasm treated with actinomycin D caused changes in the nucleoli (clubbing) of transplanted normal nuclei that are characteristic for this antibiotic; the resulting cells were not viable. Autoradiography showed that nuclei damaged by actinomycin D release the bound antibiotic in normal cytoplasm, *i.e.* that the damage is reversible. / Nature (London) *221*, 1073 (1969) / –He. [Rd 19 IE]

The "decoupling" of oxidative phosphorylation (respiratory chain phosphorylation) has been studied by *E. C. Weinbach* and *J. Garbus*. On the basis of numerous findings the authors suggest the following decoupling mechanism: The decoupler (the best known one is 2,4-dinitrophenol) crosses the mitochondrial membrane in the non-ionized state. In the mitochondrion it ionizes and interacts with the charged groups of the mitochondrial proteins, probably ε-amino groups, thus leading to conformational changes of the proteins. The differing reactions of oxidized and reduced cytochromes on trypsin, and the suppression of electron transfer by antimycin A suggest that conformational changes play a role in electron transport. This would make possible that conformational changes induced by decouplers can block the function of proteins in the coupling of phosphorylation and electron transfer. / Nature (London) *221*, 1016 (1969) / –He. [Rd 20 IE]

The first crystalline compounds of einsteinium (element 99) have been obtained and studied by *K. Fujita, B. B. Cunningham*, and *T. C. Parsons*. The extremely high radioactivity of the α-emitter ^{253}Es ($T_{1/2}$ = 20.47 d) necessitated special experimental techniques. Since the common ion-exchange resins are rapidly decomposed by high concentrations of einsteinium, the Es, which has been purified at high dilution on Dowex 50, was adsorbed onto active charcoal from 6 M HCl. Subsequent ignition of the charcoal in a stream of O_2 affords white einsteinium oxide, which reacts with HCl gas at 500 °C to give the trichloride $EsCl_3$. Reaction with a mixture of HCl gas (500 torr) and water vapor (10 torr) yields the oxide chloride EsOCl. Because of the rapid destruction of the crystal lattice by α particles, interpretable X-ray photographs can only be obtained when destruction of the lattice is compensated by a correspondingly rapid annealing of the defects, *i.e.* at high temperatures, in this case 400–435 °C. At 430 °C EsOCl possesses the tetragonal PbFCl lattice with $a = 3.97 \pm 0.01$ Å, $c = 6.75 \pm 0.02$ Å. At 425 °C $EsCl_3$ has the hexagonal UCl_3 structure with $a = 7.47 \pm 0.01$ Å and $c = 4.10 \pm 0.01$ Å; extrapolation of these figures to room temperature gave $a = 7.40 \pm 0.01$ Å and $c = 4.07 \pm 0.02$ Å. The ionic radius of Es^{3+} was found to be 0.97 Å. / Inorg. nuclear Chem. Letters *5*, 307 (1969) / –FW. [Rd 21 IE]

Determination of the equilibrium EMF in molten salts by a new galvanostatic method has been performed by *G. M. Campbell*. The metal is precipitated from a compound onto the working electrode and then removed by reversal of the current, the EMF between the working electrode and the reference electrode being recorded as a function of time. The presence of the pure metal is necessary only for a short time. The technique was used for EMF measurements on the cell

$$Pu(s,l)/PuCl_3,\ LiCl\text{–}KCl/N_2(g),\ PuN(s)$$

between 714 and 1032 °K. Reaction of Pu with N_2 hinders EMF determinations by other methods. Above the melting point of Pu, the free energy of formation of PuN is

$$-G_T^0 = 73.8 - 0.0225\ T\ (\text{kcal/mole}).$$

With the aid of additional data, it was found that S_{298}^0 (PuN) = 16.17 cal deg^{-1} mole^{-1} and $-\Delta H_{298}^0$ = 72.5 kcal/mole. The method should be of fairly general use at high temperatures; at lower temperatures problems arise from the neglect of the overpotential for oxidation and reduction of the electroactive species at the working electrode. / J. physic. Chem. *73*, 350 (1969) / –Hz. [Rd 22 IE]

The photolysis of gaseous trichlorobromomethane at 365 nm, which has been studied by *H. W. Sidebottom, J. M. Tedder*, and *J. C. Walton*, represents a convenient route to trichloromethyl radicals. The following reactions occur between 92 and 200 °C:

$$CCl_3Br \xrightarrow{h\upsilon} CCl_3^{\bullet} + Br^{\bullet} \quad (a)$$

$$CCl_3^{\bullet} + CCl_3Br \rightarrow CCl_4 + CCl_2Br^{\bullet} \quad (b)$$

$$CCl_2Br^{\bullet} + CCl_3Br \rightarrow CCl_2Br_2 + CCl_3^{\bullet} \quad (c)$$

$$CCl_3^{\bullet} + CCl_3^{\bullet} \rightarrow C_2Cl_6 \quad (d)$$

$$Br^{\bullet} + Br^{\bullet} + M \rightarrow Br_2 + M \quad (e)$$

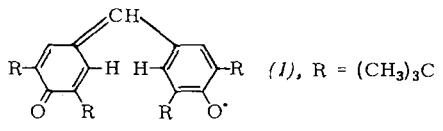
(M = third body)

No dark reaction is observed. The rate of radical formation in reactions (a)–(c) is always lower than that of the termination reactions (d) and (e). With the aid of known data for (d), the rate of (b) could be represented in the form of the Arrhenius equation

$k_b = (7.1 \pm 1.0) \times 10^6 \exp -(10500 \pm 800)/RT$ l mole^{-1} sec^{-1}.

Trans. Faraday Soc. *65*, 755 (1969) / –Hz. [Rd 25 IE]

The structure of galvinoxyl [2,6-di-*tert*-butyl-4-(3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadienylidenemethyl)phenoxyl] *(1)*, a stable phenoxyl radical, in the crystalline state has been determined by *D. E. Williams* using X-ray diffraction. In the crystal, the molecules are separated from one another by normal van der Waals distances and have a twofold axis of rotation. The CCC angle at the methine carbon atom is 134°, and the phenyl groups are twisted out of the plane of conjugation by 12° in order to avoid interaction between the two hydrogen atoms shown in formula *(1)* (separation 2.37 Å). The CO bond length is 1.27 Å and is thus intermediate between the values for C=O in aldehydes and ketones (1.215 Å) and C–O in phenols (1.36 Å). / Molecular Physics *16*, 145 (1969) / –Hz. [Rd 26 IE]



(1), R = $(CH_3)_3C$

An exceptionally reactive form of silica gel is obtained, according to *C. Morterra* and *M. J. D. Low*, when Aerosil is esterified with methanol vapor at 350 °C and the product is degassed at 600–830 °C. SiOH and SiH_2 groups are formed on the surface, which on prolonged heating and pumping off give up hydrogen leaving Si radicals in the surface, which can be detected by means of an ESR signal at $g = 2.002$. These surface radicals are able to chemisorb molecular hydrogen with dissociation, even at room temperature. SiOH and SiH_2 are re-established *via* the SiH centers in the surface. Adsorbed water does not react to any great extent with the surface silanes; they are stable towards oxygen up to 350 °C. / J. physic. Chem. *73*, 321, 327 (1969) / –Hz. [Rd 23 IE]

BOOK REVIEWS

The Refractory Carbides. By *E. K. Storms*. Vol. 2 in the Series "Refractory Materials" edited by *J. L. Margrave*. Academic Press, New York, London 1967. 1 st Edit., xiii + 285 pp., 74 figs. and 83 tables; $ 12.50.

The author gives a good account of the chemical, physical, and metallurgical properties of transition metal carbides that are stable at high temperatures. Metal-carbide systems are discussed on the basis of the literature in the case of Ti, Zr, Hf, V, Nb, Ta, Cr, Mo, W, Th, U, and Pu. The discussion comprises the preparation, phase relationships, lattice constants, crystal structure, appearance, chemical characteristics, hardness, and thermodynamic properties. The last chapter deals with these aspects in a more general manner. The magnetic and electric properties of carbides are not discussed. A subject index, an author index, and a bibliography, which contains over 600 works and extends into 1966, complete the book. This is an outstanding monograph and can be recommended to chemists, metallurgists, physicists, and materials scientists. *J. Nickl* [NB 793 IE]

Microbial Transformations of Steroids. By *W. Charney* and *H. L. Herzog*. Academic Press, Inc. New York-London 1967. 1st Edit., xi, 728 pp., $ 21.00.

Investigations on the microbial transformations of steroids were started some 30 years ago by *Mamoli* and *Vercellone*. At that time such reactions were primarily of theoretical interest, and it was not until 1950, when results concerning large-scale fermentation for the production of antibiotics became available, that the subject received new, hitherto undreamed-of impetus from Peterson and Murray's discovery that progesterone is converted almost quantitatively by molds into 11α-hydroxyprogesterone, a readily accessible starting material for the production of cortisone and hydrocortisone. Subsequently, hundreds of microorganisms were investigated to establish whether they could promote steroid reactions, and systematic studies of possible points of attack on the steroid skeleton were carried out.

The present book has succeeded admirably in collecting the results of these studies in tabular form, and covers the literature in its entirety, including United States patents, up to the end of January 1964. Moreover, a large number of further relevant scientific publications up to and including those publishing in December 1966 are also cited.

The introductory chapter on historical developments is followed by an extremely lucid description of reactions of steroids that can be carried with the aid of microorganisms: 1. Oxidation, 2. Reduction, 3. Esterification, Amide Formation, and Hydrolysis, 4. Isomerization, 5. Addition, Rearrangement, Elimination, 6. Asymmetrical Reactions, Resolutions of Racemates.

The main part of the book is taken up by two large tables. The first one "Transformation by Products" (140 pages) gives a list of the substances (arranged according to their empirical formula) obtained from steroids by microbial reaction, as well as the type of reaction, yield, microorganism, melting point, optical rotation, and literature reference.

A survey of the systematics of the microorganisms and of the typical representatives for certain reactions is given in a number of smaller tables "Taxonomy" (40 pages). The book is concluded by the largest table "Transformation by Genus" (420 pages) in which the microorganisms used for steroid reactions are arranged according to genus and subgroup species. Sources for the strains, the steroid used as substrate, the reaction performed, and the literature are all listed. – The bibliography contains 1234 references.

The book is a mine of information for anybody who has worked with microbiological reactions or intends to enter the field, and is an invaluable aid in the laboratory. Even though the literature has been considered only up to 1964, this does not detract from the value of the work since very few substantially new results have been obtained in this field since that time. Thus the book is an excellent survey and can be recommended without reservation.

J. Schmidt-Thomé [NB 805 IE]

Wasserähnliche Lösungsmittel (Water-like Solvents). By *J. Jander* and *Ch. Lafrenz*. Vol. 3 of "Chemische Taschenbücher", edited by *W. Foerst* and *H. Grünewald*. Verlag Chemie GmbH., Weinheim/Bergstrasse 1968. 1st Edit., 209 pp., 7 illustrations, 33 tables, DM 16.–.

The authors have chosen protic solvents as the first group to be discussed: ammonia, hydrogen fluoride and higher hydrogen halides, sulfuric and fluorosulfuric acid, acetic acid,

hydrogen sulfide, and hydrogen cyanide. This is followed by a section on aprotic solvents such as sulfur dioxide, halogens and interhalogen compounds, mercury bromide, dinitrogen tetroxide, and other ionizing solvents. A brief account is also given of halogen compounds of semi-metals and organic solvents, particularly amines.

Each section begins with data for the physical properties of the solvent discussed. The acid-base theory occupies a central position. The Arrhenius theory, expanded as "solvent theory", which assigns particular importance to the ions of the solvent itself, can be used in the most general way to display analogies to the aquo system, provided that the solvent undergoes even minimal self-dissociation. A special section is devoted to treatment of the relevant acid-base theories as a group, their utility being discussed with special reference to the general applicability of the ionotropy theory.

A great number of reactions is discussed in this book, showing again and again how their course can be influenced by varying the solvent used. For instance, different solubilities of reactants in water and in ammonia can reverse the direction of a reaction; and the proton affinities of the solvent molecule or of the ions derived from it can decide, for example, whether a reaction leads to salt-formation or to solvolysis. A chapter on solutions of alkali metals in liquid ammonia gives a very nice, short review of the present state of research in this field.

The book can give the advanced student an insight into the topic of water-like solvents, should he be unable to attend a special lecture course on the subject, and it is certainly apposite for this purpose. The authors have thoroughly thought out the way to cover the wide field; they have doubtless put the recently published comprehensive book on reactions in liquid ammonia to good use. This masterly exposition of water-like solvents is also to be warmly recommended to all scientists working in related fields who spurn a too detailed bibliography.

The publishing program for the Chemische Taschenbücher, which has appeared meanwhile, lists a number of interesting subjects, mainly from theoretical chemistry but also from preparative chemistry, with a long series of authors who are recognized experts. The series will doubtless direct the attention of scientists to the most varied fields of chemistry as well as to borderline areas. *R. Juza* [NB 810 IE]

Lösungsmittel-Effekte in der organischen Chemie (Solvent Effects in Organic Chemistry). By *Chr. Reichardt*. Volume 4 of "Chemische Taschenbücher", edited by *W. Foerst* and *H. Grünewald*. Verlag Chemie GmbH, Weinheim/Bergstr. 1969. 1st Edit., 180 pp., 23 figures, 22 tables, DM 16.–.

The use of solvents in chemical reactions and for the spectral examination of substances has become so commonplace that the role of the solvent is often overlooked. The reaction equations deduced from experiments are usually presented with no mention of the solvent, so that the young chemist usually has to acquire a knowledge of solvent effects by purely empirical means. In the past few decades, many series of experiments have been carried out and theoretical ideas presented on the (often dramatic) effects of the solvent, but these have rarely been treated from the same point of view. This shortcoming is made good by *Chr. Reichardt* with his introduction to the field.

The book deals first with the types of interaction that occur between solvents and solutes, clearly showing *e.g.* the difference between ionization and dissociation, and including hydrophobic interaction and selective solvation (18 pages). After a discussion of various principles for the classification of solvents (11 pages), their effect on chemical equilibria (acid-base, keto-enol) is explained (11 pages). The important and manifold solvent effects in chemical reactions, which should be familiar to every chemist to enable him to plan his experiments, are discussed at length (49 pages). Here, as elsewhere, instructive examples, often supported by tables, are used to show how the effect of the solvent on the reaction path and rate as well as on the steric course depends on the polarity and charge of the reactants and on the reaction type. 23 pages are devoted to the effect of the solvent on electronic spectra (solvatochromism) and on IR, NMR, and EPR spectra. The final chapter (27 pages) describes the empirical solvent polarity parameters, which are particularly useful in practice for the choice of solvents. An appendix presents hints on the use of organic solvents for spectroscopic and preparative purposes. A selected bibliography for further reading is found at the end of each chapter.

The text is written critically and informatively. The author avoids simplifications, but presents rules that have proved useful in sectors of this extremely complex field. The treatment leaves little to be desired, apart from a distinction between contact and solvent-separated ion pairs, as well as a detailed discussion of the resonance-solvatochromism problem. The print and formulas are easily legible. Since the book will undoubtedly see considerable use, it would probably benefit from a more durable cover. *S. Hünig* [NB 820 IE]

Ullmanns Encyklopädie der technischen Chemie, Bd. 2/2: Betriebsüberwachung mit Dokumentation und Patentrecht (Ullmann's Encyclopedia of Technical Chemistry, Vol 2/2: Process Control, and Documentation and Patent Law). Chief editor: *W. Foerst*. Editor: *Hertha Buchholz-Meisenheimer*. Urban und Schwarzenberg, München-Berlin-Wien 1968. 1st Edit., viii + 677 pp., 547 illustrations, DM 160.–.

The new Ullmann volume is a self-contained work, extracted from the alphabetically arranged Encyclopedia[1] and independent thereof. A self-coherent important complex of themes is considered under the following headings: Control Techniques (132 pp.), Measuring Processes in Industry (121 pp.), Pure Air Conservation (91 pp.), Calculation by Computer, An Introduction to Programming (60 pp.), Waste Water (57 pp.), Documentation (39 pp), Industrial Toxicology (34 pp.), Patent and Trademark Law (31 pp.), Safety in the works (26 pp.), Statistical Methods of Planning and Evaluation of Experiments (25 pp.), Non-destructive Testing of Materials (20 pp.), Dust Explosions and their Prevention (9 pp.), Waste Disposal (9 pp.).

The chapter on measuring techniques deals not only with methods for measurement of temperature, pressure, and quantities, but also with modern analytical procedures. The sections on transducers and analog-digital converters are worthy of note. The chapter on control techniques gives, in 49 pages, an elementary and instructive introduction with information that is intelligible to the user and in general sufficient for him. A second section on this subject, "Mathemathical Methods" (49 pp.) goes deeper into the matter. The chapter on "Calculation by Computer" is also written in such an elementary way that the non-expert can by himself extract the details required for use of this new method of thinking. The chapter on "Statistical Methods in the Planning and Evaluation of Experiments" provides deeper insight into what was previously called determination of error. The methods of variance and regression analysis are briefly developed, these being particularly valuable for control and optimization of complicated processes. In such cases it is often necessary to determine by purely empirical means the relation between objectives (yield, economics, quality of a product) and factors of influence thereon (pressure, temperature, throughput, concentrations of reactants, *etc.*), so that it becomes a matter of determining the relations with the minimum number of single measurements. This chapter is well written but requires concentrated reading.

The section on "Patent Rights" is especially timely because important changes in patent law became operative between January 1st and October 1st, 1968. In contrast to the previous patent law, which in chemistry permitted only the patenting

[1] Cf. Angew. Chem. *80*, 855 (1968); Angew. Chem. internat Edit. *7*, 834 (1968).

of processes, the new patent law no longer forbids the patenting of substances prepared chemically or of foods and drugs. This is a considerable reversal of German patent procedure, introduced in cooperation with neighboring European countries in order to ease agreement on uniform European patent rights.

The chapters on "Pure Air Conservation", "Waste Water", and "Waste Disposal" treat serious problems that are not the chemist's first love but can no longer be side-stepped since industrial production interferes increasingly with the maintenance of equilibria in nature. Methods for study and control of air and limitation of its pollution have developed into an exact science. Sulfur dioxide and carbon monoxide stand at the head of the list of impurities. 5.4 million tons of the former are emitted annually in England alone. Emission of CO_2 is not considered in the present chapter since it is not generally considered an impurity; yet at present 14 billion tons of CO_2 are produced annually by combustion, a quantity that suffices to increase the CO_2 content of the atmosphere by about 10 % in 15–20 years; such disturbances already exert a permanent effect on climate and vegetation and, if uncontrolled, will lead to catastrophies. The need to conserve also water is shown by the figures for water consumption and waste water given in the chapter on "Waste Water". In respect of solid waste it is noteworthy that not only is the amount per head increasing (at present 0.7 kg per person per day in the Federal Republic of Germany, but also that its calorific value increases annually by 70–80 kcal/kg.

Among the social tasks discussed in this book must be included safety at work and industrial toxicology. From the statistics of accidents in chemical industry one can see that only 10–12 % of all accidents have a specific "chemical" cause; most accidents occur during "transport and manual activity". The chapter on "Industrial Toxicology" is written by *H. Oettel* who wrote the alphabetized articles on special toxicological subjects in the complete encyclopedia and now provides a summarizing survey of this field. He shows, *inter alia*, that there is a list of notifiable "recognized occupational diseases" which the public has more or less come to accept. The statistics of the 15 diseases that were most commonly notified and compensated amounted during 1952 and 1953 to 464000 cases, of which 25 % were compensated. Apparently 3/4 of the notifications were not accepted as occupational diseases.

In its choice of subjects this book not only provides a valuable extension of the Encyclopedia but also fills a gap in the literature of industrial chemistry. Happily, all the articles are written for the layman and not for the specialist. This volume therefore is a valuable contribution to the mutual understanding between those in various modern types of work.

H. Sachsse [NB 786 IE]

Bestimmung der Isotopenverteilung in markierten Verbindungen (Determination of the Isotope Distribution in Labeled Compounds). By *H. Simon* and *H. G. Floss*. From the series: Anwendung von Isotopen in der Organischen Chemie und Biochemie (Use of Isotopes in Organic Chemistry and Biochemistry), Vol. 1. Springer-Verlag, Berlin-Heidelberg-New York 1967, 1st Edit., x, 247 pp., 5 figures, stitched DM 54.–, $ 13.50.

The rapid development of organic chemistry and biochemistry in recent years was made possible only by the introduction of new methods and their improvement. Particularly important among these methods is the use of compounds labeled with isotopes. To make use of the isotope technique, however, it is necessary to determine the distribution of the isotope over the various positions of the molecule in the reaction product as accurately as possible. The authors of this book have collected the experimental data that were formerly scattered throughout the literature, and which were sometimes difficult to find, and have presented them clearly and critically.

The book deals mainly with chemical and enzymatic degradation reactions for the location of hydrogen and carbon isotopes, while the reader is referred to reviews for oxygen, sulfur, and phosphorus isotopes.

After a survey of the principles of degradation processes, some general reactions (Kuhn-Roth reaction, iodoform reaction, *etc.*) and the manipulation of the most important fragments (CO_2, HCOOH, *etc.*) formed in degradation reactions are described. The next nine chapters describe the best degradation processes for carboxylic acids, aliphatic hydrocarbons, alcohols and amines, aldehydes and ketones, carbohydrates, aromatic compounds, cycloaliphatic compounds, heterocycles, and several groups of natural products from plants and microorganisms. Special attention is given to the difficulties, sources of error, and problems of degradation reactions. The book thus offers a very useful collection of carefully checked procedures. The use of the book is facilitated by rigid classification and a formula index arranged according to the empirical formula, which also lists the parts of the molecules that can be isolated.

The author's intention "to fill a particularly serious gap in the literature on isotope methods" has been fully realized, and it is therefore with great interest that we look forward to the second (Isotope Effects) and third (Analysis) volumes of the present series.

W. Barz [NB 804 IE]

Die Chemie der Kunststoffe (The Chemistry of Plastics). By *K. Hamann*. From the Göschen Series, Vol. 1173/1173a. Walter de Gruyter und Co., Berlin 1967. 2nd Edit., 177 pp., numerous figures, stitched DM 5.80.

This volume has long been a recognized textbook providing the chemistry student with a first glimpse of the field of macromolecular chemistry. It is therefore with pleasure that we greet this new edition, which is practically the same size as the first edition, but in which certain chapters are presented more clearly and go into greater detail, and which also takes into account more recent results (*e.g.* thermal polymerization of styrene, copolymerization, average molecular weight). It should be mentioned in particular that the chapter on anionic polymerization now contains a section on polymerization by electron transfer. A section on polymerization with complex catalysts has also been added under the title "Coordination Polymerization", as well as one on cyclopolymerization. A new chapter, "Structure and Properties", briefly explains the concepts of structure and texture and deals in particular with elementary considerations on the coil density of the macromolecule in solution. The author adheres to current nomenclature throughout the new edition. It is to be hoped that the second edition will be as well received as the first.

H. Höcker [NB 794 IE]

Anorganikum. Lehr- und Praktikumsbuch der Anorganischen Chemie mit einer Einführung in die Physikalische Chemie (Textbook of Theoretical and Practical Inorganic Chemistry with an Introduction to Physical Chemistry). Edited by *L. Kolditz*. VEB Dt. Verlag der Wissenschaften, Berlin 1967. 1st Edit., xxxiv, 1032 pp., numerous figures and tables, stitched DM 56.–.

The "Anorganikum", which now takes its place alongside the "Organikum", again carries the names of a collection of authors and, according to notes on the cover, is intended to present in one book the principles of physical chemistry as well as preparative and analytical inorganic chemistry.

The book is divided into eight sections: A. "Laboratory equipment and laboratory methods" (38 pp.), B. "Structural components of materials" (116 pp.), C.I. "Chemical kinetics and reaction mechanisms" (50 pp.), C. II. "Equilibria and chemical thermodynamics" (82 pp.), C. III. "Electrochemistry" (32 pp.), D. "Compounds and reactions in inorganic chemistry" (299 pp.), E. "Practical preparations"

(108 pp.), F. "Qualitative Analysis" (102 pp.), G. I. "Principles of quantitative analysis" (118 pp.), G. II. "Electrochemical methods in quantitative analysis" (47 pp.), G. III. "Optical methods in quantitative analysis" (10 pp.), and H. "Research by the student" (5 pp.). A bibliography and subject and author indexes are included.

It is mentioned in the Preface that the "Anorganikum" is the outcome of a desire to reorganize the basic practical textbooks in general and inorganic chemistry, and is traceable to suggestions by a number of scientists at the Humboldt-Universität, Berlin. The problem of making the study of chemistry more concise and more effective is under discussion everywhere at present, and it is therefore pleasing when the innovations tried out so far pass beyond the walls of the institutes concerned. The reviewer wholeheartedly supports the authors in their efforts to replace the historically-based amalgamation of "general and inorganic chemistry" by an introduction to physical chemistry on an exact basis at the beginning of the study. It would, however, have been preferable to provide the student with an introductory textbook of physical chemistry as well as an "Anorganikum". This would have reduced the size of the book, and would have also impressed on the student that physical chemistry is now an independent subject even in German-speaking areas.

In the discussion of the sections, some of which differ widely in their merit, the excellently written Chapter B deserves to be placed first. This section deals with the constitution of atoms and molecules and the nature of the chemical bond on the basis of modern quantum theory. The spectroscopic methods used in chemistry nowadays for structural investigations are also mentioned. Chapters C.I to C.III, which are also very valuable to students, would have benefited from the use of more examples, particularly in the discussion of reaction mechanisms. The discussion of the kinetics of redox processes and ligand exchange reactions of complexes is left for a later section, and is very brief.

Chapter D, which is probably the most important part of the book as far as students of inorganic chemistry are concerned, leaves something to be desired in the reviewer's opinion, particularly with respect to the subject matter. One pleasing point is the numerous demonstration experiments, many of which are well thought out, and which are particularly suitable for an introductory practical course. On the other hand, the arrangement of Sections D.II and D.III warrants some criticism. In a discussion *e.g.* of the elements of the third main group in three separate sections (D.II.11, D.III. 3, and D.III. 8), the relations within a group cannot be adequately described. The division of the group VIII b triad is also not altogether wise.

In addition to many omissions [HN_3, SF_4, S_n ($n \neq 8$), metal-carbonyl compounds], there are also a number of inaccuracies. For example, the first known compound of an inert gas did not have the simple formula $Xe[PtF_6]$ (p. 460); the inert gas fluorides XeF_3 and KrF_4 have not yet been verified (p. 462); the statement (foot of p. 482) that fluorine can force an element into its highest positive oxidation state is not generally true (see RuF_6, OsF_6, but RuO_4, OsO_4); the NI_3 molecule (p. 517) is not known in the free form; boranes are not restricted to the formulae B_nH_{n+4} and B_nH_{n+6} (p. 545), and finally "rhenides" (p. 598) do not exist.

The practical character of the "Anorganikum" is shown in the introductory Chapter A and in Chapters E, F, and G, the last two being of a very high level. The emphasis in the section "Qualitative analysis" is placed on semimicro techniques, and separations without the use of hydrogen sulfide are discussed. The theoretical explanations could have been more detailed in places (*e.g.* F.2.1.7). Electrochemical and optical methods (but not flame photometry) are considered in the section "Quantitative analysis".

The reviewer finds that the section "Practical preparations", unlike Chapters F and G, is not entirely satisfactory. The procedures given relate almost exclusively to the preparation of oxides, salts of oxo acids, and halides, while the synthesis of hydrides, metal complexes, and some other classes of compounds is dealt with too briefly. Transport reactions and reactions in non-aqueous solvents are not mentioned at all. Moreover, a modern inorganic practical textbook should also contain some reference to the handling of substances that are sensitive to air or that are thermally unstable.

In view of the lack of good German-language theoretical and practical textbooks on inorganic chemistry, the author had great hopes regarding the present work. To his regret, however, these hopes have not been satisfactorily fulfilled, and it is doubtful whether the "Anorganikum" in its present form can win the place that has indisputably been gained by the "Organikum". The "Anorganikum" can be recommended only with reservations. *H. Werner* [NB 802 IE]

Hagers Handbuch der Pharmazeutischen Praxis für Apotheker, Arzneimittelhersteller, Ärzte und Medizinalbeamte. 1. Bd. Allg. Teil. Wirkstoffgruppen I (Hager's Handbook of Pharmaceutical Practice for Druggists, Drug Manufacturers, Physicians, and Medical Officials. Vol. 1, General Part. Groups of Active Materials I). Edited by *P. H. List* and *L. Hörhammer* in collaboration with *H. J. Roth* and *W. Schmid*. Springer-Verlag, Berlin 1967. 4th Edit., xxxii + 1270 pp., 267 illustrations, DM 120.–.

There is always the same problem with Handbooks – enormous labor and trouble is enshrined in them, it takes years before they are finally ready, and the moment they appear they no longer correspond to the current state of knowledge. Moreover, in a collective work to which various authors have contributed it is unavoidable that a certain lack of balance will be apparent on completion – some aspects receive too much emphasis, others have insufficient weight. The present volume does not avoid these insufficiencies, which are inherent in the traditional handbook: it was "closed" in October 1966 and the Foreword begs forgiveness for the time taken in printing and difficulties of its final preparation, which were much increased by the death of the original editor, Professor *W. Kern*.

The "Handbuch der Pharmazeutischen Praxis" is to comprise seven volumes, divided into four main sections: General Part, Groups of Active Materials, Chemicals and Drugs, also Drug Forms.

It is aimed primarily at druggists and drug manufacturers; the technical side is emphasized too much for physicians and the sections that are important for the latter (*e.g.* physiological-chemical studies and pharmacological properties of the drugs dealt with as groups of active materials) are not treated in sufficient detail.

The General Part (772 pp.) contains chapters on the testing of drugs and their preparation, on general physical testing procedures, on optical methods of analysis, chromatography, and chemical detection. Quantitative methods and investigation of fats, waxes, and ethereal oils are to be treated in detail in other sections. Pharmacognostic questions, such as the evaluation of drugs and drug preparations, and the microscopical study of drugs, receive the attention they deserve. The chapter on radioactive isotopes treats the radiation properties of several isotopes and their use in pharmacy and medicine, but the section on their use in pharmaceutical research is too cursory and the references leave much to be desired. The chapter on physiological-chemical methods of investigation corresponds approximately to the content of a medical-diagnostic pocketbook.

The list of reagents (96 pp.), arranged alphabetically, contains the designations given in books on drugs and in pharmacopoeia and provides a collection that is useful and important in pharmaceutical practice.

The second Part begins its presentation of the groups of active materials with the analgesics, which are followed by anthelmintics, antibiotics, *etc.* In general, technical data required in pharmacies are given, but the pharmacological properties are treated too briefly. Of the preparations included, those currently on the German market receive particular attention,

but some of the special materials and trade names in use elsewhere are also mentioned. Not only the groups of active materials of diagnostic and therapeutic use are mentioned, but also those concerned in preservation and technical use, such as antioxidants. It is not possible, on the basis of the groups treated in the first Volume, to form a picture of the division of the total material among the groups of active materials, but one misses, for instance, analeptic drugs, antacids, and cardiac drugs – though these may well appear under other titles. The designation anticonvulsive drugs would have been preferable to antiepileptic drugs. Some preparations considered nowadays as obsolete (Filix derivatives, santonin) are treated in detail among the anthelmintics; it would perhaps be useful to emphasize the most important preparations.

Reviewing a volume of a handbook is difficult and always incomplete, since the reviewer is unable to spend sufficient time on the assembled material. Handbooks are works of reference: only those who require them for their work and use them continuously can judge whether they meet the requirements and achieve the object set.

F. Gross [NB 788 IE]

Catalysis Reviews, Volume 1. Edited by *H. Heinemann*. Marcel Dekker, Inc., New York 1968. 1st Edit., vii, 333 pp., numerous illustrations and tables, bound $ 17.50.

H. Heinemann, the research director of the M. W. Kellogg Company and expert in industrially oriented catalysis research, is the editor of the first volume of "Catalysis Reviews". Why is this new series so welcome? Handbooks written more than 20 years ago are out of date; a wealth of empirical data lies buried in patents and scattered over innumerable journals, a discouraging chaos of scientific facts that are of great technical importance since almost half of our industrial products are the outcome of catalytic processes.

The "Catalysis Reviews" are intended to cover the entire field of homogeneous and heterogeneous catalysis: the physics and chemistry of the solid state, electrochemistry, metallurgy, corrosion, polymerization, and biochemical processes, a truly tremendous undertaking. The object of this work is to replace empiricism by a comprehensive understanding of the elementary processes, which should allow the reliable prediction of the catalytic behavior of matter.

Does the first volume in this series succeed in its purpose? The first requirement is to scrutinize the data in the hope that some pattern will emerge. An excellent example of this is the article by *J. Turkevich* on "Zeolites as Catalysts" (33 pages with 44 references). Another successful article is "Reactions Catalyzed by Pentacyanocobaltate(II)" by *J. Kwiatek* (30 pages with 114 references). As might be expected from the complexity of the subject, the chapter by *E. W. Stern* on "Reactions of Unsaturated Ligands in Pd(II) Complexes" is very long (70 pages with 203 references). The article by *S. S. Grover* on "Application of Computers to Systems of Chemical Reactions" (10 pages with 14 references) is intended for specialists. *P. Mark*'s article on "Electronic Surface States of Ionic Lattices" (40 pages with 33 references) is particularly important. Two chapters for the experimental worker are "Reflection Spectroscopy as an Aid to the Study of the Surfaces of Finely Dispersed Solids" (*K. Klier*, 22 pages with 56 references) and "Static Volumetric Methods for the Determination of Adsorbed Gases on Solid Surfaces" (*Z. Knor*, 50 pages with 231 references). *F. Solymosi*'s chapter "Importance of the Electrical Properties of Support Materials to the Catalytic Properties of Adsorbed Substances" (20 pages with 39 references) is very informative. Five of the eight chapters in the first volume are by Americans and the other three by Europeans. *H. Heinemann* will undoubtedly manage to keep this gigantic work on an international basis.

L. Horner [NB 811 IE]

Kunststoff-Handbuch (Plastics Handbook). Edited by *R. Vieweg* and *E. Becker*. Volume X: Thermosets. Preparation Properties, Processing, and Use. Carl Hanser Verlag, München 1968. 1st Edit. xxii, 749 pp., 473 figures, 110 tables, cloth DM 210.–; by subscription for the complete set (12 volumes) DM 168.–.

Though the production of condensation plastics is increasing more slowly than that of polymerization plastics, thermosets account for an important fraction (about 20%) of the total production because of their special properties. After the modified natural products, the production of synthetic organic materials started with the condensation resins produced by *Baekeland* from phenol and formaldehyde. These were later joined by the urea and melamine resins. Phenol, urea, and melamine are still the mainstays of thermosetting plastics.

Volume X of the Plastics Handbook is divided into the following main sections: resins, thermosets for the bonding and processing of wood, compression molding compositions, semifinished products, laminates, and the production of compression molded objects. An introduction with an historical review and a possibly rather brief section on the economic development are followed by an excellently arranged, comprehensive section on the phenolic, urea, and melamine resins, which deals with preparation, analysis, technological testing, and use both for compression molding and for adhesives and lacquers. As was said earlier in the review of the polyamide volume[1], condensation resins for textile finishing should be discussed in a textile volume. The section on the use of thermosets as adhesives presents the chemical and physical, as well as describing the technical aspects. The chapter on compression molding compositions is divided into structure, processing, properties, and uses for the various types. Apart from semifinished products (casting resins and foams), laminates with paper, fabrics, wood, vulcanized fiber, and mica provide a wide field of application for thermosets. The book closes with a chapter on compression molding, transfer molding, and injection molding.

The collaboration of experts in this volume has again led to excellent results. Processors and users (engineers, designers, and architects), as well as chemists and development workers, are presented with numerous suggestions, and extensive reference is made to the relevant literature. The volume can be warmly recommended to all those interested.

O. Horn [NB 812 IE]

[1] Cf. Angew. Chem. 79, 1027 (1967); Angew. Chem. internat. Edit. 6, 1008 (1967).

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 4 50 75, Telex 46 1855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 7
JULY 1969
PAGES 469–534

Divalent Silicon Intermediates

By W. H. Atwell[*] and D. R. Weyenberg

Like carbenes, silylenes are assumed to occur as intermediates in many reactions. A detailed account of the reactivity of the silylenes is given and the reductive and thermolytic methods used for their preparation are discussed. Insertion and interception reactions emphasize the formal relationship between these species and the carbenes. Silacyclopropenes and silacyclopropanes have not, as yet, been isolated.

1. Introduction and Nomenclature

The considerable attention devoted to divalent carbon compounds (carbenes) has had a great impact on organic chemistry. Although the systematic and sustained investigation of the chemistry of divalent silicon compounds (silylenes) is of more recent origin and much less complete, it is already apparent that it will have an equivalent impact on the field of organosilicon chemistry.

Because these divalent species overlap the traditional domain of both organic and inorganic chemistry, several different nomenclatures are currently being used to name the specific species as well as the generic class of intermediates.

In this review compounds are referred to as "silylenes" if the silicon radical is either unsubstituted or partially substituted (*e.g.* :SiH_2 = silylene, :SiHF = fluorosilylene) or if a parent group directly attached to silicon is capable of being substituted (*e.g.* :$SiMe_2$ = dimethylsilylene). When fully substituted by groups that cannot be further substituted, derivatives of divalent silicon are frequently given inorganic binary-type names (*e.g.* :SiF_2 = silicon difluoride, :$Si(CN)_2$ = silicon dicyanide)[1].

Although the name "silenes" has been previously applied to the general class of divalent silicon intermediates, it has been recently suggested[1,2] that this generic name is inappropriate because of possible confusion with unsaturated silicon compounds, should they exist. The alternative name, "silicenes" has also been proved as inappropriate[3]. In this review, we will use the more appropriate term "silylene" when referring to the generic class of divalent silicon intermediates. Also, since the division in nomenclature based on the substituent (and its ability to be further substituted) appears to be somewhat arbitrary, we will refer to all specific intermediates as derivatives of "silylene."

While the preparation and the spectral observation of the inorganic silylenes (dichlorosilylene in particular) were reported over thirty years ago[4], only recently have detailed studies of these intermediates appeared[5]. Silylenes have been suggested as intermediates in the "direct" synthesis of chlorosilanes[6–8], and have been demonstrated as intermediates in the preparation of silicon by the hydrogen reduction of chlorosilanes[9–14].

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Midland, Mich. 48640 (USA)

[1] We wish to thank Dr. *K. L. Loening* (Chemical Abstracts Service) for this information.

[2] *P. P. Gaspar, B. D. Pate,* and *W. Eckelman,* J. Amer. chem. Soc. *88,* 3878 (1966); see also [6].

[3] For appropriate references and discussion see, *V. Bažant, V. Chvalovsky,* and *J. Rathousky:* Organosilicon Compounds. Academic Press, New York, 1965, Vol. 2.

[4] *R. Schwartz* and *G. Pietsch,* Z. anorg. allg. Chem. *232,* 249 (1937); *R. K. Asundi, M. S. Karim,* and *R. Samuel,* Proc. physic. Soc. *50,* 581 (1938).

[5] For a recent general review on the inorganic, organometallic, and organic analogs of carbenes, see *O. M. Nefedov* and *M. N. Manakov,* Angew. Chem. *78,* 1039 (1966); Angew. Chem. internat. Edit. *5,* 1021 (1966).

[6] *S. A. Golubtsov, K. A. Andrianov, R. A. Turetskaya, Z. V. Belikova, I. V. Trofimova,* and *N. G. Morozov,* Proc. Acad. Sci. USSR, Chem. Sect. (English translation) *151,* 656 (1963).

[7] *V. I. Zubkov, M. V. Tikhomirov, K. A. Andrianov,* and *S. A. Golubtsov,* Proc. Acad. Sci. USSR, Chem. Sect. (English translation) *159,* 599 (1964).

[8] *J. Joklik* and *V. Bažant,* Collect. czechoslov. chem. Commun. *29,* 603, 834 (1964).

[9] *H. Schäfer* and *J. Nickl,* Z. anorg. allg. Chem. *274,* 250 (1953).

[10] *E. G. Bylander,* J. electrochem. Soc. *109,* 1171 (1962).

[11] *E. Sirtl* and *K. Reuschel,* Z. anorg. allg. Chem. *332,* 113 (1964).

[12] *W. Steinmaier,* Philips Res. Rep. *18,* 75 (1963).

[13] *R. R. Monchamp, W. J. McAleer,* and *P. I. Pollak,* J. electrochem. Soc. *111,* 879 (1964).

[14] *O. Alstrup* and *C. O. Thomas,* J. electrochem. Soc. *112,* 319 (1965).

The objective of this review will be to discuss the reported silylene syntheses and to place in perspective those reports which contribute most to our present knowledge of the preparation, structure, and properties of these intermediates [15].

2. Methods of Preparation

Essentially all reactions used for the preparation of silylenes can be divided into two general methods: (A) The reduction of halosilanes, and (B) the thermal decomposition of appropriate substrates. Variations of each of these have been employed for the preparation of inorgano- as well as organosilylenes.

2.1. Reduction Methods

Of the reactions included under this method, the most intensely studied have been those involving the reaction of silicon with silicon tetrahalides. Reactions

$$SiX_{4(g)} + Si_{(s)} \rightleftharpoons 2\ :SiX_{2(g)}$$

of this type have been reported for a variety of silicon halides in which (X = fluorine [16,17], chlorine [9,14,18–22], bromine [23], and iodine [24–26]). These reactions take place only at temperatures above 800 °C and most of the above studies were carried out by passing the silicon tetrahalide over silicon at 1000 to 1500 °C; excellent yields of difluorosilylene (90%) [27] and dichlorosilylene (95%) [22] have been obtained at 1450 and 1350 °C, respectively. Various forms of silicon, such as silicon carbide, silicon alloys, and binary silicides of polyvalent metals have been used in the synthesis of difluorosilylene [16]. In addition, the reduction of other metal halides by silicon has been reported.

$$2\ CuCl + Si \rightarrow 2\ Cu + :SiCl_2 \qquad [7]$$

$$CaF_2 + Si \rightarrow Ca + :SiF_2 \qquad [27, 28]$$

Related vapor phase reductions have also been employed for the preparation of dimethylsilylene.

$$Me_2SiCl_2 + 2\ K_{(Na)} \xrightarrow{260-280\,^\circ C} 2\ KCl + :SiMe_2 \qquad [29]$$

Many of the products obtained from the reaction of dichlorodiorganosilanes and metals, in various aprotic solvents, have been explained in terms of silylene intermediates [5]. However, we do not feel that the formation of silylenes has been well established in many of the reactions and a more complete discussion of this area is included in Section 5 of this review.

Several reports show that the high-temperature reduction of silicon tetrachloride to silicon with hydrogen involves the intermediate formation of dichlorosilylene [10–13]. However, utilization of the dichlorosilylene produced *via* this route for other syntheses have not been reported.

$$SiCl_4 + H_2 \rightarrow 2\ HCl + :SiCl_2$$

2.2. Thermal Methods

The second general method for generating silylenes involves the thermal degradation of an appropriate substrate. Two of these methods, the thermolysis of polysilanes and of 7-silanorbornadienes, have provided a very convenient source of silylenes at moderate temperatures (170–300 °C).

The thermal degradation of hexahalodisilanes, first noted by *Friedel* and *Ladenburg* [30], gives silanes and higher polysilane compounds [5,31–33]. However, it is

$$Si_2I_6 \xrightarrow{\Delta} SiI_4 + (SiI_2)_n \qquad [30]$$

only during recent years that the intermediacy of silylenes in these thermolysis reactions has been established.

$$Si_2F_6 \xrightarrow{700\,^\circ C} SiF_4 + :SiF_2 \qquad [31]$$

The much more facile thermolysis of alkoxydisilanes [34] has rendered organosilylenes available at considerably lower temperatures. These thermolyses occur at 170

[15] A vast amount of work concerned with the suboxides and subsulfides of silicon is considered beyond the scope of this review.

[16] *D. C. Pease*, US-Pat. 2840588 (June 24, 1958); Chem. Abstr. *52*, 19245 (1958).

[17] *P. L. Timms, R. A. Kent, T. C. Ehlert*, and *J. L. Margrave*, J. Amer. chem. Soc. *87*, 2824 (1965).

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[19] *P. F. Antipin* and *V. V. Sergeev*, Ž. prikl. Chim. *27*, 737 (1954).

[20] *T. Ishino* and *A. Matsumoto*, Technol. Rep. Osaka Univ. *13*, 487 (1963); Chem. Abstr. *61*, 6449 (1964).

[21] *R. Teichmann* and *E. Wolf*, Z. anorg. allg. Chem. *347*, 145 (1966).

[22] *P. Timms*, Chem. Engng. News *45*, Nr. 39, p. 57 (1967); Inorg. Chem. (Washington) *7*, 387 (1968).

[23] a) *E. Wolf* and *C. Herbst*, Z. anorg. allg. Chem. *347*, 113 (1966); b) Z. Chem. *7*, 34 (1967).

[24] *H. Schäfer* and *B. Morcher*, Z. anorg. allg. Chem. *290*, 279 (1967).

[25] *R. C. Newman* and *J. Wakefield*, J. electrochem. Soc. *110*, 1068 (1963).

[26] *D. M. Schmeisser* and *K. Friederick*, Angew. Chem. *76*, 782 (1964); Angew. Chem. internat. Edit. *3*, 699 (1964).

[27] *J. C. Thompson* and *J. L. Margrave*, Science (Washington) *155*, 669 (1967).

[28] *A. S. Kana'an* and *J. L. Margrave*, Inorg. Chem. *3*, 103 (1964).

[29] *P. S. Skell* and *E. J. Goldstein*, J. Amer. chem. Soc. *86*, 1442 (1964); Chem. Engng. News *42*, 40 (1964).

[30] *C. Friedel* and *A. Ladenburg*, Liebigs Ann. Chem. *203*, 241 (1880).

[31] *M. Schmeisser* and *K. P. Ehlers*, Angew. Chem. *76*, 281 (1962).

[32] *N. W. Kohlschütter* and *H. Mattner*, Z. anorg. allg. Chem. *282*, 169 (1955).

[33] *A. Pflugmacher* and *I. Rohrmann*, Z. anorg. allg. Chem. *290*, 101 (1957).

[34] a) *W. H. Atwell* and *D. R. Weyenberg*, J. organometallic Chem. *5*, 594 (1966); b) Chem. Engng. News *45*, No. 38, p. 30 (1967); c) J. Amer. chem. Soc. *90*, 3438 (1968).

to 300 °C (with half-lives of 1–3 h) in sealed tubes and lead to a silane and a series of polysilanes *via* a formal redistribution of silicon-silicon and silicon-oxygen

$$n(\mathrm{MeO})\mathrm{Me_2SiSiMe_2(OMe)} \xrightarrow{225\,^\circ\mathrm{C}} (n-1)\mathrm{Me_2Si(OMe)_2} + \mathrm{MeO(SiMe_2)}_{n+1}\mathrm{OMe}$$

bonds. Recent successful attempts to intercept reactive intermediates and kinetic studies with *sym*-dimethoxytetramethyldisilane provide convincing evidence that these reactions involve a rate-determining and unimolecular thermolysis of the disilane to give a silane and a silylene.

$$\mathrm{MeO(SiMe_2)_2OMe} \xrightarrow{-\mathrm{Me_2Si(OMe)_2}} [:\mathrm{SiMe_2}]$$

$$[:\mathrm{SiMe_2}] \xrightarrow{\mathrm{MeO(SiMe_2)}_{n-1}\mathrm{OMe}} \mathrm{MeO(SiMe_2)}_n\mathrm{OMe}$$

$$[:\mathrm{SiMe_2}] \xrightarrow{\text{interceptor}} \text{adduct}$$

The thermolysis of *sym*-dimethoxytetramethyldisilane is first-order in disilane and is not accelerated by the presence of trapping agents (such as acetylenes, dienes, alcohols, *etc.*) which efficiently intercept the silylene intermediate. Although the alkoxypolysilanes offer a new and convenient source of silylenes, it should be noted that the reactivity of the starting disilane toward the silylene can be a complicating factor in synthesis, *i.e.*, the trapping agent must compete with the starting disilane. The capture of the silylene by the disilane (*via* insertion into the silicon-oxygen bond) and other trapping agents will be discussed in Section 4 of this review.

This reaction appears to be quite general for alkoxypolysilanes with the more highly alkoxylated compounds undergoing thermolysis at lower temperatures. The reactions

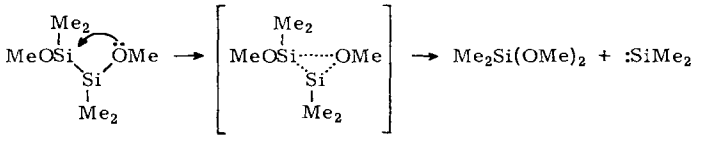
$$(\mathrm{MeO})_6\mathrm{Si_2} \xrightarrow{175\,^\circ\mathrm{C}} (\mathrm{MeO})_4\mathrm{Si} + :\mathrm{Si(OMe)_2}$$

$$(\mathrm{MeO})_2\mathrm{MeSiSiMe(OMe)_2} \xrightarrow{200\,^\circ\mathrm{C}} \mathrm{MeSi(OMe)_3} + :\mathrm{SiMe(OMe)}$$

$$(\mathrm{MeO})\mathrm{Me_2SiSiMe_2(OMe)} \xrightarrow{225\,^\circ\mathrm{C}} \mathrm{Me_2Si(OMe)_2} + :\mathrm{SiMe_2}$$

$$(\mathrm{MeO})\mathrm{Me_2SiSiMe_2SiMe_2(OMe)} \xrightarrow{275\,^\circ\mathrm{C}} \mathrm{Me_2Si(OMe)_2} + 2:\mathrm{SiMe_2}$$

also proceed quite nicely in the vapor phase at 400 °C with reaction times of only a few seconds. They most likely involve an α-elimination mechanism, *e.g.*,



and, thus, constitute another variation of the type of α-elimination reaction which leads to the formation of carbenes. This appears to be a fairly general reaction of hetero-substituted polysilanes, where the heteroatom possesses an unshared electron pair [34,35].

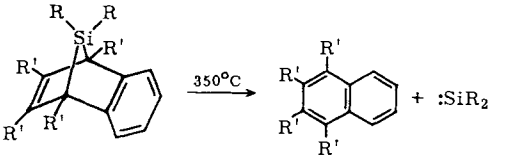
It should be noted that the above considerations are applicable to only the thermal redistributions of polysilanes. A variety of base-catalyzed redistributions of silicon-silicon bonds with silicon-halogen and silicon-oxygen bonds are known [5,36], but there is no evidence that these reactions involve silylenes [34c,36]. In fact, no silylenes have been intercepted by acetylenes in the base-catalyzed redistribution of alkoxydisilanes [34c].

The thermal decomposition of polydimethylsilylene has been reported [5,37–39] to give dimethylsilylene.

$$(\mathrm{Me_2Si})_n \xrightarrow{\approx 300\,^\circ\mathrm{C}} n:\mathrm{SiMe_2} \qquad (n \approx 55)$$

The fact that not all polydimethylsilylenes decompose with such ease [40] and that the yields of silylene "trapped" products are generally low (1–6%) [37], renders this route somewhat unattractive for the production of such intermediates [41].

A second thermal method which has been useful in elucidating the chemistry of silylenes is the thermolysis of 7-silanorbornadienes. This reaction has been utilized [5,40,42] for the preparation of dimethyl- and diphenylsilylene.



R′ = Ph, R = Me or Ph.

It has been suggested [43] that silylenes are formed in the photolytic and thermal decomposition of a variety of metal silyls.

$$\mathrm{AlMe_2(SiMe_3)} \rightarrow \mathrm{AlMe_3} + :\mathrm{SiMe_2}$$

$$\mathrm{Hg(SiMe_2)}_n \rightarrow \mathrm{Hg} + n:\mathrm{SiMe_2}$$

While the synthetic utility of such methods has not been demonstrated, their potential as photolytic or low-temperature sources of silylenes seems worthy of further investigation.

[35] *W. H. Atwell* and *D. R. Weyenberg*, unpublished.

[36] *W. H. Atwell* and *D. R. Weyenberg*, J. organometallic Chem. *7*, 71 (1967).

[37] *M. E. Vol'pin, Yu. D. Koreshkov, V. G. Dulova*, and *D. N. Kursanov*, Tetrahedron *18*, 107 (1962).

[38] *O. M. Nefedov, G. Garzo, T. Szekei*, and *V. I. Shiryaev*, Proc. Acad. Sci. USSR, Chem. Sect. (English translation) *164*, 945 (1965).

[39] a) *O. M. Nefedov* and *M. N. Manakov*, Angew. Chem. *76*, 270 (1964); Angew. Chem. internat. Edit. *3*, 226 (1964); b) Chem. Engng. News *42*, p. 40 (1964).

[40] *H. Gilman, S. G. Cottis*, and *W. H. Atwell*, J. Amer. chem. Soc. *86*, 1596 (1964).

[41] The possibility that the formation of dimethylsilylene from these polymers may be (i) due to the presence of siloxane impurities, or, (ii) related to the homolytic type of decomposition reported for hexamethyldisilane, has to our knowledge not been adequately considered.

[42] *H. Gilman, S. G. Cottis*, and *W. H. Atwell*, J. Amer. chem. Soc. *86*, 5584 (1964).

[43] *E. Wiberg, O. Stecker, H. J. Andrascheck, Z. Kreuzbichler*, and *E. Staude*, Angew. Chem. *75*, 516 (1963); Angew. Chem. internat. Edit. *2*, 507 (1963).

Silylene formation has also been suggested in the thermal decomposition of a variety of monosilanes,

$$HSiCl_3 \xrightarrow{> 1000\,^\circ C} HCl + :SiCl_2 \quad [11]$$

$$SiX_4 \xrightarrow{> 900\,^\circ C} X_2 + :SiX_2$$

X = Cl [18, 44], I [23b, 26]

$$SiH_4 \xrightarrow{\approx 400\,^\circ C} H_2 + :SiH_2 \quad [45]$$

as well as in related decompositions using other energy sources such as photolysis [46–48], glow discharge [4,49,50], and neutron irradiation [2].

$$H_3SiX \xrightarrow[\text{photolysis}]{\text{flash}} H_2 + :SiHX \quad [46]$$

X = Cl and Br

$$MeSiH_3 \xrightarrow[UV]{\text{vacuum}} H_2 + :SiHMe \quad [48]$$

$$SiF_4 \xrightarrow[\text{discharge}]{\text{glow}} F_2 + :SiF_2 \quad [49, 50]$$

3. Structure and Physical Properties

The recent and extensive studies on difluorosilylene by *Margrave* and co-workers [27] have provided our most definitive picture of the spectral and physical properties of the silylenes. Difluorosilylene with a half-life of approximately 150 seconds at ambient temperature and 0.1 torr pressure is the most stable of the silylenes and is considerably more stable than its carbon analog, difluoromethylene. This exceptional stability allows the transport of difluorosilylene away from the reaction zone in the gas phase for study of its physical properties and of its chemistry. Although quantitative data are absent, none of the related silylenes are sufficiently stable to allow this kind of treatment.

Difluorosilylene has been studied in the gas phase by microwave [27, 51], electron spin resonance [52], ultraviolet absorption [27, 53, 54], by infrared spectroscopy [55] – and in a solid matrix at low temperature by infrared spectroscopy [56]. The structures of several other silylenes have been determined from spectral studies (see Table 1). In all cases the angle (Θ) formed by the two substituents on the silicon is considerably less than the tetrahedral angle. This same phenomenon is noted in carbenes where the bond angle in difluoromethylene has been recently shown to be 104.9° [58].

Table 1. Structural parameters of silylenes.

R, R¹ Si:	Θ (°)	r_0SiR (Å)	r_0SiR¹ (Å)	Lit.
R = H, R¹ = Cl	102.8	1.56	2.06	[46]
R = H, R¹ = Br	102.9	1.56	2.23	[46]
R = H, R¹ = H	92 [b]	1.52	1.52	[47]
R = F, R¹ = F	101 [c]	1.59 [c]	1.59 [c]	[27, 51]

[a] Values refer to the singlet ground state of the molecules.

[b] Predicted value was 95° (see ref. [57]).

[c] Previous values were $\Theta = 124°$ and r_0 SiF = 1.49 Å (see ref. [50]).

The heats of formation of the dihalosilylenes are given in Table 2. These data with the reported [23, 59] heats of formation of the corresponding silicon tetrahalides give the enthalpies for the reaction,

$$Si + SiX_4 \rightarrow 2\ :SiX_2$$

which are shown in Table 2. These data suggest that $:SiF_2$, which has the greatest life-time of the halosilylenes, is actually the least stable of the halosilylenes relative to the zero- and tetravalent silicon species. This instability may be related to the previously observed thermodynamic stability associated with the accumulation of fluorine about a silicon atom [60].

Table 2. Heats of formation of dihalosilylenes and calculated heats of reaction for $Si + SiX_4 \rightarrow 2\ :SiX_2$.

$:SiX_2$	$\Delta H^0_{f,298}$ (kcal mol^{-1})	$\Delta H^0_{R,298}$ (kcal mol^{-1})
$:SiF_2$	−139 [28]	108
$:SiCl_2$	−39.5 [21, 23a] [a]	82.6
$:SiBr_2$	−10.0 [23a]	79.8
$:SiI_2$	+18.7 [23b]	86.0

[a] Cf. also [9, 19, 20].

[44] *H. Schäfer*, Z. anorg. allg. Chem. *274*, 2651 (1963).

[45] *J. H. Purnell* and *R. Walsh*, Proc. Roy. Soc. (London), Ser. A *293*, 543 (1966).

[46] *G. Herzberg* and *R. D. Verma*, Canad. J. Physics *42*, 395 (1964).

[47] *I. Dubois, G. Herzberg*, and *R. D. Verma*, J. chem. Physics *47*, 2462 (1967).

[48] a) *O. P. Strausz, K. Obi*, and *W. K. Duholke*, J. Amer. chem. Soc. *90*, 1359 (1968); b) J. Amer. chem. Soc. *91*, 1622 (1969).

[49] *J. W. C. Johns, A. W. Chantry*, and *R. F. Barrow*, Trans. Faraday Soc. *54*, 1580 (1958).

[50] *D. R. Rao* and *P. Venkateswarlu*, J. molecular Spectroscopy *7*, 287 (1967).

[51] *V. M. Rao, R. F. Curl jr., P. L. Timms*, and *J. L. Margrave*, J. chem. Physics *43*, 2557 (1965).

[52] *H. P. Hopkins, J. C. Thompson*, and *J. L. Margrave*, J. Amer. chem. Soc. *90*, 901 (1968).

[53] *V. M. Rao* and *R. F. Curl jr.*, J. chem. Physics *45*, 2032 (1966).

[54] *V. M. Khanna, G. Besenbruch*, and *J. L. Margrave*, J. chem. Physics *46*, 2310 (1967).

[55] *V. M. Khanna, R. Hauge, R. F. Curl jr.*, and *J. L. Margrave*, J. chem. Physics *47*, 5031 (1967).

[56] *J. M. Bassler, P. L. Timms*, and *J. L. Margrave*, Inorg. Chem. *5*, 729 (1966).

[57] *P. C. Jordan*, J. chem. Physics *44*, 3400 (1966).

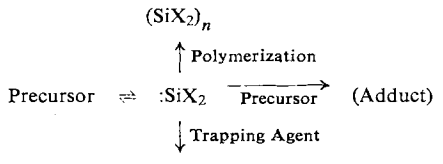
[58] *F. X. Powell* and *D. R. Lide jr.*, J. chem. Physics *45*, 1067 (1966).

[59] *J. C. McDonald, C. H. Williams, J. C. Thompson*, and *J. L. Margrave*, Proceedings of Symposium "Applications of Mass Spectrometry in Inorganic Chemistry", Advances in Chemistry Series, Washington 1966.

[60] *D. R. Weyenberg, A. E. Bey, H. F. Stewart*, and *W. H. Atwell*, J. organometallic Chem. *6*, 583 (1966).

4. Reactions

It is only in recent years that the chemistry of the silylenes has been examined and that reagents have been discovered that will intercept (trap) them. As with any highly reactive intermediate, the chemistry of a silylene is basically a consideration of the competitive reactions available to it under the conditions in which it is generated. These are summarized in Scheme 1 below, where, after generation by reduction or thermolysis (see Section 2), the silylene may either polymerize, react with its precursor, or react with a "trapping reagent" which is added to intercept the species. The fate of the silylene and the products of the reaction will depend on the relative rates of these three processes. In this



Scheme 1

section we will attempt to classify the known chemistry of silylenes into a limited number of rather general reactions. The reactions we will consider are polymerization, insertion into single bonds, and the addition to multiple bonds – three reactions which also characterize most of the known chemistry of carbenes.

4.1. Polymerization

Silylenes, when generated in the absence of other reagents, usually undergo polymerization to give polysilanes. The many examples of such silylene polymer-

$$n\ :SiX_2 \rightarrow (SiX_2)_n$$

ization include cases where X = F [16,17,31], Cl [22,23,44,61], Br [33,62], and I [24,26,30,63].

This reaction may be analogous to the dimerization of carbenes to form olefins [64], with the difference in

$$2\ :CF_2 \rightarrow F_2C{=}CF_2$$

products being due to the known [3] instability of multiple bonds between silicon atoms.

In all cases, with the possible exception of difluorosilylene, a variety of trapping agents can compete with the polymerization process. Difluorosilylene is quite unreactive in the gas phase [17] but undergoes reaction on co-condensation at low temperatures with a variety of substrates. Under these conditions the majority of products contain silicon-silicon bonds and it appears that partial polymerization (dimerization, trimerization, *etc.*) occurs prior to reaction with the added "trapping" agents. A recent electron spin resonance

$$(:SiF_2) \rightarrow (Si_2F_4) \rightarrow (Si_3F_6) \xrightarrow{etc.} (SiF_2)_n$$

study [28] of SiF_2/SiF_4 mixtures has confirmed the presence of paramagnetic species under these conditions which may represent diradical species, $[\cdot(SiF_2)_n\cdot]$.

4.2. Insertion into Single Bonds

A rather wide variety of reactions has been reported which involve the insertion of silylene into a single bond. In all cases either X or Y has been a hydrogen or one of the more electronegative elements such as a halogen or an alkoxy group.

$$R_2Si + XY \rightarrow R_2Si\begin{matrix}X\\Y\end{matrix}$$

The insertion of silylenes into a variety of MX bonds (where M represents boron, carbon, or phosphorus and X represents halogen or alkoxy) may be a rather general reaction. Both dichlorosilylene [22] and difluorosilylene [27,65] react with boron and phosphorus

$$:SiCl_2 + BCl_3 \rightarrow Cl_3SiBCl_2 \quad [22]$$

$$:SiCl_2 + PCl_3 \rightarrow Cl_3SiPCl_2 \quad [22]$$

halides. In the case of difluorosilylene and phosphorus trifluoride, unstable silicon-phosphorus compounds were formed [27]. The difluorosilylene-boron trichloride and dibromosilylene-boron trifluoride systems give similar products but are complicated by halogen exchange reactions.

$$:SiBr_2 + BF_3 \rightarrow FBr_2SiBF_2 \xrightarrow[\text{exchange}]{\text{halogen}} F_3SiBF_2 \quad [66]$$

Related reactions with alkyl halides have also been reported. Also, the reactions of difluorosilylene and

$$:SiCl_2 + CCl_4 \rightarrow Cl_3SiCCl_3 \quad [22]$$

$$n\ :SiF_2 + MeF \rightarrow MeSi_nF_{2n+1} \quad [67]$$
$$(n = 2\text{–}4)$$

trifluoroethylene or fluorobenzene (see Section 4.3.2) are formally an insertion into the carbon-fluorine bond. The anomalous behavior of difluorosilylene is

[61] *H. Schäfer* and *B. Morcher*, Colloquium Soc. inorg. Chem. internat. Union pure appl. Chem. *1954*, p. 24.

[62] *D. M. Schmeisser* and *M. Schwarzmann*, Z. Naturforsch. *11b*, 278 (1956).

[63] *E. Wolf* and *M. Schönkerr*, Z. Chem. *2*, 154 (1962).

[64] *J. Hine*: Divalent Carbon. The Roland Press Company, New York 1964; *W. Kirmse*: Carbene Chemistry. Academic Press, New York 1964.

[65] *P. L. Timms, T. C. Ehlert*, and *J. L. Margrave*, J. Amer. chem. Soc. *87*, 3819 (1965).

[66] *P. L. Timms*, unpublished.

[67] *J. L. Margrave*, unpublished studies presented at the "Polysilane Symposium", University of Pennsylvania, Philadelphia, Pa., April 15, 1967.

again illustrated in the above examples, however, 1:1 adducts being obtained with other MX compounds.

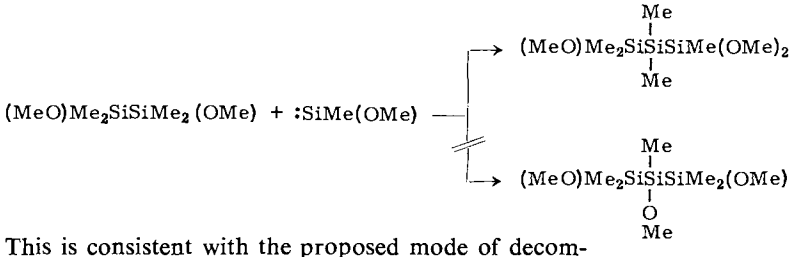
$$:SiF_2 + Br_2 \rightarrow Br_2SiF_2 \quad [16]$$

There are now several examples of silylenes reacting with alkoxy- or halo-substituted polysilanes. While

$$MeO(SiMe_2)_nOMe + :SiMe_2 \rightarrow MeO(SiMe_2)_{n+1}OMe \quad (n \geqslant 2) \quad [34a]$$

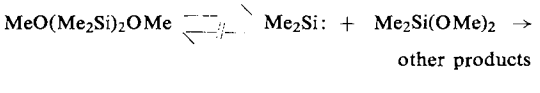
$$Cl(SiCl_2)_nCl + :SiCl_2 \rightarrow Cl(SiCl_2)_{n+1}Cl \quad (n \geqslant 2) \quad [32]$$

the above products could arise *via* reaction with the silicon-silicon bond, the following example shows that this reaction proceeds *via* insertion in the Si–X bond.



This is consistent with the proposed mode of decomposition of these alkoxy-substituted polysilanes which involves an α-elimination of the terminal silicon, *i.e.*, the reverse of the above silicon-oxygen insertion reaction [34c].

While the above data suggest that the reaction of silylenes with the silicon-oxygen or silicon-halogen bonds of polysilanes is rather general, several attempts to carry out related reactions with monosilanes have been unsuccessful. Thus, silicon tetrafluoride did not react with difluorosilylene, and the reaction of dimethylsilylene with dimethyldimethoxysilane was shown to be kinetically unimportant in the thermolysis of the corresponding disilane [35]. With additional data on the relative reactivities of various SiX bonds, this



reaction could become a valuable synthetic route to polysilanes.

Silylenes react with a variety of X–H bonds to give 1:1 adducts:

$$:SiMe_2 + Me_3SiH \rightarrow Me_3SiSiMe_2H \quad [29, 35]$$

$$:SiH(SiMe_3) + Me_3SiH \rightarrow (Me_3Si)_2SiH_2 \quad [68]$$

$$:SiMe(OMe) + MeOH \rightarrow MeHSi(OMe)_2 \quad [35]$$

$$:Si(OMe)_2 + MeOH \rightarrow HSi(OMe)_3 \quad [35]$$

$$2{:}SiF_2 + HBr \rightarrow HF_2SiSiF_2Br \xrightarrow[\text{exchange?}]{\text{halogen}} HF_2SiSiF_3 \quad [69]$$

$$:SiF_2 + H_2S \rightarrow HF_2SiSH \quad [67]$$

$$3{:}SiF_2 + 2GeH_4 \rightarrow H_3GeSiF_2H + H_3GeSiF_2SiF_2H \quad [66]$$

[68] *P. S. Skell* and *P. W. Owen*, J. Amer. chem. Soc. *89*, 3933 (1967).

[69] *A. G. MacDiarmid* and *Y. L. Baay*, unpublished.

The last two reactions are additional examples of 1:1 adducts from difluorosilylene. It has been suggested that the "direct" synthesis of trichlorosilane from silicon and hydrogen chloride involves this type of insertion reaction.

$$:SiCl_2 + HCl \rightarrow HSiCl_3 \quad [8]$$

The similarity of these reactions of silylenes to the reactions of carbenes with hydrogen halides [70], alcohols [64, 70, 71], and silicon and germanium hydrides [70] is very striking. However, insertion into carbon-hydrogen bonds, which is a common reaction with carbenes, has not been observed with silylenes. The low efficiency of dimethylsilylene insertions into the

(ref. [35])

carbon-hydrogen bonds of ethane and trimethylsilane has been cited in support of the suggested decreased reactivity of this silylene relative to methylene [29].

4.3. Carbon-Carbon Multiple Bonds

Certainly the most popular and probably the most general method for intercepting carbenes involves trapping with unsaturated hydrocarbons. Most of our information regarding carbene chemistry has come from these reactions which yield cyclopropanes or cyclopropenes. Silylenes also appear to react with a variety of unsaturated organic compounds; however, to date, no stable, isolable silacyclopropanes or silacyclopropenes are known [72].

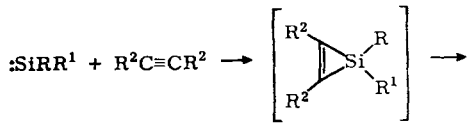
4.3.1. Alkynes

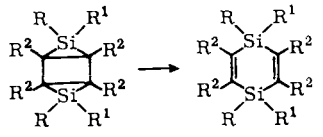
Since the initial report [37] that diphenylacetylene could be employed as a "trapping" agent for dimethylsilylene and the original incorrect assignment of the structure of the products was corrected [5, 34c], a variety of acetylenes and silylenes have been employed in this reaction. In all cases the product is the corresponding 1,4-disilacyclohexadiene. It is generally assumed that the disilacyclohexadiene arises *via* a silacyclopropene and it has been further suggested [40] that a dimerization through the π-system was involved.

[70] *D. Seyferth* in: Proc. R. A. Welch Foundation Conference Chem. Res. IX Organometallic Compounds, Robert A. Welch Foundation, Houston, Texas, 1966, p. 84ff.

[71] *A. M. Trozzolo, W. A. Yager, G. W. Griffin, K. Kristinsson*, and *I. Sarkar*, J. Amer. chem. Soc. *89*, 3357 (1967).

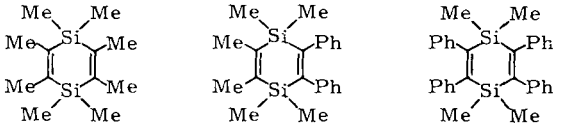
[72] *K. A. Andrianov* and *L. M. Khanashvili*, Organometallic Chem. Rev. *2*, 141 (1967).





R = R¹ = Me, R² = Ph [5, 34, 37, 40]
R = R¹ = Me, R² = Et [35]
R = R¹ = Ph, R² = Ph [42]
R = Me, R¹ = OMe, R² = Ph [34]
R = Me, R¹ = OMe, R² = Me [35]
R = Me, R¹ = OMe, R² = H [35]

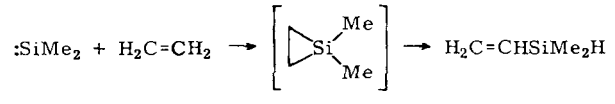
However, reaction of dimethylsilylene with a mixture of dimethyl and diphenylacetylene gave only three disilacyclohexadienes. The structure of the "mixed" disilacyclohexadiene eliminated from further consideration the π-dimerization mechanism for disilacyclohexadiene formation. An alternative route involving



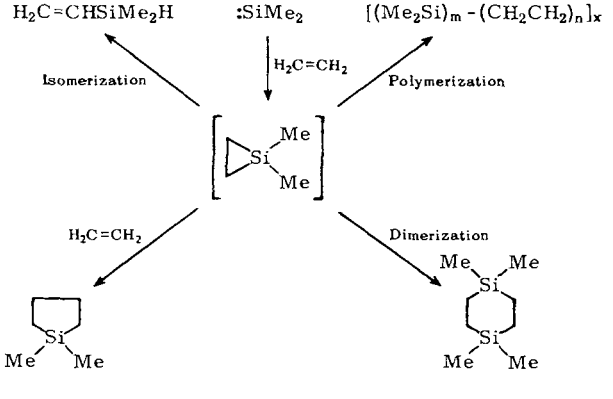
a rather specific dimerization across the carbon-silicon ring bonds of the silacyclopropene intermediates has been suggested [34c].

4.3.2. Alkenes

The reaction of dimethylsilylene with ethylene in the vapor phase has been reported [29]. While the product isolated is vinyldimethylsilane, it has been suggested [29]

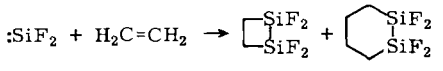


that this reaction involves formation and isomerization of 1,1-dimethyl-1-silacyclopropane rather than direct insertion of the silylene into the carbon-hydrogen bond. The condensed phase reaction of dimethyl silylene (from 7-silanorbornadienes) and ethylene

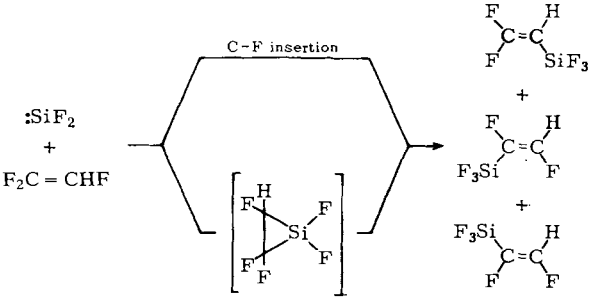


gives, in addition to vinyldimethylsilane, cyclic and polymeric products which are also viewed as derivatives of the silacyclopropane [5]. It should be noted that although the above examples demonstrate that dimethylsilylene reacts with simple olefins, the non-conjugated olefins cannot successfully compete with simple alkoxydisilanes for the silylenes, and, therefore, this convenient source of silylenes is not satisfactory for this class of reactions. The relative reactivities of various unsaturated organic compounds are compared in Section 4.4.

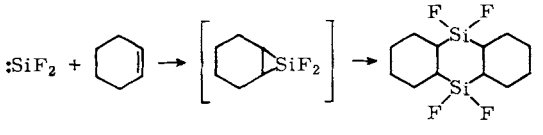
The reactions of difluorosilylene with ethylene [16], acrylonitrile [16], and tetrafluoroethylene [16, 73] had been reported to give solid polymeric products. In a recent study, however, two monomeric products were identified from the ethylene reaction [73].



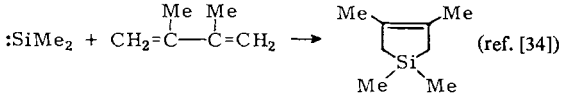
Reaction of difluorosilylene and trifluoroethylene gave several vinylsilane derivatives [73]. While these products may be accounted for *via* insertion into the

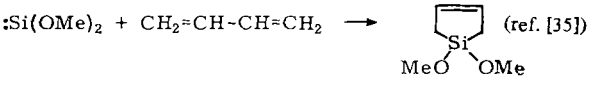


C–F bonds (see Section 4.2), their formation may also be rationalized by isomerization of a silacyclopropane intermediate. The reaction of difluorosilylene and cyclohexene has been thoroughly studied [74], and, again, the products are most easily explained *via* dimerization of a silacyclopropane.



Conjugated olefins such as butadienes have also been utilized as trapping agents. Difluorosilylene and 2,3-dimethylbutadiene gave only solid polymeric products [16]. Silylenes generated *via* pyrolysis of alkoxydi-

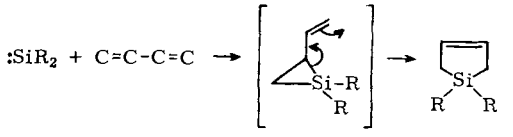




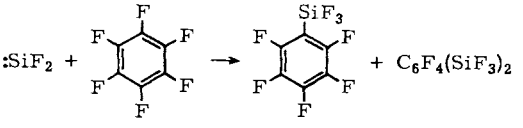
[73] *J. C. Thompson, P. L. Timms,* and *J. L. Margrave,* Chem. Commun. *1966,* 566.

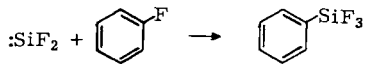
[74] *A. G. MacDiarmid* and *F. M. Rabel,* unpublished.

silanes and of 7-silanorbornadienes, however, gave silacyclopentenes. The dienes, like the acetylenes, compete successfully with the alkoxydisilanes for the silylenes. While the silacyclopentene is formally a product of 1,4-addition of the silylene, a reaction path involving formation and thermal isomerization of a vinyl-substituted silacyclopropane is favored [34].

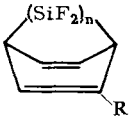


Dimethylsilylene from the pyrolytic methods is not intercepted by simple aromatic compounds [35,40,42]. However, a variety of derivatives have been isolated from the co-condensation of difluorosilylene with





benzene or fluorobenzenes [75]. Reaction with benzene or toluene, however, follows a different path to give structures of the type shown below.



R = H, $n = 3$
R = Me, $n = 3$
R = Me, $n = 2$

4.4. Relative Reactivities

The trapping of silylenes from the pyrolysis of methoxydisilanes provides some insight into the relative reactivity of the trap, for it must always compete with the precursor disilane for the silylene. From these and related studies with the 7-silanorbornadienes, we see that saturated hydrocarbons and benzene are quite inert and do not compete with the polymerization of the silylene. Ethylene reacts with the silylene but cannot compete with the disilane. Acetylenes and conjugated dienes are more reactive than the methoxydisilane with the dimethylsilylene. Thus, we have the following series of relative reactivities toward dimethylsilylene.

benzene < ethylene < dimethoxytetramethyldisilane < dienes and alkynes

5. Concerning the Proposed Intermediacy of Silylenes in Other Organosilicon Reactions

A number of organosilicon reactions are known (in addition to those previously discussed) which involve the formal transfer of an $R_2Si=$ moiety. Although some of these reactions are closely related to known methods of generating silylenes and have been interpreted in terms of silylene intermediates, present evidence suggests alternative mechanisms. In some cases, even the intermediacy of "silylenoid" [76] species is unlikely.

5.1. Catalyzed Disproportionation of Polysilanes

A number of base-catalyzed disproportionation reactions of substituted polysilanes have been reported [79]. Silylene intermediates have been suggested [5] for some of these reactions which are formally similar to the thermal disproportionations (Section 2.2) – reactions known to involve silylenes.

$$n\ Si_2Cl_6 \xrightarrow{\text{amine or ammonium halide}} n\ SiCl_4 + (SiCl_2)_n \quad [80, 81]$$

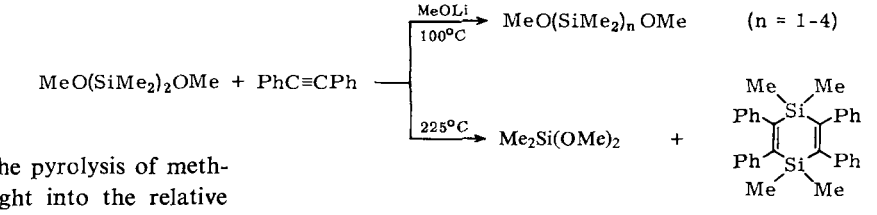
$$n\ EtCl_2SiSiCl_3 \xrightarrow{Me_3HNCl} n\ EtSiCl_3 + (SiCl_2)_n \quad [80]$$

$$4\ Si_2Cl_6 \xrightarrow{Me_3HNCl} 3\ SiCl_4 + Si_5Cl_{12} \quad [82, 83]$$

$$n\ Me_3SiSiMe_2CN \xrightarrow{\Delta} (n\text{-}1)\ Me_3SiCN + Me_3Si(SiMe_2)_nCN \quad [84]$$
$$n = 2\text{–}5$$

$$2\ MeO(SiMe_2)_2OMe \xrightarrow{MeOLi} Me_2Si(OMe)_2 + MeO(SiMe_2)_3OMe \quad [36]$$

However, to date, there is no direct evidence to support this suggestion and the one attempt to examine this point suggests a quite different mechanism. Thus, while the thermolysis of 1,2-dimethoxytetramethyldisilane in the presence of diphenylacetylene gives a disilacyclohexadiene derivative, none of the latter is obtained in the base-catalyzed reaction of this disilane [34c].



These base-catalyzed reactions are best explained in terms of a silicon-silicon (SiSi) and silicon-ligand (SiL) redistribution of the general type [36,79,85]:

$$-\overset{*}{Si}Si- + SiSiL \rightarrow \overset{*}{Si}-L + -SiSiSi-$$

---

[75] *P. L. Timms, D. D. Stump, R. A. Kent,* and *J. L. Margrave,* J. Amer. chem. Soc. *88*, 940 (1966).

[76] The term "silylenoid" analogous to "carbenoid" [77, 78] is suggested for the general class of intermediates which exhibit reactions qualitatively similar to those of silylenes without necessarily being free divalent silicon species.

[77] *G. L. Closs* and *R. A. Moss,* J. Amer. chem. Soc. *86*, 4042 (1964).

[78] *G. Köbrich,* Angew. Chem. *79*, 15 (1967); Angew. Chem. internat. Edit. *6*, 41 (1967).

[79] *M. Kumada* and *K. Tamao,* Advances organometallic Chem. *6*, 19 (1968).

[80] *C. J. Wilkins,* J. chem. Soc. (London) *1953*, 3409.

[81] *G. D. Cooper* and *A. R. Gilbert,* J. Amer. chem. Soc. *82*, 5042 (1960).

[82] *G. Urry,* J. inorg. nuclear Chem. *26*, 409 (1964).

[83] *E. Wiberg* and *A. Neumaier,* Angew. Chem. *74*, 514 (1962); Angew. Chem. internat. Edit. *1*, 517 (1962).

[84] *J. V. Urenovitch* and *A. G. MacDiarmid,* J. Amer. chem. Soc. *85*, 3372 (1963).

[85] An exception to this may be the thermally induced reactions of the cyano-substituted polysilanes [84].

5.2. Reaction of R_2SiX_2 with Metals

Although some of the most convincing evidence for dimethylsilylene has come from the reaction of dichlorodimethylsilane and potassium in the gas phase[29] (Section 2.1), the nature of the reaction of alkali metals and dihalodiorganosilanes in the condensed phase is much more obscure. Dihalodiorganosilanes react rapidly with alkali metals in a variety of solvents to yield polysilanes[79,86], and a similar reaction occurs more slowly with halotriorganosilanes[79,86].

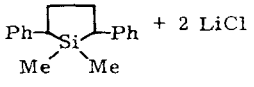
$$R_2SiCl_2 + 2\ M \rightarrow (R_2Si)_n + 2\ MCl$$

$$2\ R_3SiCl + 2\ Na \rightarrow R_3SiSiR_3 + 2\ NaCl$$

An attempt to intercept silylene intermediates in the reaction of dichlorodiphenylsilane and lithium using cyclohexene was unsuccessful[87].

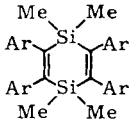
Of specific interest is the class of reactions where the combination of an alkali metal, a dichlorodiorganosilane, and an unsaturated organic compound yield organic products containing the $R_2Si=$ unit. The reactions have been cited[5] as examples of syntheses involving silylenes.

$$Me_2SiCl_2 + 2\ PhCH{=}CH_2 + 2\ Li \rightarrow$$



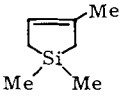
$+ 2\ LiCl$ [5,88]

$$2\ Me_2SiCl_2 + 2\ ArC{\equiv}CAr + 4\ Na \rightarrow$$



$+ 4\ NaCl$ [37,89]

$$Me_2SiCl_2 + CH_2{=}CH{-}\underset{\displaystyle Me}{\underset{|}{C}}{=}CH_2 + 2\ Na \rightarrow$$



$+ 2\ NaCl$ [90]

It is highly unlikely that any of the above reactions involve silylenes as nearly identical reactions are obtained in each case with a chlorotriorganosilane. These reactions involve the trapping, *via* reaction with a chlorosilane, of short-lived organometallic reagents from the alkali metal made olefin, *i.e.*, a "disilylation" reaction[88,90]. This latter scheme is more consistent with the effects of stoichiometry, solvent, and metal on the structure and stereochemistry of the products than is one involving silylene intermediates.

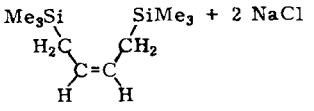
$$2\ Me_3SiCl + 2\ PhCH{=}CH_2 + 2\ Li \rightarrow$$

$$Me_3SiCHCH_2CH_2\overset{\displaystyle Ph}{\overset{|}{C}}HSiMe_3 + 2\ LiCl \quad [88]$$

$$2\ Me_3SiCl + PhC{\equiv}CPh + 2\ Na \rightarrow$$

$$(Me_3Si)PhC{=}CPh(SiMe_3) + 2\ NaCl \quad [91]$$

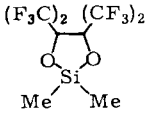
$$2\ Me_3SiCl + CH_2{=}CH{-}CH{=}CH_2 + 2\ Na \rightarrow$$



$+ 2\ NaCl$ [90]

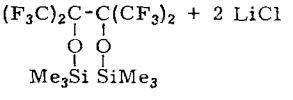
Likewise, the related reaction with hexafluoroacetone was initially thought[92] to involve a silylene, but most likely involves initial reaction of the alkali metal and the ketone[93,94].

$$Me_2SiCl_2 + 2\ (CF_3)_2CO + 2\ Li \rightarrow$$



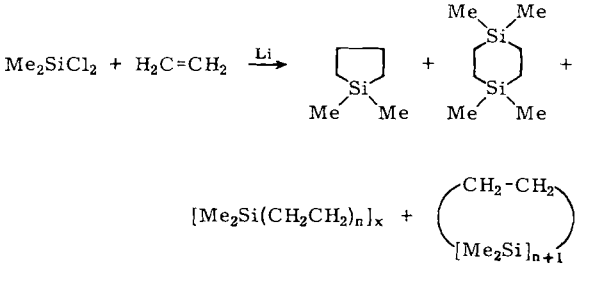
$+ 2\ LiCl$ [92,93]

$$2\ Me_3SiCl + 2\ (CF_3)_2CO + 2\ Li \rightarrow$$



$+ 2\ LiCl$ [93]

Related reactions with olefins which react less readily with alkali metals may indeed involve initial reaction between the chlorosilane and metal. Particularly, the reaction of dimethyldichlorosilane, lithium, and ethylene is more consistent with



a silylene or "silylenoid" intermediate (Section 4.3)[39a]. Because of these complicating factors, the reaction of alkali metals and halosilanes in aprotic solvents has been of limited value in the study of silylenes.

The authors are grateful to Drs. A. G. MacDiarmid, J. L. Margrave, and P. L. Timms for allowing use of their data prior to publication.

Received: July 8, 1968 [A 702 IE]
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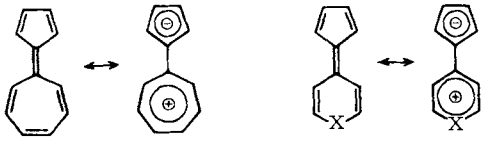
Hetero Analogs of Sesquifulvalene[1]

By G. Seitz[*]

Heterosesquifulvalenes containing sulfur or oxygen as hetero atom may be prepared, e.g., by condensation of cyclopentadienes with thiopyrones or pyrones in acetic anhydride. Heterosesquifulvalenes containing nitrogen can be obtained from the oxygen compounds by O,N-exchange. The ground state of all these compounds is determined mainly by the nonpolar resonance formula.

1. Introduction

Both the increasing pharmacological significance of cyclopentadienylidenes [2] and the considerable interest shown by theoretical chemists have provided impulse to the search for new syntheses of heterosesquifulvalenes [3]. These compounds are formally derived from sesquifulvalene *(1)* [4], replacement of a $-CH=CH-$ group of the carbocyclic seven-membered ring by a hetero atom such as oxygen [5,4c], sulfur [5,4c], or nitrogen [6], giving cyclopentadienylidenepyrans, -thiopyrans, and -1,4-dihydropyridines, respectively. Compound *(1)* and its hetero analogs *(2)* are characterized by cyclic cross-conjugated π-bond systems, which can be described to a first approximation by a covalent resonance structure and a dipolar one.



(1) *(2)*

X = O, S, N-R

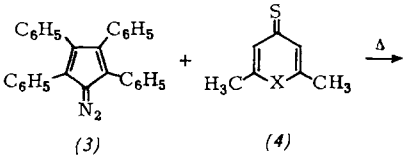
If the dipolar form were to make a large contribution to the resonance hybrid, a situation that would be favored by the gain in resonance energy of two aromatic 6π systems, then stable molecules having high dipole moments would result and the bond order of the intercyclic C=C double bond would be reduced. Such predictions [7], based on simple HMO calculations, prove inapplicable [4a] to sesquifulvalene, which is in fact a highly unstable compound whose properties resemble more those of a reactive polyolefin. In contrast, the nitrogen-containing heterosesquifulvalenes *(2)*, having X = N–R [6], are relatively stable.

With this in mind, our interest became focused on the chemical behavior of the oxygen and sulfur analogs. The present article reports on a simple method of synthesis and a number of chemical and physical properties of these heterosesquifulvalenes.

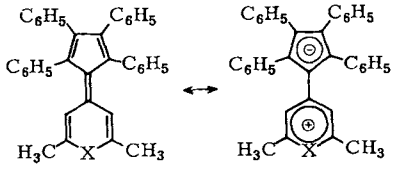
2. Synthesis of Heterosesquifulvalenes containing Oxygen and Sulfur as Hetero Atoms

Two methods for the preparation of cyclopentadienylidenepyrans and -thiopyrans have hitherto become known. The first method is restricted to phenyl-substituted cyclopentadienes and is based on the reaction of diazocyclopentadienes *(3)* with 4-thiopyrones *(4)* in xylene at elevated temperatures to give *(5)* [5].

The second synthetic route utilizes the finding that substituents exhibiting a –M or –I effect increase the



(3) *(4)*



(5)

X = O, S

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[1] From the Habilitation Thesis by *G. Seitz*, Universität Marburg 1968, also Part 4 of Cyclopentadienylidenes. – Part 3: Tetrahedron Letters *1968*, 2305.

[2] *C. T. Bahner, H. Kinder, D. Brotherton, J. Spiggle*, and *L. Gutmann*, J. med. Chem. *8*, 390 (1965); *P. W. Thies*, Dtsch. Apotheker-Ztg. *107*, 1411 (1967).

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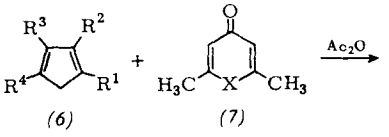
[4] a) *H. Prinzbach*, Angew. Chem. *73*, 169 (1961); *H. Prinzbach, D. Seip, L. Knothe*, and *W. Faisst*, Liebigs Ann. Chem. *698*, 34 (1966); b) *Y. Kitahara, I. Murata*, and *S. Katagiri*, Angew. Chem. *77*, 345 (1965); Angew. Chem. internat. Edit. *4*, 353 (1965); c) *G. Seitz*, Angew. Chem. *79*, 96 (1967); Angew. Chem. internat. Edit. *6*, 82 (1967); d) *E. Koerner v. Gustorf, M. C. Henry*, and *P. V. Kennedy*, Angew. Chem. *79*, 616 (1967); Angew. Chem. internat. Edit. *6*, 627 (1967).

[5] *D. Lloyd* and *F. J. Wasson*, Chem. and Ind. *1963*, 1559; J. chem. Soc. (London) *C 1966*, 1086.

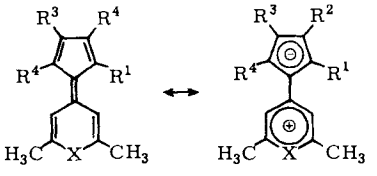
[6] a) *F. Kröhnke, K. Ellegast*, and *E. Bertram*, Liebigs Ann. Chem. *600*, 176 (1956); *D. N. Kursanov, N. K. Baranetskaja*, and *V. N. Setkina*, Proc. Acad. Sci. USSR, Chem. Sect. (English translation) *113*, 191 (1957); *J. A. Berson, E. M. Evleth*, and *Z. Hamlet*, J. Amer. chem. Soc. *87*, 2887 (1965); b) *G. V. Boyd* and *L. M. Jackman*, J. chem. Soc. (London) *1963*, 548.

[7] *J. D. Roberts, A. Streitwieser*, and *C. M. Regan*, J. Amer. chem. Soc. *74*, 4579 (1952).

reactivity of the cyclopentadienes *(6)* and promote their condensation with ketones such as *(7)*, X = O,S, or –CH=CH–, in acetic anhydride[4c,1]. A number of heterosesquifulvalenes *(8a)–(8e)* that have been prepared by the "anhydride method"[8] are listed in Table 1.



(6) *(7)*

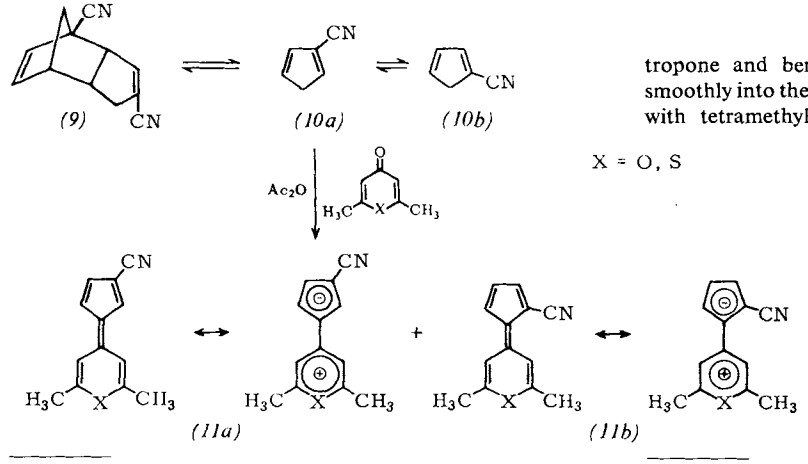


(8)

Table 1. Cyclopentadienylidenepyrans and -thiopyrans prepared by the "anhydride method".

(8)	R^1	R^2	R^3	R^4	X	M.p. (°C)	Yield (%)
(a)	CO_2CH_3	CO_2CH_3	CO_2CH_3	CO_2CH_3	O	227	52
(b)	Cl	Cl	Cl	Cl	O	>150 (decomp.)	45
(c)	CO_2CH_3	H	CO_2CH_3	H	S	171	12
(d)	CN	CN	H	H	O	>260 (decomp.)	25
(e)	CN	H	H	H	S	168	19

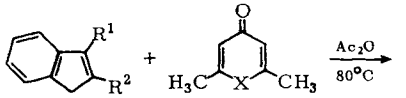
Even those cyclopentadienes formed by retro-Diels-Alder reaction at elevated temperatures are activated sufficiently by only one such substituent, and can consequently be intercepted in the equilibrium *(9)* ⇌ *(10)* by pyrone or thiopyrone. The resulting monosubstituted heterosesquifulvalenes *(11a)* and *(11b)* are also stable compounds; the major product *(11b)* can be separated from the minor component of the isomeric mixture by adsorption chromatography on silica gel.



(9) *(10a)* *(10b)*

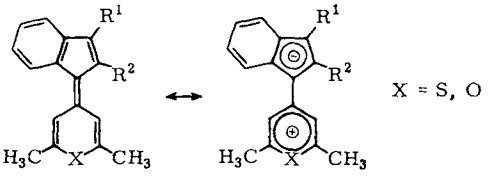
(11a) *(11b)*

Provided that the indene system *(12)* carries electron-attracting substituents, the anhydride method can also be used for the synthesis of the hetero analogs of 9,10-benzosesquifulvalenes[10], indenylidenepyrans and -thiopyrans *(13)*, X = O,S[9].



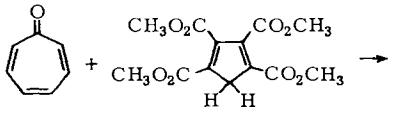
(12a), $R^1 = CO_2CH_3$, $R^2 = H$

(12b), $R^1 = R^2 = CO_2C_2H_5$

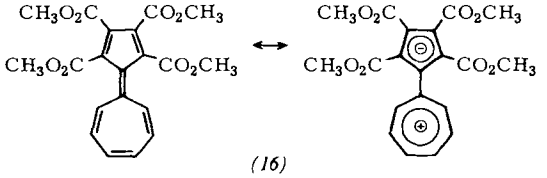


(13)

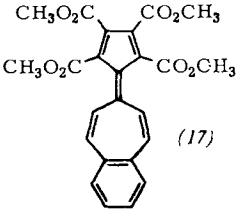
The success of these experiments provided some justification for the expectation that, like the heterocyclic ketones, the iso-π-electronic system tropone *(14)* should also condense with activated cyclopentadienes in acetic anhydride. Indeed, both



(14) *(15)*



(16)



(17)

tropone and benzotropone could be converted extremely smoothly into the sesquifulvalenes *(16)* and *(17)* by treatment with tetramethyl cyclopentadienetetracarboxylate[11] *(15)*.

[8] Regarding condensation reactions of other CH acids with 4-pyrones, cf. *L. L. Woods*, J. Amer. chem. Soc. *80*, 1440 (1958); *F. Eiden*, Angew. Chem. *71*, 747 (1959); Arch. Pharmaz. *293*, 404 (1960); *M. Ohta* and *H. Kato*, Bull. chem. Soc. Japan *32*, 707 (1959); *J. Kelemen* and *R. Wizinger*, Helv. chim. Acta *45*, 1908 (1962).

[9] *G. Seitz*, Arch. Pharmaz. *300*, 1016 (1967).

[10] *H. Prinzbach*, *D. Seip*, and *G. Englert*, Liebigs Ann. Chem. *698*, 57 (1966).

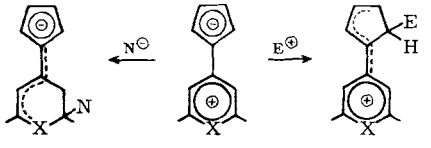
[11] *G. Seitz*, Angew. Chem. *78*, 680 (1966); Angew. Chem. internat. Edit. *5*, 670 (1966).

An analogous synthesis of the tetrachloro derivative *(16)*, Cl instead of CO_2CH_3, has also been reported[12].

The synthesis of substituted heterosesquifulvalenes and a number of hetero analogs of 9,10-benzosesquifulvalene, as well as the condensation of tropone and benzotropone, illustrate the scope of the anhydride method. The limitations of this synthetic technique become apparent when one considers the unsuccessful attempts to condense unsubstituted cyclopentadiene, indene, or fluorene with pyrones.

3. Reactivity of Heterosesquifulvalenes

A highly polar ground state of the heterosesquifulvalenes, in line with the dipolar formula *(18)*, would suggest amphoteric character and therefore permit electrophilic reactions in the five-membered ring and nucleophilic reactions in the six-membered ring.

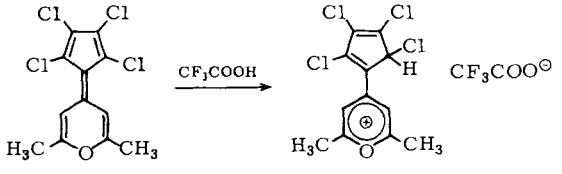


(18)

Both such reactions do take place, as shown in the following examples.

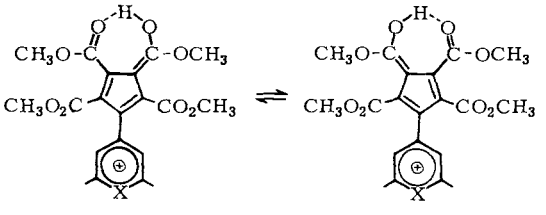
3.1. Electrophilic Addition

Heterosesquifulvalenes are relatively strong "π bases". For instance, in strong acids, such as perchloric acid or trifluoroacetic acid, *(8b)* undergoes regiospecific



(8b) *(19)*

quantitative *C*-protonation to give *(19)*[1,4a,5,6b,13]; the structure of the product is proved by NMR and UV spectra.

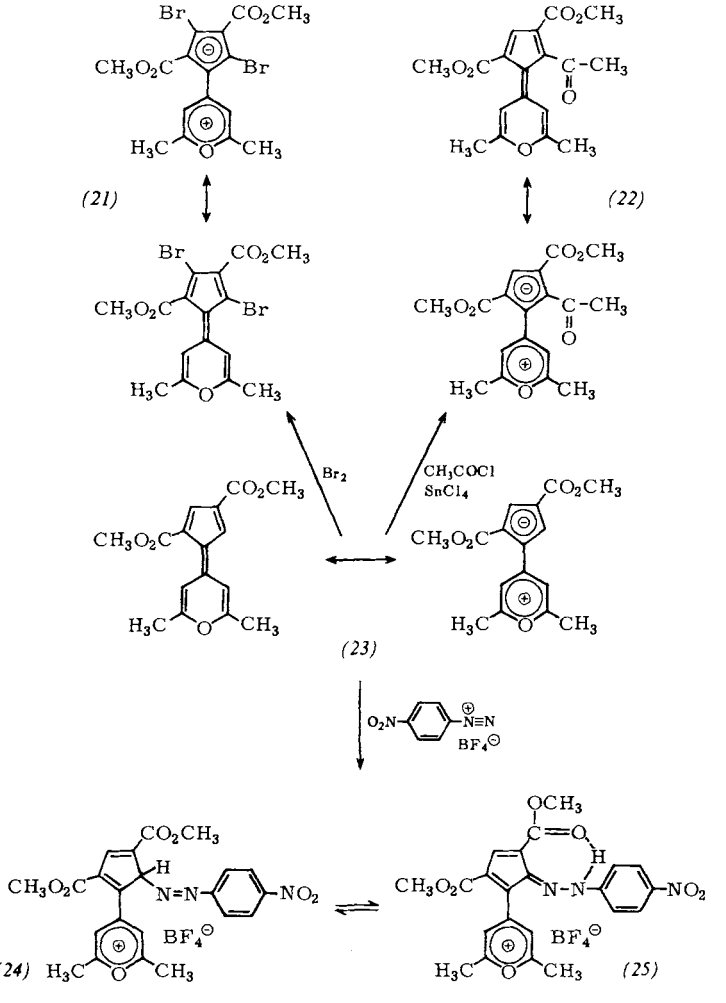


(20a), X = O
(20b), X = S
(20c), X = -CH=CH-

(8a), the analog having X = S, and *(16)* are all protonated in a uniform manner, though at the ester carbonyl group; NMR and electronic spectra suggest the structures *(20a)*, *(20b)*, and *(20c)*, having a symmetrical hydrogen bond[1,4d].

3.2. Electrophilic Substitution

Electrophilic substitutions occur in good yields, even at room temperature. Friedel-Crafts acylation of *(23)* with acetyl chloride/$SnCl_4$ affords the monoacetylated compound *(22)*. An excess of bromine converts *(23)* into the dibromo derivative *(21)*, whereas reaction with *p*-nitrobenzenediazonium fluoroborate probably yields the phenylhydrazone *(25)*, which is tautomeric with *(24)*.



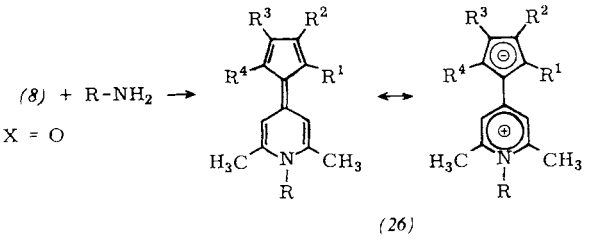
(21) *(22)* *(23)* *(24)* *(25)*

3.3. Nucleophilic Reactions

Pyrones and pyranylidene compounds are known to be readily convertible into pyridine derivatives by treatment with primary amines[5,14]. By analogy, replacement of oxygen in cyclopentadienylidenepyrans should also be feasible. Indeed, heterosesquifulvalenes containing oxygen as hetero atom react almost quantitatively, irrespective of substituents, with aliphatic amines to give the aza analogs *(26)*. This nucleophilic

[12] *E. D. Bergmann*, Chem. Reviews *68*, 74 (1968).
[13] *E. D. Bergmann* and *I. Agranat*, Tetrahedron *22*, 1275 (1966).

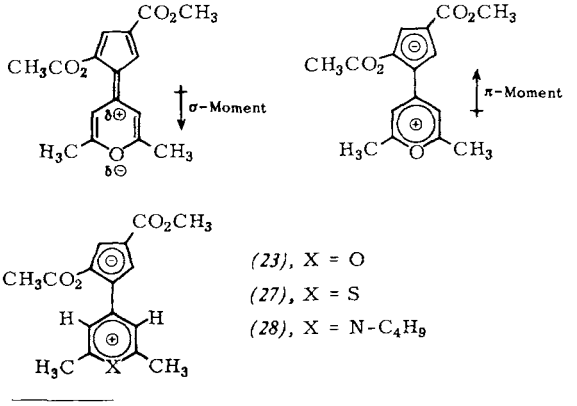
substitution proves a useful addition to the known syntheses of unsubstituted or annelated nitrogen analogs of sesquifulvalene.



4. Polarity and Electron Distribution

NMR data provide no unequivocal information regarding the shielding of the protons attached to the five- and six-membered rings of heterosesquifulvalenes; the anisotropic effects of the substituents do not permit direct relationships to be observed between the chemical shifts and the π-electron density distribution. On the other hand, solvatochromism effects[15] should at least furnish qualitative information about the polarity of the ground state. All the heterosesquifulvalenes having oxygen or sulfur as hetero atom that have been isolated so far show, to a greater or lesser extent, a pronounced positive solvatochromism. The ground state is therefore determined primarily by the nonpolar resonance formula. However, measurements of dipole moments and determination of the free energy of activation $\Delta G_c^{\neq}$ for rotation around the central C–C double bond suggest that the dipolar form also contributes to the resonance hybrid.

Compound *(23)* has a dipole moment of 5.1 D (20 °C, benzene), a finding that becomes all the more remarkable when one considers that the sense of the σ moment (disregarding the effect of the two ester groups, which is not readily estimable) is opposed to that of the π moment[16].



The heterosesquifulvalenes *(23)*, *(27)*, and *(28)*, whose five-membered rings are substituted in two positions, are suitable for determination of the free energy of activation $\Delta G_c^{\neq}$ for rotation around the intercyclic bond. (Figure 1 reproduces sections of the relevant NMR spectra measured at 40 °C.)

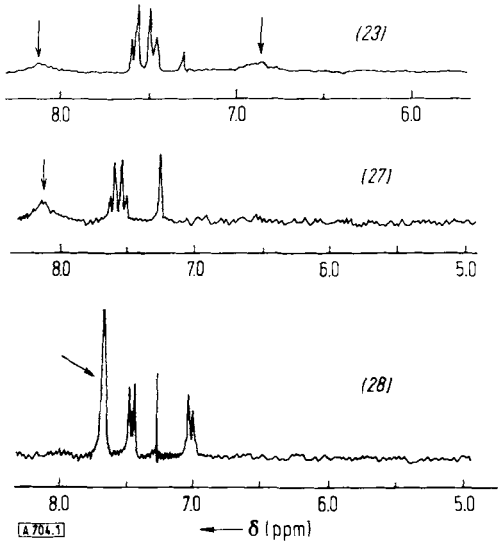


Fig. 1. Partial NMR spectra (60 MHz) of *(23)*, *(27)*, and *(28)*. The signals due to the pyran protons are indicated by arrows.

In addition, $\Delta G_c^{\neq}$ was also determined for the acylated product *(22)* and *(8e)*. The different rates of rotation around the central bond can be calculated from the signals of the pyran protons (shown by arrows). The shapes and positions of the peaks are temperature dependent (Figure 2).

The relevant $\Delta G_c^{\neq}$ values could be calculated from the temperature of coalescence T_c and the maximum

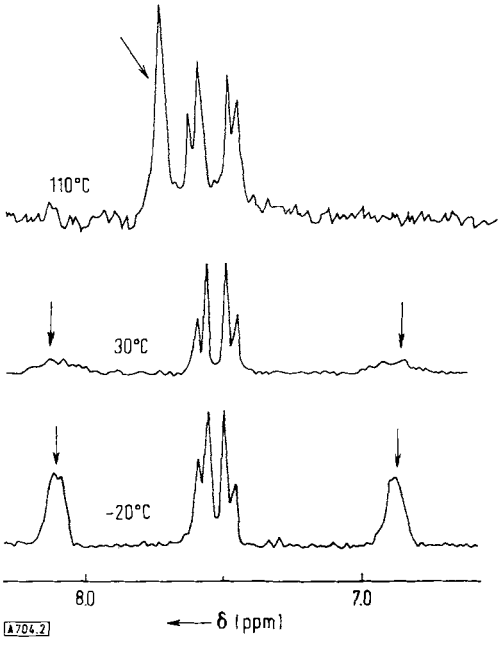


Fig. 2. Temperature dependence of the peaks due to the pyran protons (shown by arrows) in *(23)*.

[14] *K. Dimroth*, Angew. Chem. *72*, 331 (1960), and further literature cited there; *F. Eiden*, Naturwissenschaften *47*, 60 (1960); Arch. Pharmaz. *295*, 607 (1962).

[15] For recent reviews see p. 336 in *H. A. Staab*: Einführung in die theoretische organische Chemie, 1st Edit., Verlag Chemie, Weinheim/Bergstr. 1959; *C. Reichardt*, Angew. Chem. *77*, 30 (1965); Angew. Chem. internat. Edit. *4*, 29 (1965).

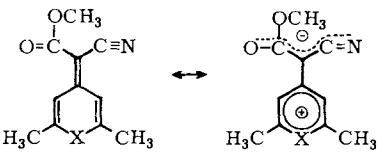
[16] Cf. *A. Streitwieser*: Molecular Orbital Theory. *J. Wiley*, New York 1962, p. 139ff.

Table 2. $\Delta G_c^{\neq}$ values [17] (solvent $CDCl_3$; D_3CSOCD_3 for *(8e)*).

Cpd.	Δν (Hz)	T_c (°K)	$\Delta G_c^{\neq}$ (kcal/mole)	X
(22)	47	279	13.7	O
(23)	73	339	16.5	O
(27)	48	280	13.8	S
(8e)	52	384	19.0	S

splitting Δν of the signals at low temperature by means of the Eyring equation [17] (see Table 2).

The low $\Delta G_c^{\neq}$ values obtained for all the heterosesquifulvalenes investigated indicate participation of the dipolar structure in the ground state. The results demonstrate quite impressively that the bond order of the central C–C double bond depends both on the number of electron-accepting groups attached to the five-membered ring and on the donor properties of the hetero atom. The nitrogen atom in *(28)* proves to be the best electron donor; rotation around the central bond is still so fast at −50 °C that the two protons on the six-membered ring in *(28)* are equivalent in the NMR spectrum. As expected, the sulfur atom is more readily polarizable than the more electronegative oxygen. In this connection it is interesting to note that $\Delta G_c^{\neq}$ for *(29)* is 17.7 kcal/mole, while the energy barrier for the corresponding oxygen compound *(30)* is so high that no rotation occurs, even at temperatures as high as 160 °C, in dimethyl sulfoxide [18].



(29), X = N-C_4H_9

(30), X = O

5. Conclusion and Outlook

Within certain limits the anhydride method has proved a simple and effective process for the preparation of substituted sesquifulvalenes and of the iso-π-electronic cyclopentadienylidenepyrans and -thiopyrans. Only a selection of the possible reactions has been described in this article. Preliminary experiments have shown that various other ketones that are iso-π-electronic with tropone and contain more than one hetero atom also undergo condensation to heterosesquifulvalenes by the same synthetic route. Similarly, the benzotropone analogs furo[3,4-*d*]tropone and thieno[3,4-*d*]-tropone can also be converted into heterosesquifulvalenes that may be considered as vinylogs of the cyclopentadienylidenepyrans and -thiopyrans, respectively.

The author wishes to thank the Deutsche Forschungsgemeinschaft for their support of his investigations described in this article.

Received: October 4, 1968 [A 704 IE]
German version: Angew. Chem. *81*, 518 (1969)

[17] Regarding method of calculation cf. *J. A. Pople, W. G. Schneider*, and *H. J. Bernstein*: High Resolution Nuclear Magnetic Resonanz. McGraw-Hill, New York 1959, p. 223; *S. Glasstone, K. J. Laidler*, and *H. Eyring*: The Theory of Rate Processes. McGraw-Hill, New York 1941, p. 194.

[18] *G. Seitz*, unpublished experiments.

Thiiranium Ions as Reaction Intermediates

By Wolfgang H. Mueller[*]

The addition of sulfenyl chlorides or sulfur dichloride to unsaturated compounds proceeds via thiiranium ions. The present article reviews the electronic and steric factors influencing the nature of these ions and their effects on subsequent ring opening and product formation. For the purpose of this discussion results primarily from electrophilic ring opening have been chosen to illustrate these factors. Solvent and temperature effects have been disregarded.

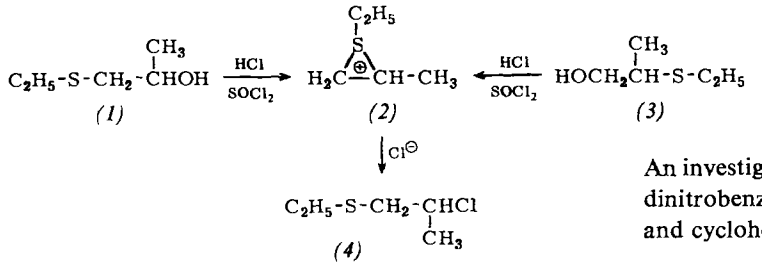
1. Introduction

Thiiranium ions (episulfonium ions) as chemical intermediates were first proposed during studies of the neighboring group effect of sulfur in extremely reactive β-haloalkyl thioethers of the "mustard gas" type, $S(CH_2CH_2Cl)_2$ [1,2]. For instance, the intervention of a thiiranium ion *(2)* was postulated [1] to account for a single product *(4)* obtained on chlorination of the isomeric alcohols *(1)* and *(3)*.

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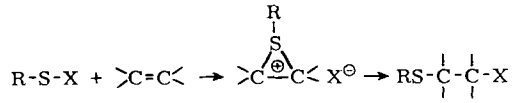
[1] *R. C. Fuson, C. C. Price*, and *D. M. Burness*, J. org. Chemistry *11*, 475 (1946).

[2] *P. D. Bartlett* and *C. G. Swain*, J. Amer. chem. Soc. *71*, 1406 (1949).



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

Similarly, thiiranium ion intermediates *(5)* have been proposed for the polar addition of sulfenyl halides to double bonds [3–6].

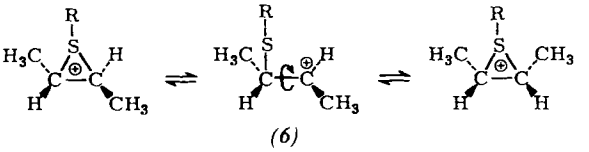


(5)

The present review will concern itself mainly with the factors influencing the nature of thiiranium ions formed in the course of such additions and the less extensively studied reaction of thiiranes (episulfides) with electrophiles. These reactions frequently allow a differentiation between kinetic and thermodynamic factors controlling the ring opening. An abundance of data obtained in the same or similar solvents is available and thus excludes the added complication of solvent effects.

2. Formation of Thiiranium Ions

Support in favor of the proposed intermediacy of thiiranium ions during sulfenyl chloride additions was derived from the almost exclusive *trans*-stereospecific addition observed with *cis*- and *trans*-2-butene [7–9]. Although in some cases the possibility of contributions from open ions cannot be ruled out [10], strong evidence against a nonrotating open carbonium ion *(6)* has recently been supplied by the stereospecific uniformity of this addition reaction over a wide temperature range [11].



(6)

An investigation of the kinetics of the reaction of 2,4-dinitrobenzenesulfenyl chloride or bromide with styrene and cyclohexene revealed it to be second order [12–14]:

$$-\mathrm{d\,RSX/d}t = k[\mathrm{RSX}]\,[\mathrm{olefin}]$$

Enhanced rates were observed in more polar solvents, *e.g.*, the addition proceeded 1400 times faster in acetic acid than in carbon tetrachloride. In addition, a salt effect was observed; the presence of sodium perchlorate in acetic acid further enhanced the reaction rate. The sum of the kinetic evidence is consistent with the development of charge in the rate determining transition state, but does not require the general postulate of a thiiranium ion intermediate. More recently, an examination of the reaction rates of addition of several *para*-substituted, *ortho*-nitrobenzenesulfenyl chlorides to cyclohexene demonstrated the need to allow for an enhanced mesomeric electron release from *para*-substituents by the use of σ^+ values (Fig. 1) [15]. This

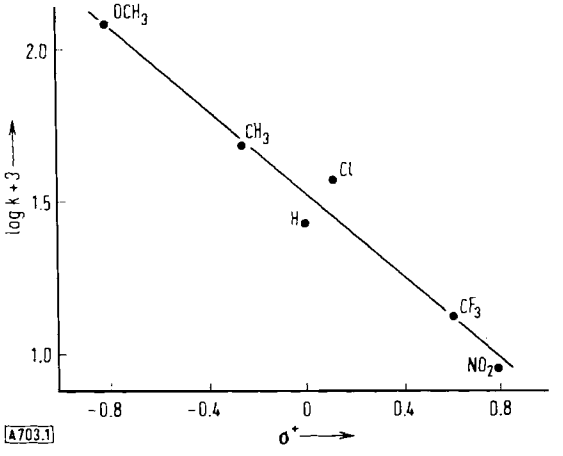
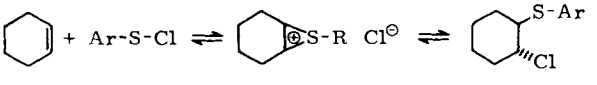


Fig. 1. Hammett relationship for the addition of *p*-substituted *o*-nitrobenzenesulfenyl chloride to cyclohexene in acetic acid at 25 °C; $\rho = -0.714$ [15].

strongly supports the postulate of an intermediate thiiranium ion, rather than an open carbonium ion. A rate-limiting first step involving a transition state closely resembling the intermediate *(7)*, stabilized by electron releasing *para*-substituents, was invoked to explain the sign and magnitude of ρ.



(7)

[3] *N. Kharasch* and *C. M. Buess*, J. Amer. chem. Soc. *71*, 2724 (1949).

[4] *N. Kharasch* in *N. Kharasch*: Organic Sulfur Chemistry. Pergamon Press, New York, N.Y., 1961, Vol. 1., pp. 375–396.

[5] *P. B. D. De La Mare* and *R. Bolton* in *C. Eaborn*: Reaction Mechanisms in Organic Chemistry, Monograph 4. Elsevier Publishing Co., New York, N.Y., 1966, pp. 166–173.

[6] *N. Kharasch et al.*, Quart. Rep. Sulfur Chem. *1*, 93 (1966).

[7] *D. J. Cram*, J. Amer. chem. Soc. *71*, 3383 (1949).

[8] *N. Kharasch* and *A. J. Havlik*, J. Amer. chem. Soc. *75*, 3734 (1953).

[9] *A. J. Havlik* and *N. Kharasch*, J. Amer. chem. Soc. *78*, 1207 (1956).

[10] *A. Streitwieser*, Chem. Reviews *56*, 571 (1958).

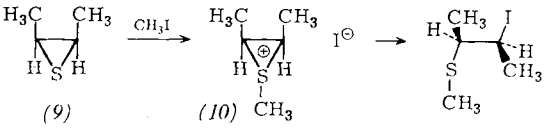
[11] *G. H. Schmid* and *V. M. Szismadia*, Canad. J. Chem. *44*, 1338 (1966).

[12] *W. L. Orr* and *N. Kharasch*, J. Amer. chem. Soc. *75*, 6030 (1953).

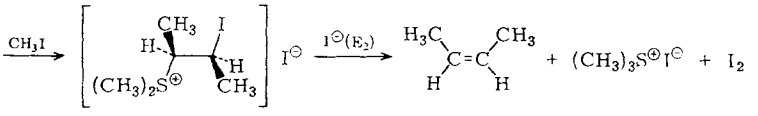
[13] *D. R. Hogg* and *N. Kharasch*, J. Amer. chem. Soc. *78*, 2728 (1965).

[14] *D. S. Campbell* and *D. R. Hogg*, J. chem. Soc. (London) *(B)*, 109 (1966).

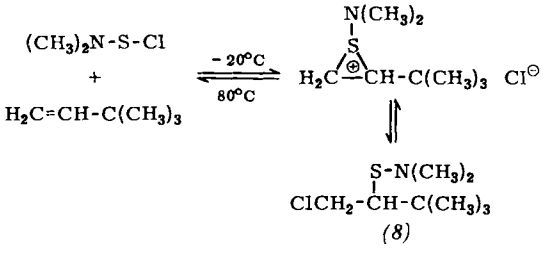
[15] *C. Brown* and *D. R. Hogg*, Chem. Commun. *1965*, 357.



(9) (10)



The reversible formation of an intermediate analogous to *(7)* has been observed as an unusual case in the reaction of dimethylaminosulfenyl chloride and 3,3-dimethyl-1-butene[16]. Attempts to distill compound *(8)* under reduced pressure afforded 85% of the starting materials.



(8)

A study of relative rates of the addition of methanesulfenyl chloride (and chlorine[18]) to a variety of methyl-substituted olefins has also provided further insight into the first step, the formation of the thiiranium ions[17] (Table 1). It is obvious that the rate of addition of chlorine is directly related to the relative

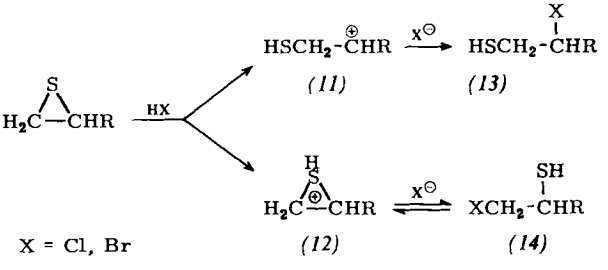
Table 1. Relative reactivities of olefins toward methanesulfenyl chloride and chlorine in nonpolar media [17].

Olefin	k_{rel} Cl_2	k_{rel} CH_3SCl
1-Butene	1.0	1.0
cis-2-Butene	63	13.0
trans-2-Butene	50	0.72
Isobutylene	58	0.75
2-Methyl-2-butene	11000	8.26
2,3-Dimethyl-2-butene	430000	12.9

nucleophilicity of the olefin, *i.e.*, to the number of electron releasing substituents on the double bond. The data for methanesulfenyl chloride, however, show that the reaction with this compound is considerably less sensitive to the electronic environment of the double bond. This implies that in the transition state little or no charge is being developed on the carbon atoms of the double bond and, therefore, that methyl substituents do not significantly lower the transition state energy. This is again consistent with the formation of a thiiranium ion, the positive charge residing mostly on sulfur. The rate enhancement observed with *cis*-2-butene relative to *trans*-2-butene clearly shows the importance of steric effects which somewhat obscure the net electronic effect.

The reaction of electrophilic reagents with thiiranes has been considered to involve either thiiranium ions or open carbonium ions, depending on the reagent. The stereospecific desulfurization of *cis*-2,3-dimethylthiirane *(9)* to *cis*-2-butene with methyl iodide was explained by a mechanism involving the formation of a thiiranium ion *(10)* in the first step[19,20].

A carbonium ion intermediate *(11)* was proposed for the reaction of anhydrous hydrogen chloride and hydrogen bromide with substituted thiiranes[21]. This proposal was based on the reaction's second order kinetics[21] and the reported formation of primary thiols *(13)*[22]. A recent reinvestigation[23] of this reaction, however, revealed that the kinetically controlled products are predominantly primary halogen compounds *(14)* which can isomerize to the primary thiols *(13)*. These data are more consistent with a thiiranium ion intermediate *(12)* undergoing ring opening at the least substituted carbon atom to form the kinetically controlled product *(14)*.



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

This compound may then isomerize through *(12)* to the thermodynamically favored product *(13)*. Similar results (discussed in Section 3.3) obtained for a variety of electrophiles allow the general postulate of a thiiranium ion intermediate rather than that of an open ion.

Very convincing support for the existence of thiiranium ions has been provided by the successful preparation of several crystalline thiiranium salts *(5)*. The 2,4,6-trinitrobenzenesulfonate[24a] or the hexafluoroantimonate[24b] have been found to be suitable anions permitting the isolation of such salts.

[16] *W. H. Mueller* and *P. E. Butler*, J. org. Chemistry *33*, 2111 (1968).

[17] *W. A. Thaler*, J. org. Chemistry *34*, 871 (1969).

[18] *M. L. Poutsma*, Science (Washington) *157*, 997 (1967).

[19] *G. K. Helmkamp* and *D. J. Pettitt*, J. org. Chemistry *25*, 1754 (1960).

[20] *G. K. Helmkamp* and *D. J. Pettitt*, J. org. Chemistry *27*, 2942 (1962).

[21] *A. Oddon* and *J. Wylde*, Bull. Soc. chim. France *1967*, 1607.

[22] *W. Davis* and *W. E. Savige*, J. chem. Soc. (London) *1950*, 317; *1951*, 747.

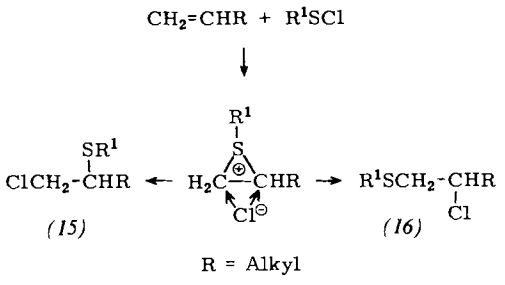
[23] *N. V. Schwartz*, J. org. Chemistry *33*, 2895 (1968).

[24] a) *O. J. Pettitt* and *G. K. Helmkamp*, J. org. Chemistry *29*, 2702 (1964); b) *J. F. King* and *K. Abikar*, private communication.

3. Effects on Thiiranium Ion Ring Opening

3.1. Steric Effects

Recent studies on the addition of sulfenyl chlorides to terminal olefins have revealed that steric factors can control the ring opening of the thiiranium ion intermediate [25,26]. With olefins of the type CH_2=CH-Alkyl the kinetically controlled products were predominantly of the anti-Markovnikov structure *(15)* [27].



The selectivity to this type of adduct increases with the size of the alkyl substituent R (Table 2), thus demonstrating the importance of the steric requirements of the alkyl substituents on the ring carbon atoms.

Table 2. Percentage isomer ratio from ring opening of alkyl substituted thiiranium ions by chloride ion.

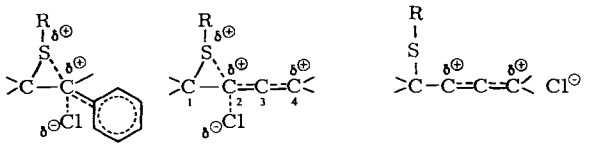
R \ R^1	*(15)* CH_3	*(15)* C_6H_5	*(15)* $(CH_3)_2N$	*(16)* CH_3	*(16)* C_6H_5	*(16)* $(CH_3)_2N$
CH_3	82	68	78	18	32	22
$CH(CH_3)_2$	94	87	>90	6	13	<10
$C(CH_3)_3$	95		95	5		5

This finding is unambiguous evidence for a bridged thiiranium ion and is completely consistent with the expectation of a nucleophilic attack of the chloride ion on the thiiranium ion intermediate. In these cases little positive charge seems to be developed on the ring carbons in the transition state.

3.2. Polar Effects of Substituents on Carbon

Phenyl substituents on the ring carbon atoms of a thiiranium ion cause ring opening at the benzylic position leading to Markovnikov [27] oriented adducts [3,12,28]. This effect is caused by a lower transition-state energy of *(17)* relative to that arising from attack of the chloride on the terminal carbon.

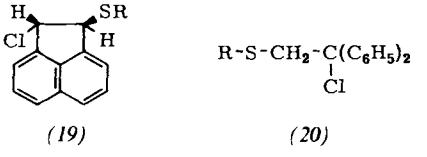
Stabilization of the transition state *(17)* is due to π-bond overlap of the p orbital of the electron-deficient



α-carbon with the π cloud of the phenyl ring. A similar transition-state *(18a)* also explains the kinetically controlled formation of 1,2-Markovnikov adducts from sulfenyl chlorides and conjugated dienes [29], *e.g.*,

$$R\text{-}S\text{-}Cl + CH_2\text{=}CH\text{-}CH\text{=}CH_2 \rightarrow R\text{-}S\text{-}CH_2\text{-}CHCl\text{-}CH\text{=}CH_2$$

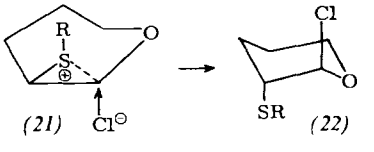
Strong sulfur bridging to the exclusion of contributions from an allylic or benzylic carbonium ion can be deduced from several observations made during sulfenyl chloride additions to conjugated systems. Acenaphthylene afforded exclusively *trans*-adducts *(19)*, and 1,1-diphenylethylene exhibits a lower selectivity (90%) for the Markovnikov adduct *(20)* than was found with styrene (98%). Apparently, two geminal phenyl groups cause some competition between the steric requirements and the electronic factors governing the ring opening. This would be less likely for an S_N1-type reaction.



The kinetically favored attack of the chloride on C-2 rather than on C-4 of the thiiranium ion intermediate is derived from the relative degree of electron deficiency of the two carbons in question. The partial positive charge residing on C-2 receives its enhanced stabilization from overlap of the electron deficient orbital on carbon with the sulfur orbitals.

The lower reactivity of dienes *versus* simple olefins toward sulfenyl chlorides [17,30] is also in accord with a transition-state *(18a)* where relatively little positive charge is developed on carbon. Higher reactivity of dienes would be expected from the participation of a resonance stabilized allylic carbonium ion *(18b)*.

As one might expect in the light of the previous examples, ring opening of thiiranium ions *(21)* derived from vinylic ethers takes place exclusively on the carbon *alpha* to the hetero atom [31].



[25] *W. H. Mueller* and *P. E. Bulter*, J. Amer. chem. Soc. *88*, 2866 (1966).

[26] *G. M. Beverly* and *D. R. Hogg*, Chem. Commun. *1966*, 138.

[27] In the present paper "Markovnikov" orientation indicates adducts with the chlorine on a secondary or tertiary carbon atom while "anti-Markovnikov" adducts have the chlorine on the terminal carbon.

[28] *W. H. Mueller* and *P. E. Butler*, J. Amer. chem. Soc. *90*, 2075 (1968).

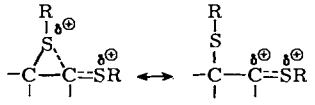
[29] *W. H. Mueller* and *P. E. Butler*, Chem. Commun. *1966*, 646.

[30] *W. H. Mueller* and *P. E. Butler*, J. org. Chemistry *33*, 2642 (1968).

[31] *M. J. Baldwin* and *R. K. Brown*, Canad. J. Chem. *46*, 1093 (1968); *45*, 1195 (1967).

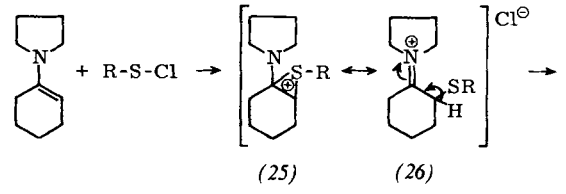
In a similar manner to that shown in the transition states *(17)* and *(18)*, oxygen orbitals stabilize the transition state by overlap with the p orbital of the electron deficient carbon. The *trans*-stereochemistry of product *(22)* appears to rule out significant contributions by an open ion.

Addition of sulfenyl chloride to vinylic thioethers[32] results in the same adduct orientation as that observed with vinylic ethers. There are, however, no data available which would allow one to differentiate between the bridged intermediate *(23)* or the stabilized carbonium ion *(24)*.

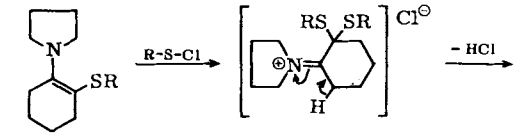


(23) *(24)*

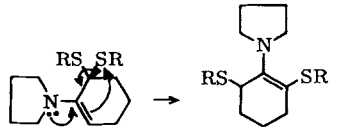
The addition of sulfenyl chlorides to enamines yields products *(27)* and *(30)* with the mercapto group *beta* to nitrogen[33]. Monoadducts such as *(27)* have been isolated only in special cases and the involvement of a thiiranium ion *(25)* seems unlikely. The preponderant ability of nitrogen *versus* that of sulfur to stabilize a positive charge on an adjacent carbon can be assumed and serves to explain the formation of products *(30)*. Addition of a second equivalent of sulfenyl chloride to compound *(27)*, dehydrochlorination of *(28)*, and subsequent rearrangement of the enamine *(29)* has been postulated[33b].



(25) *(26)*

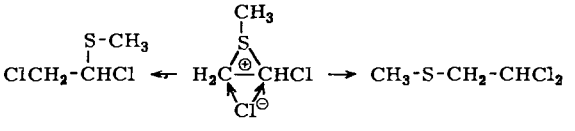


(27) *(28)*



(29) *(30)*

Chloride substituents play well-recognized dual roles in the stabilization (destabilization) of an electron-deficient center; however, a chloride substituent on carbon has little apparent influence on the charge distribution in a thiiranium ion *(32)*[28].



(31) 77% *(32)* *(33)* 23%

[32] *W. H. Mueller*, unpublished results.

[33] a) *G. H. Alt* and *A. J. Speziale*, J. org. Chemistry *29*, 789 (1964); b) *M. E. Kuehne, ibid. 28*, 2124 (1963).

Predominant anti-Markovnikov orientation of the ring opening product *(31)* indicates that overlap of the central p orbital of the α-carbon with a p orbital of the adjacent chlorine does not contribute significantly to the lowering of the energy of the transition state resonance hybrid. Rather, destabilization of an electron deficient α-carbon by the electron withdrawal, along with possible steric hindrance to attack by the incoming nucleophile, explains the product distribution.

Reactions of sulfenyl chlorides with several other ethylenes substituted with electronegative groups have already been reviewed[34]; however, later reports have been somewhat contradictory[35]. A recent reinvestigation of a number of these cases has allowed a correlation of the seemingly unrelated results[36]. A marked difference exists in the ability of electronegative groups on the thiiranium ion ring to direct the attack of chloride ion. Examination of Table 3 reveals that the

Table 3. Isomer distribution (%) from ring opening of functionally substituted episulfonium ions by chloride ion.

	$CH_3SCH_2-C(Cl)-RX$		$ClCH_2-C(S-CH_3)-RX$	
X	R = H	R = CH_3	R = H	R = CH_3
COCl	94	52	6	48
CO_2CH_3	83	24	17	76
CN	51	–	49	>98
SO_2CH_3	–	–	>98	–

tendency for a functional group to favor formation of the Markovnikov isomer follows the same order as the reactivity of the functional group toward solvolysis. Thus the decreasing reactivity of the functional groups toward nucleophiles (COCl > $COOCH_3$ > CN > SO_2CH_3) is paralleled by the decrease in the relative amount of Markovnikov isomer from sulfenylchloride addition to the corresponding substituted ethylene. This order of reactivity is also reminiscent of nucleophilic displacement reactions of α-halocarbonyls and related compounds. Dramatic activation of the α position to nucleophilic attack, in which the activating ability of the functional groups follows the above sequence, is well established[37,38]. The enhanced rate of nucleophilic substitution on α-halocarbonyl compounds has been attributed to the important contribution of transition state structures in which the incoming nucleophile is bonded to both the carbonyl carbon and the α-carbon simultaneously[38,39].

[34] *K. D. Gundermann*, Angew. Chem. *75*, 1194 (1963); Angew. Chem. internat. Edit. *2*, 674 (1963), and references therein.

[35] *I. L. Knunyants, M. G. Lin'kova*, and *N. D. Kuleshova*, Izvest. Akad. Nauk SSSR, Ser. chim. *1966*, 1069; *I. L. Knunyants, M. G. Lin'kova*, and *N. L. Veller, ibid. 1966*, 1075; *V. Hasserodt*, Chem. Ber. *100*, 1482 (1967).

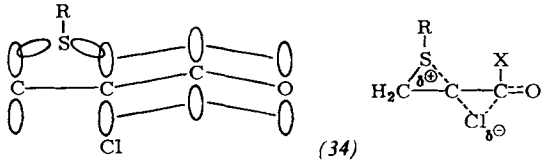
[36] *W. A. Thaler, W. H. Mueller*, and *P. E. Butler*, J. Amer. chem. Soc. *90*, 2069 (1968).

[37] *P. D. Bartlett* and *E. N. Trachtenberg*, J. Amer. chem. Soc. *80*, 5908 (1958); *A. Streitwieser, Jr.*: Solvolytic Displacement Reactions. McGraw Hill, New York, N.Y., 1962, p. 28.

[38] *M. S. Newman*: Steric Effects in Organic Chemistry. Wiley, New York, N.Y., 1956, pp. 103–106.

[39] *M. J. S. Dewar*: The Electronic Theory of Organic Chemistry. Clarendon Press, Oxford 1949, p. 73; *S. Winstein, E. Grunwald*, and *H. W. Jones*, J. Amer. chem. Soc. *73*, 2700 (1951).

The striking resemblance between α-activation in nucleophilic displacement on α-halocarbonyl compounds and α-activation in the direction of thiiranium ion ring opening suggests that similar transition state structures *(34)*, in which the carbonyl group is at right angles to the entering and leaving groups, are important and serve to lower the energy for α attack (Markovnikov product formation).



(delocalized orbitals) *(34)* (localized orbitals)

As the ability of the functional group to accommodate a nucleophile decreases, contribution of such resonance structures to the transition state also diminishes and a progressively greater amount of β attack (anti-Markovnikov product) occurs.

The tendency is to favor sterically controlled β attack by chloride ion; therefore, only those electrophilic substituents which can most effectively participate in a transition state such as *(34)* are capable of extensively diverting the attack by chloride ion to the α position. Functional groups such as sulfones, which do not effectively participate in such structures, exhibit strong steric effects which deactivate the α position [40,41].

The importance of steric effects on the ring opening of thiiranium ions again becomes evident in the rather drastic change in the product ratio that occurs on introduction of a methyl substituent *alpha* to the carbonyl group (Table 3, R = CH_3). In this case, ring opening on the unsubstituted β-carbon becomes increasingly favored.

3.3. Polar Effects of Substituents on Sulfur

The nature of the substituent on sulfur also has an important influence on the ring opening of thiiranium ions. This can be most dramatically demonstrated in the addition of various sulfenyl chlorides to isobutylene [28,42,43] and by the reaction of 2,2-dimethylthiirane with certain electrophilic reagents [23]. Both reactions can produce products *(35)*, *(37)*, and *(38)*. From Table 4 it becomes apparent that the product ratio is strongly dependent on the nature of R.

As expected, the adduct distribution from methanesulfenyl chloride and isobutylene shows little difference from that of propylene (see Table 2), *i.e.*, sterically controlled ring opening of the thiiranium ion favors the formation of product *(35)*. Similar, although less

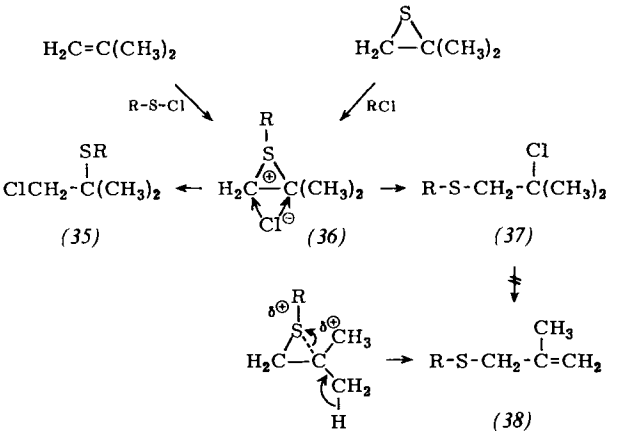


Table 4. Influence of the group R attached to sulfur on the product distribution.

R	*(36)* (%)	*(37)* (%)	*(38)* (%)
CH_3 [a]	80	20	0
H [b]	66	34	0
CH_3CO-S [a]	32	68	0
$(CH_3O)_2P(O)$ [a]	19	57	21
CH_3CO [b]	9	60	31

[a] Sulfenyl chloride addition. [b] Reaction of 2,2-dimethylthiirane with HCl or CH_3COCl.

pronounced, is the result obtained from ring opening of 2,2-dimethylthiiranium *(36)*, R = H. In contrast, the electron-withdrawing effect of an acetylthio group [*(36)*, R = CH_3-CO-S] tends to destabilize the positive charge on the ring sulfur atom contributing to the development of an electron-deficient center on the substituted carbon atom of *(36)*, which results predominantly in the formation of the Markovnikov oriented compound *(37)*. Although no evidence for a true carbonium ion intermediate had been detected in an extensive study of acetylthiosulfenyl chloride additions to a variety of unsaturated compounds [42], it appears that in the case of isobutylene the transition state must have significant charge on carbon in order to be stabilized by the methyl substituents.

The effect of an electron-withdrawing R group on the charge distribution in the thiiranium ion *(36)* becomes even more apparent when R = $(CH_3O)_2P(O)$ or CH_3CO. In contrast to R = CH_3-CO-S, here the electronegative phosphoryl or acetyl group is directly bonded to the sulfur atom participating in the thiiranium ion. This evidently impairs the sulfur's bridging ability to such an extent as to allow for the formation of olefin *(38)*. The expulsion of a proton and formation of product *(38)* is strongly reminiscent of the disciplines observed in carbonium ion chemistry, particularly since no indication for its formation *via* dehydrohalogenation of *(37)* has been found.

In summary, sterically controlled ring opening decreases with the decreasing ability of R to support a positive charge on sulfur in the following order: $CH_3 > H > CH_3-CO-S > (CH_3O)_2P(O) > CH_3CO$ (Table 4).

Additional data demonstrating the above tendency have been obtained from the reaction of methylthi-

[40] *D. I. Relyea*, J. org. Chemistry *31*, 3577 (1966).

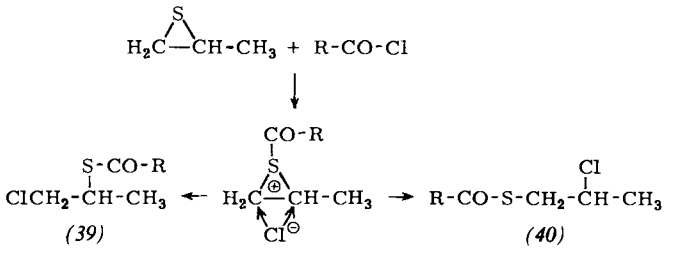
[41] *F. G. Bordwell* and *W. T. Braunen*, J. Amer. chem. Soc. *86*, 4645 (1964).

[42] *W. H. Mueller* and *P. E. Butler*, J. org. Chemistry *32*, 2925 (1967).

[43] *W. H. Mueller*, *R. M. Rubin*, and *P. E. Butler*, J. org. Chemistry *31*, 3537 (1966).

irane with hydrogen halides or acyl chlorides (Table 5)[23].

Although the effect observed with various *para*-substituted benzoyl chlorides is relatively small, the decreasing proportion of product *(39)* can be correlated directly with the electron-withdrawing ability of the electrophilic group.

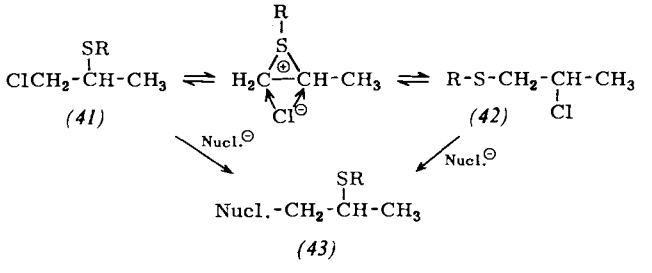


(39) *(40)*

Table 5. Influence of the group R attached to sulfur on the product distribution.

R	*(39)* (%)	*(40)* (%)
H	76	24
CH_3CO	54	46
p-CH_3O–C_6H_4–CO	71	29
p-CH_3–C_6H_4–CO	67	33
C_6H_5–CO	64	36
p-Cl–C_6H_4–CO	59	41
p-NO_2–C_6H_4–CO	57	43

Further evidence for the important influence of R on the sulfur atom participating in the thiiranium ion stems from the differing propensity for rearrangement of the initial kinetically controlled ring opening products *(41)* to the thermodynamically more stable Markovnikov products *(42)*.

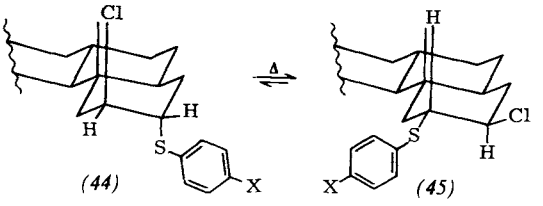


(41) *(42)* *(43)*

Ready isomerization is observed when R is methyl. Phenylthio compounds, however, rearrange much more slowly[28], whereas little or no tendency for post-isomerization has been found when R is acetylthio[42] or *O,O*-dimethylphosphoryl[43], respectively. Increasing electronegativity of R decreases the availability of unshared electrons on the sulfur atom and impairs or prevents participation in S_N2 displacement of the chlorine.

Strong support for the intermediacy of a bridged ion during the rearrangement is derived from displacement reactions with various nucleophiles, *e.g.*, acetate ion[28] or thiourea[23], on compound *(41)* or *(42)*. Displacement on either the anti-Markovnikov oriented compound *(41)* or the Markovnikov compound *(42)* affords products of identical composition. The reaction leads to the isomer *(43)* in high selectivity, and to a similar product ratio as was obtained from kinetically controlled ring opening by chloride ion, provided that the nature of nucleophile (Nucl.) does not allow post-isomerization of product *(43)*.

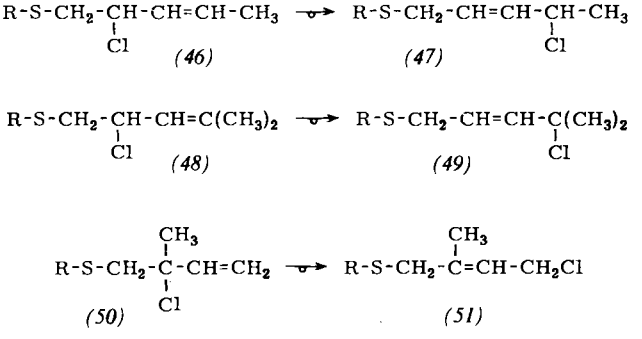
Quantitative data on the influence of the electronic nature of R on this rearrangement was obtained with *para*-substituted benzenesulfenyl chloride adducts of α-cholest-2-ene. The kinetically controlled diaxial adduct *(44)* rearranges on heating to the diequatorial compound *(45)*[44]. The first order rate constants of



(44) *(45)*

this rearrangement were found to vary with the nature of the *para*-substituent X and to follow the sequence $CH_3O > H > NO_2$[45]. This finding is in accord with the qualitative assessment of the relative propensity for the rate of rearrangement to depend on the availability of the unshared electrons on sulfur for the S_N2 displacement of chlorine[28].

This tendency for post-isomerization has also been detected with certain 1,2-Markovnikov adducts, *e.g.* *(46)* and *(48)*, derived from sulfenyl chloride additions to conjugated dienes[29, 30].



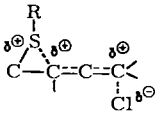
(46) *(47)* *(48)* *(49)* *(50)* *(51)*

Two major factors determing the rate of rearrangement were recognized with the models investigated:

(i) Only adducts with R = CH_3 rearrange while none of those having R = C_6H_5 rearranges under the same conditions.

(ii) Methyl substituents on C-4 or C-2 of the initial adduct facilitate this rearrangement.

This differing propensity for rearrangement depending on the nature of R is strong evidence that the rearrangement involves the same thiiranium ion intermediate as the initial addition reaction. It also follows that formation of this intermediate is reached through transition state *(18)*. Isomerization then proceeds through a higher energy transition state, such as *(52)*, to form the thermodynamically favored 1,4-products *via* S_N2' displacement by the chloride.



(52)

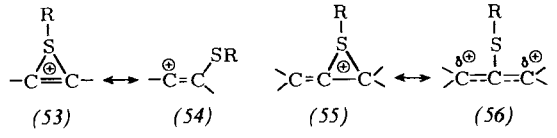
[44] *J. F. King* and *K. Abikar*, Canad. J. Chem. *46*, 1 (1968).
[45] *J. F. King* and *K. Abikar*, Canad. J. Chem. *46*, 9 (1968).

This step is essentially irreversible since it would require an unfavorable S_N2' displacement of a chlorine atom on C-4 by the methylthio group.

The methyl substituents effect additional stabilization of the transition state *(18)* by electron release at C-2 or C-4. In compounds bearing methyl substituents on C-1 or C-3 no contribution by the substituent to lowering the transition state energy would be expected. This is consistent with the failure of such compounds to rearrange[30]. Furthermore, methyl substituents on C-4 can also contribute to lowering the energy of the transition state *(52)* by stabilizing a partial positive charge on C-4. This finds support in the greater ease of rearrangement of *(48)* to *(49)* compared to that of *(46)* to *(47)*.

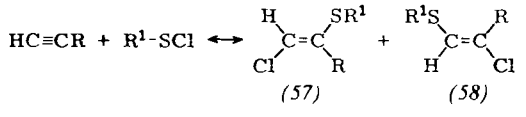
4. Unsaturated Thiiranium Ions

This section will deal with thiiranium ions containing endo- or exocyclic double bonds. The involvement of such species, whose existence is not well-established, may be postulated for sulfenyl chloride additions to acetylenes, allenes, and ketenes.



(53) *(54)* *(55)* *(56)*

The possibility of forming intermediates such as *(53)* has to be considered in a discussion of sulfenyl chloride additions to acetylenes. From terminal acetylenes and either arene-[46–48] or alkanesulfenyl chlorides[16,43,49,50], adducts of predominantly anti-Markovnikov orientation *(57)* have been reported.



(57) *(58)*

In solvents such as chlorinated hydrocarbons or ethyl acetate both alkyl- and aryl-substituted acetylenes afford mostly products of structure *(57)*. However, in acetic acid the reaction of phenylacetylene with either 2,4-dinitrobenzenesulfenyl chloride[51] or methanesulfenyl chloride[50] produced predominantly the opposite adduct orientation *(58)*. A similar dependence of the adduct orientation on solvent has also been observed in a study with *para*-nitrobenzenesulfenyl chloride and phenylacetylene[52a]. *trans*-Configuration of these adducts has been established in only a few cases[53]. NMR spectral evidence supports a *trans*-structure *(57)* in the case of the major *O,O*-dimethoxyphosphorylsulfenyl chloride-propyne adduct[43], and for both positional isomers obtained from 2,4-dinitrobenzenesulfenyl chloride and 1-phenylpropyne[54]. As an added complication one has to deal with the possible *trans-cis* isomerization of such adducts[49].

The addition of 2,4-dinitrobenzenesulfenyl chloride to either phenylacetylene or 3-hexyne follows second order kinetics, as in its addition to olefins[51]. The formally equivalent reactions, however, appear to differ in details. In contrast to the addition of *para*-substituted benzenesulfenyl chlorides to olefins[15], which follows the Hammett relationship when Brown σ^- values are used, no definite trend was observed with either aryl-[52b] or alkyl-substituted acetylenes[55]. The rate constants increase, however, by an order of magnitude from *para*-nitro to *para*-methoxy substituents, which is consistent with some positive charge being developed on sulfur. The rate of addition of *para*-toluenesulfenyl chloride to *para*-substituted diphenylacetylenes correlates well with Brown σ^+ values (Figure 2) at fairly high negative values of ρ[52b]. This suggests an intermediate in which there is development of an electron deficient carbon *alpha* to the *para*-substituted phenyl ring. It is also in accord with the nucleophilic role of acetylenes as reflected by the ~10 times faster addition of methanesulfenyl chloride to 2-butyne relative to propyne[17].

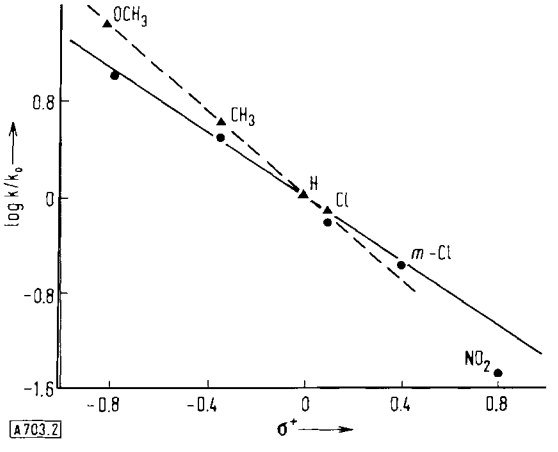


Fig. 2. Hammett relationship for the addition of *p*-toluenesulfonyl chloride to *p*-substituted diphenylacetylenes; in ethyl acetate at 25 °C (▲); $\rho = -1.8$; in chloroform (●), $\rho = -1.3$ [52b].

While the anti-Markovnikov adduct orientation, as in *(57)*, could be attributed to an intermediate such as *(53)* with the positive charge mainly on sulfur, some of the kinetic data suggest the intervention of vinylic carbonium ions *(54)* or at least a strong development of charge on the vinylic carbon in the case of bridged species.

[46] *A. Dondoni, G. Modena,* and *G. Scorrano,* Boll. sci. Fac. Chim. ind. Bologna *22,* 26 (1964).

[47] *L. I. Zacharkin,* Izvest. Akad. Nauk. SSSR, Otdel. chim. Nauk *1959,* 437.

[48] *W. E. Truce, H. E. Hill,* and *M. M. Boudakian,* J. Amer. chem. Soc. *78,* 2760 (1956).

[49] *W. H. Mueller* and *P. E. Butler,* J. org. Chemistry *33,* 1533 (1968).

[50] *V. Calò, G. Modena,* and *G. Scorrano,* Chim. e Ind. (Milano) *49,* 776 (1967).

[51] *N. Kharasch* and *C. N. Yinnaios,* J. org. Chemistry *29,* 1190 (1964).

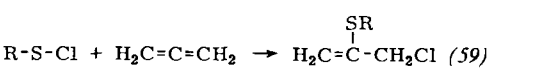
[52] a) *V. Calò, G. Modena,* and *G. Scorrano,* Tetrahedron Letters *1965,* 4399; b) *L. Di Nunno, G. Melloni, G. Modena,* and *G. Scorrano,* Tetrahedron Letters, *1965,* 4405.

[53] *L. Benati, M. Tiecco,* and *A. Tundo,* Boll. sci. Fac. Chim. ind. Bologna *21,* 177 (1963); *F. Montanari, ibid. 16,* 31 (1958); *L. Maioli, G. Modena,* and *F. Taddei, ibid. 18,* 58 (1960); *W. E. Truce* and *M. M. Boudakian,* J. Amer. chem. Soc. *78,* 2748 (1956).

[54] *G. H. Schmid* and *M. Heinola,* J. Amer. chem. Soc. *90,* 3466 (1968).

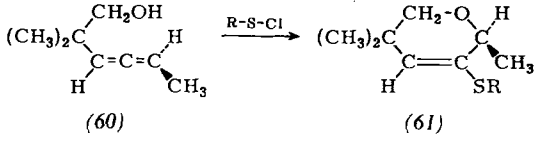
[55] *A. Dondoni, G. Modena,* and *G. Scorrano,* Ric. Sci., Parte II, Sez. A *34,* 665 (1964).

Structure *(59)* has been assigned to the initial adducts obtained from sulfenyl chlorides and allenes[49,56].



The existence of substantial coupling of the allylic and vinylic protons with the phosphorus nucleus supplied unambiguous NMR evidence for structure *(59)* when R is $(CH_3O)_2P(O)$[57].

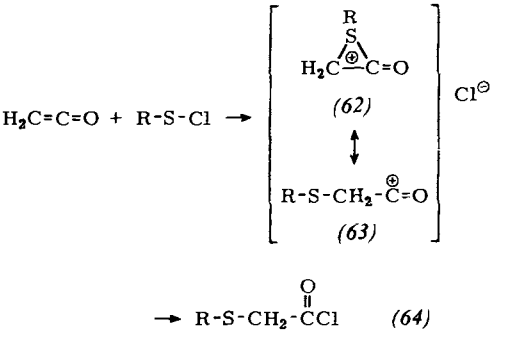
Products of structure *(59)* would be expected from ring opening of a bridged intermediate *(55)* at the terminal sp^3 carbon or from an allylic carbonium ion *(56)*. Addition of 2,4-dinitrobenzenesulfenyl chloride to the optically active allene *(60)* afforded the optically active product *(61)*[58]. This is strong support for a



(60) *(61)*

bridged ion intermediate such as *(55)*. However, the possibility of an allylic ion *(56)* cannot be rigorously ruled out since the optical purity of neither starting material *(60)* nor product *(61)* is known.

Sulfenyl chloride additions to ketene may also involve an thiiranium ion intermediate *(62)* having an sp^2 hybridized ring carbon[59,60].

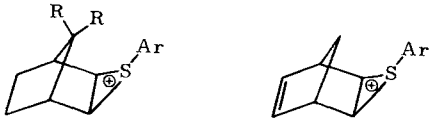


The formation of the acid chloride *(64)* is consistent with contributions by structures *(62)* and *(63)* to the intermediate but does not allow an assessment of their relative importance. Ring opening of the thiiranium ion *(62)* would be expected to take place preferentially at the carbonyl carbon, in analogy with nucleophilic displacement reactions on chloroacetyl chloride. The products *(64)* are most likely those of kinetic control since chloromethyl thioacetate does not isomerize to methylthioacetyl chloride[61].

5. Thiiranium Ions Fused on to Bicyclic Systems

The contribution of sulfur bridging in reaction intermediates derived from the addition of sulfenyl chlorides or sulfur dichloride to either unsaturated cyclic compounds or systems leading to cyclic products comprises a subject of recent interest. Frequently the stringent geometric requirements in these systems accommodate only a distorted thiiranium ion with unsymmetrical carbon-sulfur bonds in the ring. These cases may closely resemble a carbonium ion.

The addition of benzene- or substituted benzenesulfenyl chlorides to norbornene[57,62,63], 7,7-dimethylnorbornene[28], and norbornadiene[62] involves the *exo*-thiiranium ions *(65a)*, *(65b)*, and *(66)*, respectively. Ring opening by the chloride ion subsequently

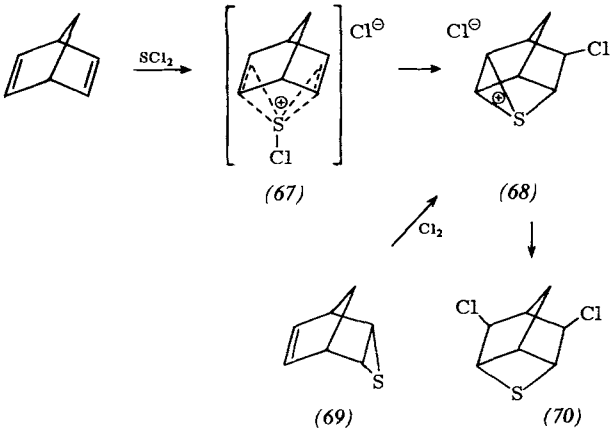


(65a), R = H
(65b), R = CH_3

(66)

takes place by attack from the *endo*-side. The formation of a thiiranium ion on the *exo*-side is particularly remarkable in the case of the reaction of 7,7-dimethylnorbornene *(65)*, R = CH_3, with the relatively bulky benzenesulfenyl chloride.

Sulfur dichloride, however, approaches norbornadiene from the *endo*-side to give product *(70)*[64], which is also obtained from chlorinolysis of the thiirane *(69)*[65]. A transition state such as *(67)* leading to the intermediate *(68)* would most readily explain the observed *endo*-attack. Similar transition states may be invoked to explain the preponderant transannular addition of sulfur dichloride to both 1,4-cyclohexadiene[66] and 1,5-cyclooctadiene[66–68]. Structures such as



(67) *(68)* *(69)* *(70)*

[56] *T. L. Jacobs* and *R. N. Johnson*, J. Amer. chem. Soc. *82*, 6397 (1960).

[57] *P. E. Butler, W. H. Mueller*, and *J. J. R. Reed*, Environ. Sci. Technol. *1*, 315 (1967).

[58] *T. J. Jacobs, R. Macomber*, and *D. Zunker*, J. Amer. chem. Soc. *89*, 7001 (1967).

[59] *H. Böhme, H. Bezzenberger*, and *H. D. Stachel*, Liebigs Ann. Chem. *602*, 1 (1957).

[60] *F. Šorm, J. Smrt*, and *J. Beránek*, Collect. czechoslov. chem. Commun. *20*, 721 (1955); Chem. Abstr. *49*, 15773d (1955); Chem. Listy *49*, 573 (1956); Chem. Abstr. *50*, 2429h (1956).

[61] *W. H. Mueller*, unpublished results.

[62] *S. J. Cristol, R. P. Arganbright, G. D. Brindell*, and *R. M. Heitz*, J. Amer. chem. Soc. *79*, 6035 (1957).

[63] *H. Kwart* and *R. K. Miller*, J. Amer. chem. Soc. *78*, 5658 (1956).

[64] *F. Lautenschlaeger*, J. org. Chemistry *31*, 1679 (1966).

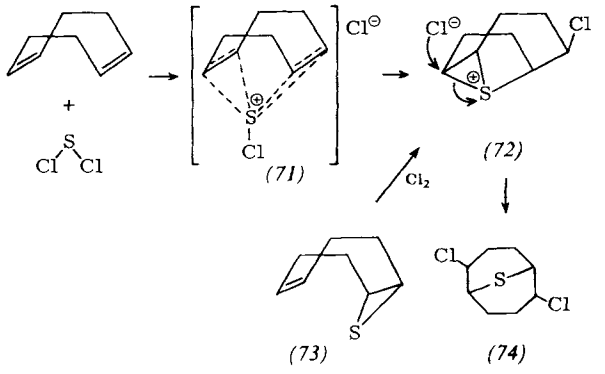
[65] *F. Lautenschlaeger*: Novel Bicyclic Sulfides. Paper read to the Princeton University Conference on the Chemistry of Sulfides, on June 29, 1966.

[66] *E. J. Corey* and *E. Block*, J. org. Chemistry *31*, 1663 (1966).

[67] *E. D. Weil, K. J. Smith*, and *R. J. Gruber*, J. org. Chemistry *31*, 1669 (1967).

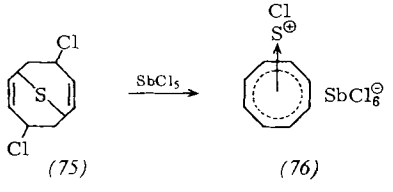
[68] *F. Lautenschlaeger*, Canad. J. Chem. *44*, 2813 (1966).

(71), reminiscent of transition metal π-complexes, may be envisioned for the reaction of sulfur dichloride with the tub-shaped 1,5-cyclooctadiene. Ring opening of the thiiranium ion *(72)*, which is also obtained from chlorinolysis of the thiirane *(73)*[69], produces 4,8-dichloro-1,5-epithiocyclooctane *(74)*.



(71) *(72)* *(73)* *(74)*

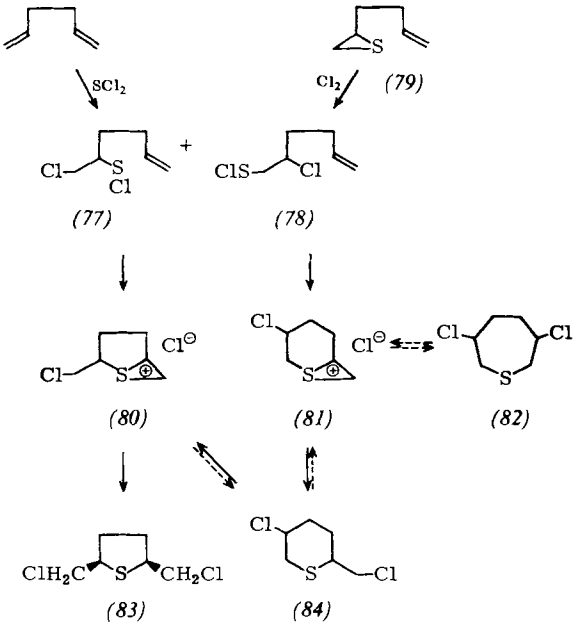
Product *(75)*, which was obtained from sulfur dichloride and cyclooctatetraene[70], forms an unstable coordination complex with antimony pentachloride in benzene[65]. Its NMR spectrum in nitromethane shows only a singlet which is 1.7 ppm downfield from the olefinic protons of cyclooctatetraene. These NMR data are consistent with a planar ring structure *(76)* and lend strong support to the transition states discussed above whose geometry allows simultaneous interaction of two double bonds with electrophilic sulfur.



(75) *(76)*

The reaction of sulfur dichloride with linear diolefins is an excellent route to cyclic sulfides[69]. The heterocycles formed appear to be, in most cases, the thermodynamically favored products. From the examples investigated thus far, it seems that formation of five-membered rings is strongly preferred. Unless additional steric or electronic factors are introduced, which make it necessary sometimes to consider open ions rather than thiiranium ion intermediates, the following order of preference for ring formation is observed: $5 > 6 \gg 7 > 8$-membered.

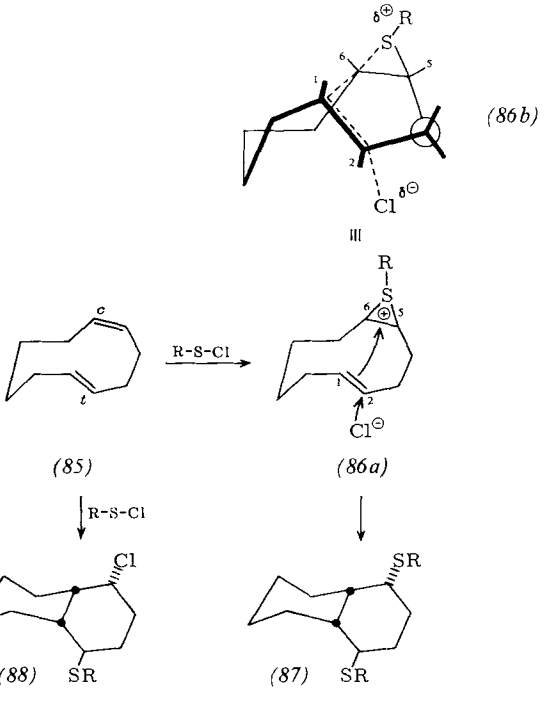
The thiiranium ions and possible equilibria in such systems are exemplified by the reaction of sulfur dichloride with 1,5-hexadiene or chlorinolysis of the thiirane *(79)*. Both reactions afford the tetrahydrothiophene derivative *(83)*. Based on the considerations discussed above (Section 3.3) one would expect initial formation of both intermediate products *(77)* and *(78)* from either reaction, with *(77)* being somewhat predominant in the product mixture[71]. Internal attack on the second double bond would then lead to the ions *(80)* and *(81)*.



(77) *(78)* *(79)* *(80)* *(81)* *(82)* *(83)* *(84)*

Ring opening of these thiiranium ions at the least hindered side by chloride affords products *(83)* and *(84)*, respectively. [The kinetically less favored ring opening on the more substituted carbon would produce either product *(84)* or *(82)*.] If one accepts the very likely formation of isomer *(78)* in the first step, then one also has to postulate the involvement of the thiiranium ion *(81)* and the transient formation of product *(84)* during cyclization. The isolation of *(83)* as the sole product, however, can be reconciled with post-isomerization of *(84)* through the thiiranium ion *(80)*. The fact that the chloromethyl substituents on *(83)* have a *cis* stereorelationship further supports thiiranium ion-product equilibria resulting in the thermodynamically most stable structure. It appears that a quasi-equatorial position of *cis*-2,5-substituents in this five-membered ring is thermodynamically preferred, as is the case with 1,3-substituted cyclohexanes[72].

Finally, a unique case of transannular carbon-carbon bond formation during methanesulfenyl chloride addition to *cis*,-



(86b) *(85)* *(86a)* *(88)* *(87)*

[69] *F. Lautenschlaeger*, Quart. Rep. Sulfur Chem. *2*, 285 (1967); J. org. Chemistry *33*, 2620 (1968).

[70] *F. Lautenschlaeger*, J. org. Chemistry *33*, 2627 (1968); *P. Y. Blanc*, *P. Diehl*, *H. Fritz*, and *P. Schläpfer*, Experientia *23*, 896 (1967).

[71] The addition of sulfur dichloride to propylene occurs with ~65% anti-Markovnikov orientation.

[72] *M. Mousseron* and *R. Granger*, Bull. Soc. chim. France *5*, 1618 (1938); *E. L. Eliel*: Stereochemistry of Carbon Compounds McGraw Hill, New York, N.Y., 1962.

trans-1,5-cyclodecadiene *(85)* has recently been reported[73]. The interaction of a double bond with a cationic center across the ring is well established in this and other ring systems[74]. A similar behavior with a thiiranium ion, however, is unprecedented and particularly surprising in the case of the strongly bridging methylthio group, since all evidence regarding such ions points toward little charge being developed on carbon (Section 3.1).

It is not known whether one or both of the stereoisomeric *cis*-decalins are formed. Compound *(88)* would arise from attack on the *trans* double bond of *(85)* which has been shown to be the preferred reaction site with addends not involving a carbonium ion intermediate. However, on the basis of the considerably faster rate of sulfenyl chloride addition to *cis*-butene compared to its *trans*-isomer[17] one would expect preferential attack at the *cis* double bond of *(85)* and subsequent formation of decalin *(87)*.

The possibility of initial 1,2-addition, as in the case of conjugated dienes, and transannular post-isomerization to *(87)* or *(88)* must also be considered. It is, therefore, tempting to suggest transition state *(86b)* which is strongly reminiscent of the intermediate *(52)* previously proposed for the rearrangement of the 1,2-adducts from methanesulfenyl chloride and conjugated dienes. Inspection of a model shows that C-1 and C-6 in *(86b)* can approach sufficiently closely for the lobe of the p orbital on C-1 to overlap with the electron deficient orbital on C-6.

Received: July 3, 1968 [A 703 IE]
German version: Angew. Chem. *81*, 475 (1969)

[73] *J. G. Traynham, G. R. Franzen, G. A. Knesel*, and *D. J. Northington, jr.*, J. org. Chemistry *32*, 3285 (1967).

[74] *A. C. Cope* and *P. E. Peterson*, J. Amer. chem. Soc. *81*, 1643 (1959); *R. M. Gipson, H. W. Guin, S. H. Simonsen, C. G. Skinner*, and *W. Shive*, J. Amer. chem. Soc. *88*, 5366 (1966); *I. Tabushi, K. Fjuita*, and *R. Oda*, Tetrahedron Letters, 3815 (1967); *R. K. Sharma, B. A. Shoulders*, and *P. D. Gardner*, Chem. and Ind., 2087 (1962).

Topochemical Investigations on Peptide Systems[**]

By **M. M. Shemyakin, Yu. A. Ovchinnikov, and V. T. Ivanov**[*]

The basic principles of the topochemical approach to the investigation of the structure-function relation in peptide systems are formulated. This approach makes use of the new possibility of transforming natural peptides, consisting in the modification of the molecule as a whole and utilization of the resultant analogs to elucidate the boundaries of the stereoelectronic complementarity of the biologically active peptide to the corresponding receptor. In particular, on the example of depsipeptide antibiotics and their topochemical analogs the fruitfulness of using such compounds as tools in elucidating the physicochemical basis of functioning of biological membranes is shown. The topochemical principle has also been applied in preparing specific competitive inhibitors of proteolytic enzymes, whose study may shed light on the nature of the forces binding the substrate to the contact site of the corresponding enzyme.

1. Introduction

The structure-function relation of biologically active compounds, one of the cardinal problems in modern chemistry and biology, owes its importance not only to the fact that knowledge of such a relation is essential for the rational search of compounds with valuable physiological properties, but in no less degree to the fact that it serves as guide into the innermost details of the mechanism of interaction between the biologically active substance and the corresponding receptor.

It is common knowledge that such an interaction requires not only steric correspondence between the molecules but also an appropriate electron density distribution, in the absence of which interaction, if it takes place at all, is reduced by several orders of magnitude. It stands to reason, therefore, that for the rational search for substances with similar, modified, or antagonistic biological effects, and also for the proper understanding of their mode of action, one must know the limits of such stereoelectronic complementarity requirements of the molecules participating in the given biochemical act.

In order to determine the complementarity boundaries it has been usual to modify stepwise the biologically active molecule and to see how the structural changes affect the biological activity. Such a largely empirical approach, probably the only possible one in the early stages of investigating this problem, has of course been ineffective. Only occasionally has it yielded tangible results and still more rarely has it lead to concepts of a predictive nature.

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[**] This paper is an enlarged version of the reports read to the 8th European Symposium on Peptide Chemistry (Nordwijk, Holland, 1966), to the 1st, 2nd European Meetings on Stereochemistry (Bürgenstock, Switzerland, 1966, 1967) and to the 1st All-Union Symposium on peptide chemistry (Riga, 1967).

Peptide systems have been no exception here, and "trial and error" methods are still widely prevalent. In biologically active peptides, chiefly hormones and antibiotics[1–3], one amino acid is replaced by another. While many hundreds of preparations have been synthesized during the last decade, most of them proved to be completely inactive. True, a few active preparations had been found (some of whose activity even exceeded that of the parent compound) and a certain number of them have found practical application; however such an approach could not be expected to give rise to rational methods, nor could it yield information elucidating the underlying principles of the action of biologically active compounds. At best only a few limited relationships could be established (see, *e.g.*[4]).

At first, our work on the structure-antimicrobial relation of enniatin antibiotics[5–7] also bore the same empirical character. From a critical survey of the results, however, we were able to recognize the outlines of the topochemical principles, which later proved to be generally applicable to a wide variety of peptide systems, both cyclic and linear.

2. Enniatin Antibiotics and Their Analogs

The investigations involved, first of all, the synthesis of linear and cyclic analogs of enniatin antibiotics, differing in the size of the chain or of the ring and in the nature and configuration of the amino and hydroxy acid constituents (see Table 1).

Table 1 [a]. Antimicrobial activity of the enniatins and some of their analogs [b].

No.	Compound	Minimal growth inhibiting concentration (μg/ml)				
		Staph. aureus	*Sarcina lutea*	*Bac. mycoides*	*Mycob. phlei*	*Cand. albicans*
(1)	(L-MeVal-D-HyIv)$_2$	>100	>100	>100	>100	>100
(2)	(L-MeIle-D-HyIv)$_3$ enniatin A	1.5	2.5	4.5	1.5–2.5	6.0
(3)	L-MeIle → L-MeVal	2.0	4.5	9.0	1.5–2.0	9.0
(4)	(D-MeIle-L-HyIv)$_3$ enantio-enniatin A	1.5	2.5	4.5	1.5–2.5	6.0
(5)	(D-MeVal-L-HyMev)$_3$ "false" enniatin A	75–100	37	75	37	>100
(6)	(L-MeVal-D-HyIv)$_3$ enniatin B	9.0	18	25–37	9–12	9–12
(7)	L-MeVal → L-MeLeu	9.0	12	25	9.0	18
(8)	L-MeVal → L-Val	25	37–50	50–75	25–37	75
(9)	D-HyIv → D-HyIc	>100	50–75	>100	>100	>100
(10)	L-MeVal → D-MeVal	>50	>50	>50	>50	>50
(11)	D-HyIv → L-HyIv	>50	>50	>50	>50	>50
(12)	(D-MeVal-L-HyIv)$_3$ enantio-enniatin B	9.0	18	25–37	9–12	9–12
(13)	(L-MeLeu-D-HyIv)$_3$ enniatin C	>50	>50	>50	>50	>50
(14)	(L-MeVal-D-HyIv)$_4$	3.0	4.5	>100	18–25	>100

[a] The standard symbols and abbreviations for amino acids are used in the Table; HyIv, HyMev and HyIc designate α-hydroxyisovaleric, α-hydroxy-β-methylvaleric and α-hydroxyisocaproic acid residues respectively. The arrows indicate substitution of one amino or hydroxy acid for another; thus compound *(7)* is an analog of enniatin B in which one *N*-methyl-L-valine residue has been replaced by an *N*-methyl-L-leucine residue.

[b] All the linear analogs of the compounds tabulated here are completely devoid of antimicrobial activity.

As can be seen from the table the antimicrobial activity of the cyclodepsipeptides is strongly dependent on the ring size. The highest activity and broadest spectra are displayed by the cyclohexadepsipeptides [naturally occurring antibiotics *(2)* and *(6)* and their analogs *(3)*, *(7)*, and *(8)*]; the cyclotetradepsipeptides *(1)* and the actadepsipeptides *(14)* exhibit the opposite behavior. Furthermore, it can be seen that the structure of the amino acid radicals of the antibiotic molecules can be modified considerably (albeit on a limited part of the chain) without marked loss of activity [compounds *(3)* and *(7)*]. On the other hand modification of the hydroxy acid residues [cf. *e.g.*, compound *(9)*] causes

[1] *J. Meienhofer*, Chimia (Zürich) *16*, 385 (1962).

[2] *H. C. Beyermann*, *A. van de Linde*, and *W. Maassen van den Brink*: Peptides. Proceedings of the Eighth European Peptide Symposium. North-Holland Publishing Company, Amsterdam 1967, p. 197ff.

[3] *E. Schröder* and *K. Lübke*: Peptides. Academic Press, New York 1965.

[4] *R. Walter*, *J. Rudinger*, and *I. S. Schwartz*, Amer. J. Med. *42*, 653 (1967).

[5] *M. M. Shemyakin*, *Yu. A. Ovchinnikov*, *A. A. Kiryushkin*, and *V. T. Ivanov*, Tetrahedron Letters *1962*, 301.

[6] *M. M. Shemyakin*, *Yu. A. Ovchinnikov*, *A. A. Kiryushkin*, and *V. T. Ivanov*, Tetrahedron Letters *1963*, 885.

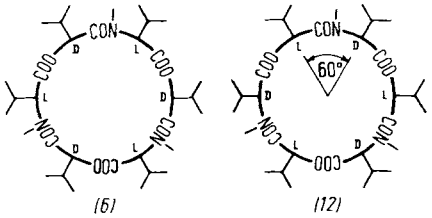
[7] *M. M. Shemyakin*, *Yu. A. Ovchinnikov*, *A. A. Kiryushkin*, and *V. T. Ivanov*, Izvest. Akad. Nauk SSSR, Ser. chim. *1965*, 1623.

sharp loss of activity. Finally, changes in the configuration of even one of the amino and hydroxy acid residues [compounds *(10)* and *(11)*] lead to complete loss of activity[8,9], Analogous relations were obtained with the cyclododecadepsipeptide valinomycin [10].

2.1. Topochemistry of the Enniatins

These results show the important role played by steric factors in the manifestation of biological activity by these compounds, and they lead to the conclusion that the mode of action of the enniatin and valinomycin antibiotics is connected with a biochemical process, which demands that the entire molecule as an integral whole must correspond to a certain site in the receptor. Further conclusions could not be drawn from the data at our disposal. In pursuit of further information we found that not only certain parts but the entire molecule could be so modified that the general features of the spatial structure, *i.e.* the topology of the new molecule would remain similar to that of the initial molecule; however, the electron density distribution among the individual functional centers would more or less differ. Such a topochemical approach to the structure-activity relation is applicable not only to depsipeptides but to peptides as well (see Sections 3 and 4).

One of the first substances to be synthesized by a topochemical approach was the enantiomer of enniatin B *(6)*, enantio-enniatin B *(12)*, in which all the amino and hydroxy acid residues are of opposite configuration to those in the natural antibiotic.



(6) *(12)*

Since enantio-enniatin B is the mirror image of the naturally occurring compound a stereoselective receptor would be expected to behave quite differently to the two stereochemically non-equivalent molecules.

Provided no fundamentally different mechanism for the biological action existed (cf. the L-isomer of the antibiotic cycloserine [11]) one would suppose enantio-enniatin B to be biologically inactive. The same holds for the antipodes of such naturally occurring peptides as bradykinin [12,13], angiotensin [14], oxytocin [15], actinomycin C_1 [16], *etc.*

Nevertheless, it appeared likely to us that enantio-enniatin B should display a biological activity equal or close to that of enniatin B. In fact, if one of the formulas *(6)* or *(12)* be turned by 60° in the plane of the drawing all the like chirality centers become superimposed; each ester group takes the place of an *N*-methylamide group and *vice versa*. Hence the antipodes differ with respect to the receptor not spatially, but only structurally. However, the ester group not only models the amide group quite well spatially, but also electronically [17,18]. Since both these topochemically similar antipodes display the same high complementarity to one and the same stereoselective receptor one would expect them to exhibit similar activities. This assumption is supported by the fact that in many naturally occurring peptides the amide group could can be substituted by the ester group and *vice versa* without essentially affecting their biological activity [19–23].

Enantio-enniatin B *(12)* was synthesized by the same method as was used for the synthesis of enniatin B *(6)* [6]. Compound *(12)* proved to be identical to the naturally occurring antibiotic in all physicochemical properties (excepting the rotatory dispersion curves, which, although of the same shape are of opposite sign). As expected, microbial tests showed that with all the microorganisms studied enantio-enniatin B displayed exactly the same activity, both qualitatively and quantitatively as enniatin B (see Table 1) [24].

This is the first proven example of a polyasymmetric naturally occurring compound and its antipode having equivalent activity along the entire microbial spectrum. The latter circumstance practically precludes any difference in the mode of action of the two compounds.

In the example of enniatin B and its antipode we have a special case since the molecules are very similar both

[8] *M. M. Shemyakin, Yu. A. Ovchinnikov, V. T. Ivanov, A. A. Kiryushkin, G. L. Zhdanov*, and *I. D. Ryabova*, Experientia *19*, 566 (1963).

[9] *I. I. Mikhaleva, I. D. Ryabova, T. A. Romanova, T. I. Tarasova, V. T. Ivanov, Yu. A. Ovchinnikov*, and *M. M. Shemyakin*, Ž. obšč. Chim. *38*, in press.

[10] *M. M. Shemyakin, E. I. Vinogradova, M. Yu. Feigina, N. A. Aldanova, N. F. Loginova, I. D. Ryabova*, and *I. A. Pavlenko*, Experientia *21*, 548 (1965).

[11] *J. Ciak* and *F. E. Hahn*, Antibiotics and Chemotherapy *9*, 47 (1959).

[12] *J. M. Stewart* and *D. W. Woolley*, Nature (London) *206*, 619 (1965).

[13] *K. Vogler, P. Lanz, W. Lergier*, and *W. Haefely*, Helv. chim. Acta *49*, 390 (1966).

[14] *K. Vogler* and *R. O. Studer*, Helv. chim. Acta *48*, 1407 (1965).

[15] *G. Flouret* and *V. du Vigneaud*, J. Amer. chem. Soc. *87*, 3775 (1965).

[16] *H. Brockman* and *W. Schramm*, Tetrahedron Letters *1966*, 2331.

[17] *R. Huisgen, H. Brade, H. Walz*, and *I. Glogger*, Chem. Ber. *90*, 1437 (1957).

[18] *R. Huisgen* and *H. Ott*, Tetrahedron *6*, 253 (1959).

[19] *L. A. Shchukina, G. A. Ravdel, M. P. Filatova*, and *A. L. Zhuze*, Acta chim. Acad. Sci. hung. *44*, 205 (1965).

[20] *L. A. Shchukina, G. A. Ravdel*, and *M. P. Filatova*, Chim. prirodynch Soedinenij *1966*, 265.

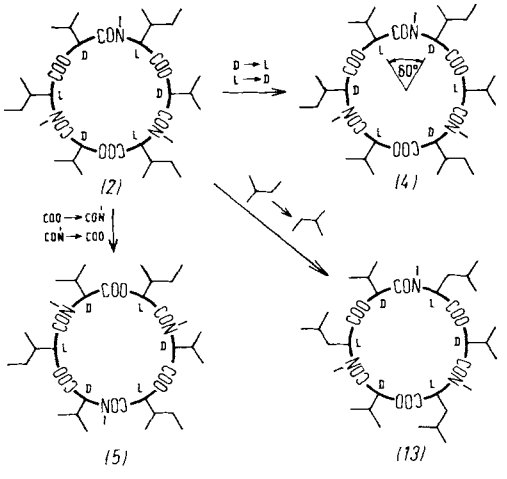
[21] *M. M. Shemyakin, L. A. Shchukina, G. A. Ravdel, E. I. Vinogradova*, and *Yu. A. Ovchinnikov*, Experientia *22*, 535 (1966).

[22] *G. A. Ravdel, M. P. Filatova, L. A. Shchukina, T. S. Pskhina, M. S. Surovikina, S. S. Trapesnikova*, and *T. P. Egorova*, J. med. Chem. *10*, 242 (1967).

[23] *L. A. Shchukina* and *A. L. Zhuze*, Ž. obšč. Chim. *37*, 1980 (1967).

[24] *M. M. Shemyakin, Yu. A. Ovchinnikov, V. T. Ivanov*, and *A. V. Evstratov*, Nature (London) *213*, 413 (1967).

topologically and with respect to the nature of their functional groups. Retaining the latter and changing only the effective size of the radicals in the depsipeptide molecule renders possible a study of the degree of topological correspondence between biologically active compound itself and the receptor. Thus, the antipode of enniatin A *(2)*, enantio-enniatin A *(4)* (Fig. 2), which we synthesized [25], was found to have the same antimicrobial activity as the parent compound (see Table 1). This is not surprising if one takes into account the topological similarity of the valine and isoleucine side chains in eniatins A and B (branching at the β-carbon atom in both compounds). In fact not



only the similarity but the constancy of the optical rotatory dispersion curves of enniatins A *(2)* and B *(6)* in various solvents bears evidence on the similarity of their preferred conformations in these solvents [26] (see Fig. 1).

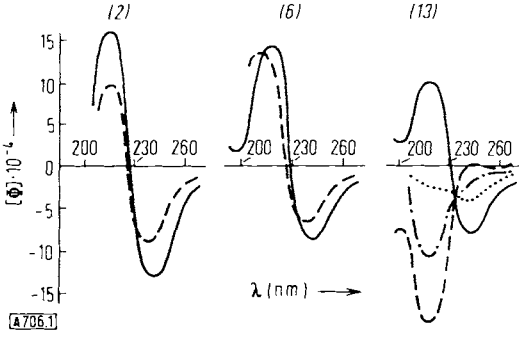


Fig. 1. Optical rotatory dispersion curves of enniatin A *(2)*, enniatin B *(6)*, and enniatin C *(13)*.
Solvent: ———— heptane; ····· heptane/ethanol (94:6); —·—·— heptane/ethanol (92:8); — — — heptane/ethanol (50:50).

However, if all the *N*-methylvaline residues in enniatin B are replaced by *N*-methylleucine residues, the resultant compound, known as enniatin C *(13)* [27], turns out to be practically inactive (see Table 1). The reason for this apparently lies in the stereochemical specificity of the valine and isoleucine residues, the β-branched chains of which, in contrast to the γ-branched chains of leucine, have a strong steric screening effect [28]. One could expect therefore that the side chains of enniatins A and B fix the relative orientation of the radicals and groups, giving rise to a sufficiently rigid conformation of the 18-membered ring, whereas enniatin C should have a more flexible structure and be more easily subjected to conformational changes. This was confirmed by optical rotatory dispersion studies of enniatins A, B, and C [26]. As is shown in Fig. 1 all three enniatins have similar conformations in a non-polar solvent (heptane). Solvents of higher polarity (heptane with increasing amounts of ethanol) have very little effect on the conformations of enniatins A and B, but considerably change the conformations of enniatin C. Apparently, under conditions obtaining in the biological medium enniatin C assumes a conformation not suitable for interaction with the receptor for enniatins A and B.

In this connection it should be emphasized that with the topochemical analogs of the naturally occurring peptides, obtained by modifying the entire molecule, one could expect the occurrence of biological activity only when the modification does not entrain changes in the biologically specific conformation of the peptide. Hence transformations of the molecule based only on formal structural principles may lead to abrupt change in or to disappearence of the biological activity, for even very small structural modification of the molecule can cause marked changes in its conformation.

Another striking illustration of this behavior, besides the case of enniatin C, is afforded by cyclohexadepsipeptide *(5)* [25]. This depsipeptide can be regarded as an analog of enniatin A in which all the ester groups are replaced by *N*-methylamide groups and *vice versa*.

Formally, almost all requirements of topochemical correspondence appear to be fulfilled, but the minute structural differences between compound *(5)* on the one hand and enantio-enniatin A *(4)* or enantio-enniatin B *(12)* on the other proved sufficient to impart considerably differing conformations to the compounds (as evidenced in the optical rotatory dispersion curves, Fig. 2). As a consequence the compounds differ greatly in antimicrobial properties;

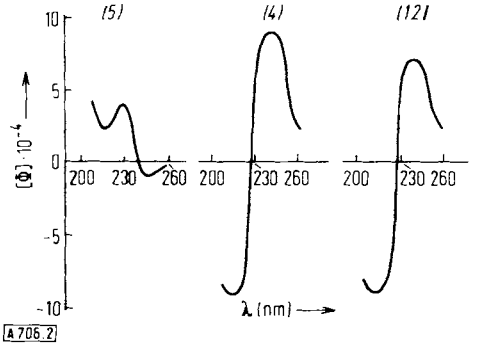


Fig. 2. Optical rotatory dispersion curves of "false" enniatin A *(5)*, enantio-enniatin A *(4)*, and enantio-enniatin B *(12)*.
Solvent: heptane/ethanol (50:50).

[25] *Yu. A. Ovchinnikov, V. T. Ivanov, A. V. Evstratov, I. I. Mikhaleva, L. V. Sumskaya*, and *E. E. Meshcheryakova*, unpublished.

[26] *M. M. Shemyakin, Yu. A. Ovchinnikov, V. T. Ivanov, V. K. Antonov, A. M. Shkrob, I. I. Mikhaleva, A. V. Evstratov*, and *G. G. Malenkov*, Biochem. biophysic. Res. Commun. *29*, 779 (1967).

[27] *Pl. A. Plattner* and *U. Nager*, Helv. chim. Acta *31*, 2203 (1948).

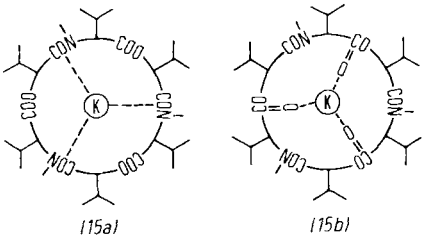
[28] *E. R. Blout, C. de Loze, S. M. Bloom*, and *C. D. Fasman*, J. Amer. chem. Soc. *82*, 3787 (1960).

compound *(15)*, in contrast to enniatins A and B and their enantiomers, displays low activity against all microorganisms studied (see Table 1) – a fact that led to its being named "false" enniatin A.

2.2. Mode of Action of Enniatins

Besides the above described studies on enniatin antibiotics the topochemical principles were also useful in the study of the problem of the mode of action of these and other depsipeptide antibiotics. According to *Pressman* depsipeptide antibiotics are capable of selectively inducing the active transport of some monovalent ions in mitochondria[29,30]. Further joint study of this phenomenon by *Pressman* and us on a number of valinomycin and enniatin analogs synthesized in our laboratory led to the conclusion that there is a definite parallelism between the antimicrobial activity of the depsipeptides and their ability to induce active cation transport – a parallelism that is not only of a qualitative nature (active transport of K^+, but not Na^+), but, to a certain degree, also of a quantitative nature.

These results suggested that the antibiotic activity of the depsipeptides is connected with their interaction with the receptors (lipoproteids) of the biological membranes controlling the active cation transport[8,10,31]. Another inference that could be drawn was that the depsipeptide antibiotics influence the ion transport not only by stereospecific interaction with the receptor in the membrane, but also by interaction with the corresponding cation. Cyclodepsipeptides appear to form complexes with monovalent metal ions such that the ion is included in the internal sphere of the cyclic molecule by means of ion-dipole interaction with the amide and/or ester groups, reproduced schematically in formulas *(15a)* and *(15b)*.



(15a) *(15b)*

This we were able to demonstrate experimentally[26] (cf.[32,33]), showing not only the fact of complex formation in solution and the participation of ester groupings in the complex (Fig. 5)[*], but also that there is a correspondence between the ability of enniatin cyclodepsipeptides to form complexes, their conformational states in solutions, and their antibiotic activity. The complexes were either isolated in the crystalline state or their formation in solution was established by electroconductivity and ORD measurements.

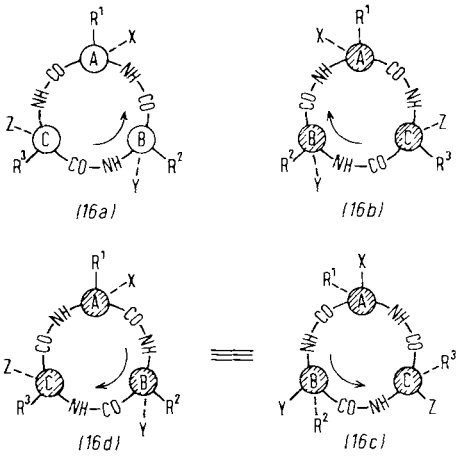
Whereas enniatins A and B, and their enantiomers, all belong to a single topochemical group and readily form complexes with potassium ions, the cyclohexapeptide *(5)* was found in general to be incapable of forming complexes with alkali metal ions. This is in accord with the results of the optical rotatory dispersion measurements on these compounds (cf. Figs. 1 and 2), and also with their biological properties.

The results served as a starting point in the investigation of the mechanism of membrane functioning. One of the first results of these studies was discovery of the fact that complexation of the enniatins and valinomycin with cations occurs only in a lipophilic medium[26], *i.e.* takes place on the membrane after the binding of the depsipeptide molecule to the latter.

3. Topochemical Investigations on Other Peptides

The topochemical approach to the structure-function relations may be useful not only with such highly symmetric systems as the anniatin antibiotics, but in principle can be applied to cyclopeptides regardless of their symmetry. This is clearly illustrated in the transformations of the hypothetical cyclopeptide *(16a)*.

For the sake of simplicity a tripeptide is depicted in the figure, but conclusions hold for any ring size and for any set of configurations of the amino acid residues.



(16a) *(16b)* *(16d)* *(16c)*

Compound *(16b)* is the antipode of this cyclopeptide and compound *(16c)* [which is identical with *(16d)*] is the retro-form of *(16b)* with reversed direction of acylation (cyclodiastereomer according to *Prelog's* nomenclature[34,35]). It can easily be seen that the cyclopeptides *(16a)* and *(16d)* are very similar topologically, differing only by reversed arrangement of the atoms in the amide groups (CO–NH and NH–CO); in other words they are topochemical analogs. The

[29] *C. Moore* and *B. C. Pressman*, Biochem. biophysic. Res. Commun. *15*, 562 (1964).

[30] *B. C. Pressman*, Proc. nat. Acad. Sci. USA *53*, 1076 (1965).

[31] *B. C. Pressman*, private communication.

[32] *P. Mueller* and *D. O. Rudin*, Biochem. biophysic. Res. Commun. *26*, 398 (1967).

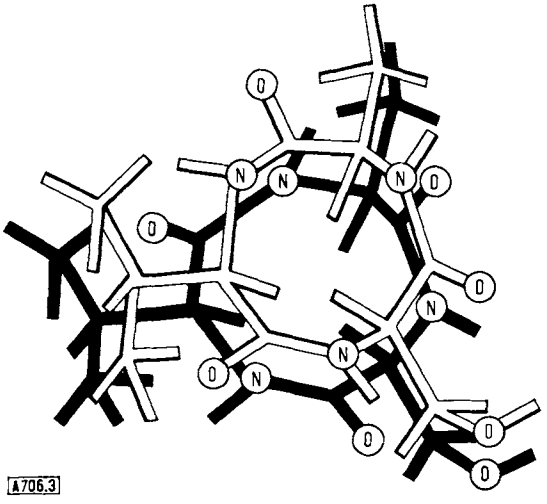
[33] *H. K. Wipf, L. A. Pioda, Z. Stefanac*, and *W. Simon*, Helv. chim. Acta *51*, 377 (1968).

[*] This shows why the biological properties of the enniatins and valinomycin are so strongly dependent upon the nature of the hydroxy residues, but not on the nature of the amino acid residues.

[34] *V. Prelog* and *H. Gerlach*, Helv. chim. Acta *47*, 2288 (1964).

[35] *H. Gerlach, J. A. Owtschinnikov*, and *V. Prelog*, Helv. chim. Acta *47*, 2294 (1964).

similarities and differences between cyclopeptide *(16a)* and its retro-enantiomer *(16d)* come particularly to the fore in Fig. 3, which depicts the latter compound

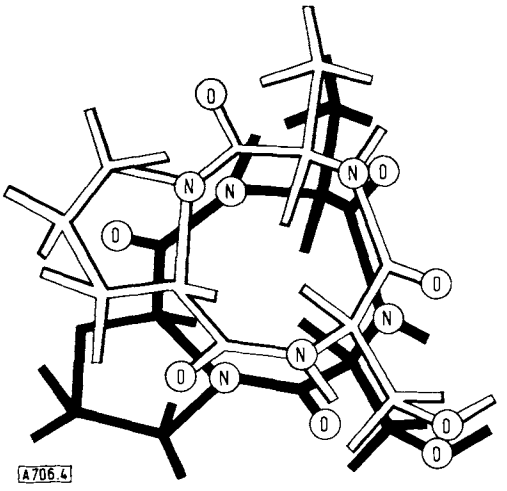


A706.3

Fig. 3. Structural and spatial relationships between a cyclopeptide and its retro-enantiomer.

as the "shadow", or replica, as it were, of the former, thus showing why it can play the role of a "double" in biological processes and may often possess closely similar biological properties to the parent compound. The highly biologically active Gly^5, Gly^{10}-gramicidin S *(17)* [37, 38] and its retro-enantio analog *(18)* (Fig. 8) furnished further proof of the validity of this assumption [36].

Gly^5, Gly^{10}-gramicidin S was chosen instead of the naturally occurring gramicidin S since it does not contain the proline residues of the latter, that would introduce extra complications in the topochemical



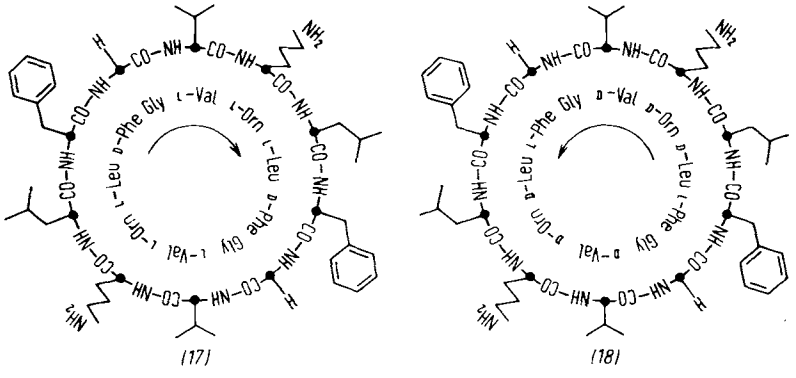
A706.4

Fig. 4. Topological difference between a proline-containing cyclopeptide and its retro-enantiomer.

Retro-enantio-Gly^5,Gly^{10}-gramicidin S *(18)* was synthesized by stepwise construction of the peptide chain, beginning with the C-terminus, and using the doubling reaction to cyclize the linear penta peptide. As predicted, the resultant compound displayed high antimicrobial activity, comparable with the activity of gramicidin S.

4. Topochemical Investigations on Linear Peptides

Of particular interest would be extension of the principles discussed here to linear peptides since this could open up new possibilities in the studies of many important peptide bioregulators. For the topochemical transformation principles to be effective in the case of



(17) *(18)*

transformations. Indeed, with the proline residues the retro-enantio isomer would differ much more greatly in the topochemical sense from the initial compound, because, as can be seen in the example of the proline-containing cyclotripeptide (Fig. 4), the proline rings would not coincide on superimposing the two molecules.

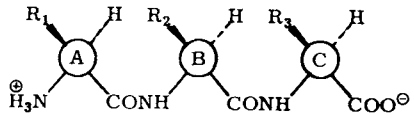
linear peptides certain prerequisites must be fulfilled. For instance the principles cannot be applied to peptides with free carboxyl and amino end groups. While considerable topological conformity is retained on the antiparallel superposition of the hypothetical linear peptide *(19)* and its retro-enantiomer *(20)*, these two, contrary to the internally compensated cyclopeptides (Fig. 6), still differ by the reversed position of the charged end groups.

Naturally such difference in the compounds of type *(19)* and *(20)* should cause them to behave differently from the receptor and it would be difficult to expect the retro-enantiomer *(20)* to display the biological activity

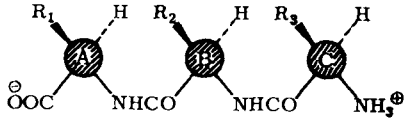
[36] *M. M. Shemyakin, Yu. A. Ovchinnikov, V. T. Ivanov,* and *I. D. Ryabova,* Experientia *23,* 326 (1967).

[37] *H. Aoyagi, T. Kato, M. Ohno, M. Kondo,* and *N. Izumiya,* J. Amer. chem. Soc. *86,* 5700 (1964).

[38] *H. Aoyagi, T. Kato, M. Ohno, M. Kondo, M. Waki, S. Makisumi,* and *N. Izumiya,* Bull. chem. Soc. Japan *38,* 2139 (1965).



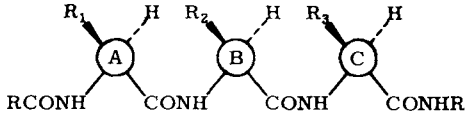
(19)



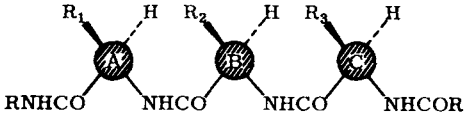
(20)

of the linear peptide *(19)*. Herein probably lies the reason for the inability of *Vogler et al.*[13] and *Stewart*[39] to detect any essential biological activity in the retro-enantio-bradykinin they have synthesized (cf. also[40]).

We believe that such difficulties could often be overcome by appropriately blocking the end groups. With suitable choice of the blocking groups the conditions could be created for establishing the same topochemical correspondence as in the case of cyclopeptides. In the case of the substituted amides of acyl peptides the topochemical analogs *(21)* and *(22)* differ only by reversal of the amide groups, including the end groups.



(21)



(22)

Thus one can also put the search for analogs of biologically active linear peptides, in particular of some peptide hormones and antibiotics (for instance α-melanophoro-stimulating hormone, gastrin and its highly active C-terminal fragments, and gramicidin A) on a rational footing. Since the retro-enantiomers of such peptides are built up of only D-amino acid residues they should be resistant towards the inactivation by the proteolytic enzymes in the organism and consequently should have a more durable biological action.

With respect to linear peptides we considered it of particular interest to apply the topochemical concept in making specific analogs of substrates and inhibitors of proteolytic enzymes, which could yield additional valuable information on the nature of the enzyme-substrate interaction.

If the protected dipeptide *(23)* serves as a specific substrate, its topochemical analog *(24)*, which is practically its equal with respect to the hydrophobic and functional periphery, will differ from it only in the reversed disposition of the atoms in the amide groupings (see Table 2). Therefore, such an analog [*(24)*]

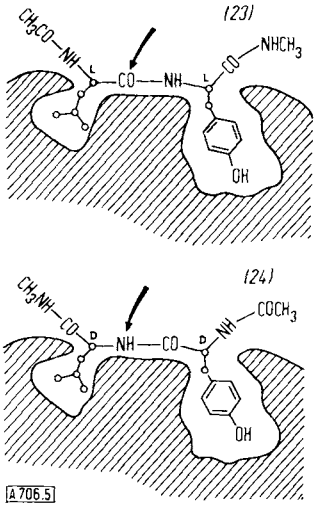


Fig. 5. Schematic representation of a specific substrate of a proteolytic enzyme — protected peptide *(23)* — and its retro-enantiomer *(24)*, both complementarily bound to the binding site of the enzyme.

should in all probability bind with the same efficacy to the same contact site of the enzyme as compound *(23)* (see Fig. 5); such an assumption is supported by the numerous data that show that the major role in the binding process belongs to hydrophobic interactions. But this retro-enantio isomer *(24)*, built up of D-amino acid residues should not be subject to enzymatic hydrolysis, owing to the high configurational specificity of this reaction (cf. however[41]). Hence such a compound should prove to be an effective competitive inhibitor. Kinetically its behavior would be manifested in its inhibiting constant K_I being close in value to the Michaelis constant for the corresponding substrate, *i.e.* $K_I \simeq K_M$.

With this in mind we synthesized a number of C- and N-terminus protected leucine and tyrosine containing dipeptides [compounds *(23)* to *(29)* in Table 2] and carried out a kinetic study of their interaction with pepsin[42] and chymotrypsin[43]. The results, treated according to the Lineweaver-Burk method, are presented in Table 2.

As predicted, the dipeptide *(24)* which is the retro-enantiomer of the substrate *(23)* proved to be an effective inhibitor of pepsin with an inhibiting constant very close to that of the Michaelis constant of the substrate. A similar behavior is displayed by the pairs of related dipeptides *(25)* and *(26)*, and *(27)* and *(28)* which are in retro-enantio relations to each other and possess practically identical K_I values. These results assume a particular significance in the light of the be-

[39] *J. M. Stewart, D. W. Wolley, E. Erdös, N. Back,* and *F. Sicuteri*: Hypotensive Peptides. Springer-Verlag, New York 1966, p. 23.

[40] *D. Chung* and *C. H. Li*, Biochim. biophysic. Acta *135*, 570 (1967).

[41] *G. E. Hein* and *C. Niemann*, J. Amer. chem. Soc. *84*, 4487 (1960).

[42] *V. I. Tsetlin, E. N. Shepel, V. T. Ivanov,* and *Yu. A. Ovchinnikov*, unpublished.

[43] *E. M. Bogomolnaya, N. F. Kazanskaya, I. V. Beresin, V. I. Tsetlin, E. N. Shepel, V. T. Ivanov,* and *Yu. A. Ovchinnikov*, unpublished.

Table 2. Kinetic constants of peptide-enzyme interaction.

No.	Peptide	Pepsin (K_M or K_I, mole/l)	Chymotrypsin (K_I, mole/l)
(23)	Ac-Leu-Tyr-$NHCH_3$ LL	$K_M = 2.7 \times 10^{-3}$	1.9×10^{-2}
(24)	Ac-Tyr-Leu-$NHCH_3$ DD	K_I [a] $= 5.8 \times 10^{-3}$	1.6×10^{-2}
(25)	Ac-Leu-Tyr-$NHCH_3$ LD	K_I [b] $= 1.2 \times 10^{-2}$	—
(26)	Ac-Tyr-Leu-$NHCH_3$ LD	K_I [b] $= 1.3 \times 10^{-2}$	4.3×10^{-2}
(27)	Ac-Leu-Tyr-$NHCH_3$ DL	K_I [b] $= 1.5 \times 10^{-2}$	—
(28)	Ac-Tyr-Leu-$NHCH_3$ DL	K_I [b] $= 1.8 \times 10^{-2}$	—
(29)	Ac-Leu-Tyr-$NHCH_3$ DD	K_I [b] $= 7.5 \times 10^{-3}$	$\sim 10^{-1}$

[a] Competitive inhibition. [b] Mixed inhibition.

havior of all the dipeptides *(25)–(29)* which are not topochemical analogs of *(23)*. Their interaction with pepsin cannot be described by equations for competitive inhibition. These peptides exhibit "mixed" inhibition with noncompetitive inhibition strongly predominating ($\alpha = 1.8$–3.2).

Even more definite results were obtained in studies of the interaction of protected dipeptides *(23)*, *(24)*, *(26)*, and *(27)* with chymotrypsin. The process studied was the inhibition by these dipeptides of chymotrypsin-catalyzed hydrolysis of *p*-nitrophenyl pivalate. In this case the inhibition constants of the dipeptides could be compared without determination of the Michaelis constant which gives only an approximated picture of the binding of the substrate to the enzyme. As is shown in Table 2, the K_I values for the retro-enantiomers *(23)* and *(24)* coincide within the limits of experimental error. The dipeptide *(26)* binds with chymotrypsin less efficiently, and compound *(29)*, which is an antipode of the dipeptide *(23)*, and is usually *a priori* regarded as an inhibitor, showed no inhibiting effect under the experimental conditions.

Received: July 8, 1968 [A 706 IE]
German version: Angew. Chem. *81*, 523 (1969)

Hydration Structure and Intermolecular Interaction in Polyelectrolytes

By G. Zundel[*]

In hydration, the intermolecular interaction is of decisive importance, since the ions modify the properties of the hydration water molecules, and the water molecules in turn have a strong influence on the interaction between the ions. These processes can be studied in detail with the aid of IR spectroscopy, which in addition provides a picture of the hydration structure. IR spectroscopy also shows that the excess protons are in energy bands and allows the detection of the proton dispersion forces acting between tunneling protons. The results of IR studies on polyelectrolytes contribute to our understanding of the many biological processes that depend on the behavior of ions.

1. Introduction

In biological events, intermolecular interaction is just as important as chemical bonding. This "intermolecular" interaction is due to weak bonds, *e.g.* hydrogen bonds, linking molecules or the functional groups of a macromolecule. It is important in particular to the hydration processes, and hence to all biological processes involving ions.

Methods of molecular physics that have little effect on the system are particularly suitable for the investigation of intermolecular interaction. Since IR quanta have relatively low energies, they cause no appreciable changes in the systems, and IR spectroscopy accordingly offers a promising method.

The intramolecular vibrations occur in the middle infrared region. The bands in this region provide information about the changes in the molecules due to the intermolecular interactions, since these interactions influence the potential wells in the molecules and so displace the IR bands. Moreover, the bands due to intermolecular vibrations can be observed in the far infrared. This could yield direct information about the intermolecular bonds, which are very important to our knowledge of the nature of the liquid state. Practically no such investigations in the far infrared have however been carried out as yet.

One difficulty that arises in the spectroscopic study of homogeneous liquid electrolyte solutions is that in addition to the water of hydration, such solutions usually also contain water that is influenced little or not at all by the ions, and the IR bands of this water mask the bands due to the water of hydration. IR spectroscopy is therefore best suited to the investigation of very concentrated solutions, and particularly to the study of polyelectrolytes.

The present article deals with investigations on organic ion exchangers (salts and acids derived from polystyrene). In these substances, the ions of the one kind are fixed to a polymeric network (fixed ions), while

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those of the other kind move more or less freely in this network. Ion exchangers of this type are simple model substances for systems of biopolymers.

A brief survey of the IR bands that provide information about the intermolecular interaction in these substances [*] will serve as a basis for later discussion. These are firstly the bands due to vibrations in the anions. Figure 1 shows the antisymmetric (1200 cm^{-1})

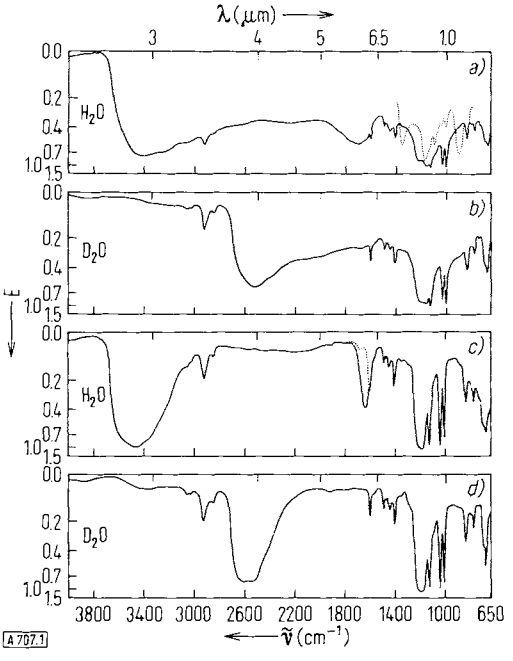


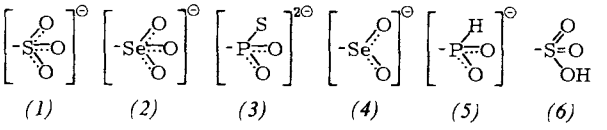
Fig. 1. IR spectra of a) polystyrenesulfonic acid hydrated with H_2O — — at 98% relative humidity [*], ... thoroughly dried membrane; b) polystyrenesulfonic acid hydrated with D_2O —— at atmospheric humidity over saturated $BaCl_2$ solution in D_2O; c) Na^+ salt of polystyrenesulfonic acid hydrated with H_2O —— at 98% relative humidity .... thoroughly dried membrane; d) Na^+ salt of polystyrenesulfonic acid hydrated with D_2O —— at atmospheric humidity over saturated $BaCl_2$ solution in D_2O. For positions of the bands due to vibrations of the anions and acid groups see Table 1. Stretching vibrations H_2O (3700—2800 cm^{-1}), D_2O (2750—2050 cm^{-1}), scissor vibrations H_2O (about 1640 cm^{-1}), D_2O (about 1206 cm^{-1}, masked in Fig. 1).

[*] The spectrum was recorded while the membrane was in equilibrium with water vapor.

and the symmetric (1040 cm^{-1}) SO stretching vibrations of the $-SO_3^-$ ions *(1)* in the sodium salt of polystyrenesulfonic acid, as well as the antisymmetric and the symmetric stretching vibrations of the S=O double bonds (1350 and 1172 cm^{-1}) and the stretching vibration of the SO single bond (907 cm^{-1}) of the $-SO_2OH$ group *(6)* in the undissociated polystyrenesulfonic acid. Secondly there are the bands due to the water of hydration (stretching vibrations and scissor vibration). Thirdly, interesting information can be derived from an absorption continuum in the case of the acids if they are dissociated. If the acids are not dissociated, but associated, this is shown by a pair of bands due to the OH or OD groups of the acid (see Fig. 5).

2. The Salts

The fixed ions *(1)–(5)* each contain either three or two substantially equivalent XO bonds (Fig. 2 together with Table 1). The mesomeric bond resonance



is therefore very extensive in the anions. The $-SO_3^-$ and $-SeO_3^-$ ions, so far as they are isolated from their surroundings, thus have a pyramidal structure, *i.e.* C_{3v} symmetry.

2.1. Cation-Anion Interaction [7]

The antisymmetric stretching vibration of a group having C_{3v} symmetry is degenerate, *i.e.* two vibrations have the same wave number [8]. However, in the spectra of thoroughly dried membranes of the salts of polystyrenesulfonic acid a doublet is found (Fig. 3) instead of the expected single band at 1200 cm^{-1} [*], showing that the degeneracy is removed. This splitting generally increases as the cation becomes smaller and as its valency increases, *i.e.* as the field of the cation at the anion increases. It is greater for the $-SO_3^-$ than for the $-SeO_3^-$ ion, and hence increases with increasing polarizability of the anion. The removal of the degeneracy is due to asymmetrical polarization of the anions by the cations, *i.e.* to a disturbance of the mesomeric bond resonance in the anions. It is therefore closely connected with the cation-anion ion-induced dipole interaction.

Other types of cation-anion interaction increase the splitting of the bands if they change the structure of the anion *e.g.* the covalent interaction. The splitting in the presence of transition element ions is thus much greater than one would expect from the cation field. This is illustrated by comparison of the Zn^{2+} ion with Mg^{2+} ion in Fig. 3a. Finally, the splitting with very small polyvalent cations is not so great as it should be on the basis of the cation field. This is due to the influence of the fields of the neighboring anions [1].

2.2. Location of the Cations with Respect to the Anions

The cation must be situated asymmetrically with respect to the O atoms of the $-SO_3^-$ ion, since only then can it disturb the C_{3v} symmetry. It can also be deduced

[*] For the preparation of the substances and methods of investigation, see [1–6].

[1] *G. Zundel*: Hydration and Intermolecular Interaction. Academic Press, New York 1969.

[2] *G. Zundel*, *H. Noller*, and *G.-M. Schwab*, Z. Naturforsch. *16b*, 716 (1961).

[3] *G. Zundel*, Z. Naturforsch. *23b*, 119 (1968).

[4] *G. Zundel*, Kunststoff-Rdsch. *15*, 166 (1968).

[5] *G. Zundel*, *A. Murr*, and *G.-M. Schwab*, Z. Naturforsch. *17a*, 1027 (1962).

[6] *G. Zundel*, Chemie-Ing.-Techn. *35*, 306 (1963).

[7] *G. Zundel* and *A. Murr*, Z. Naturforsch. *21a*, 1640 (1966).

[8] *K. Nakamoto*: Infrared Spectra of Inorganic and Coordination Compounds. Wiley, New York 1963, p. 87.

[*] A vibration of the benzene ring is superimposed at 1128 cm^{-1} [1].

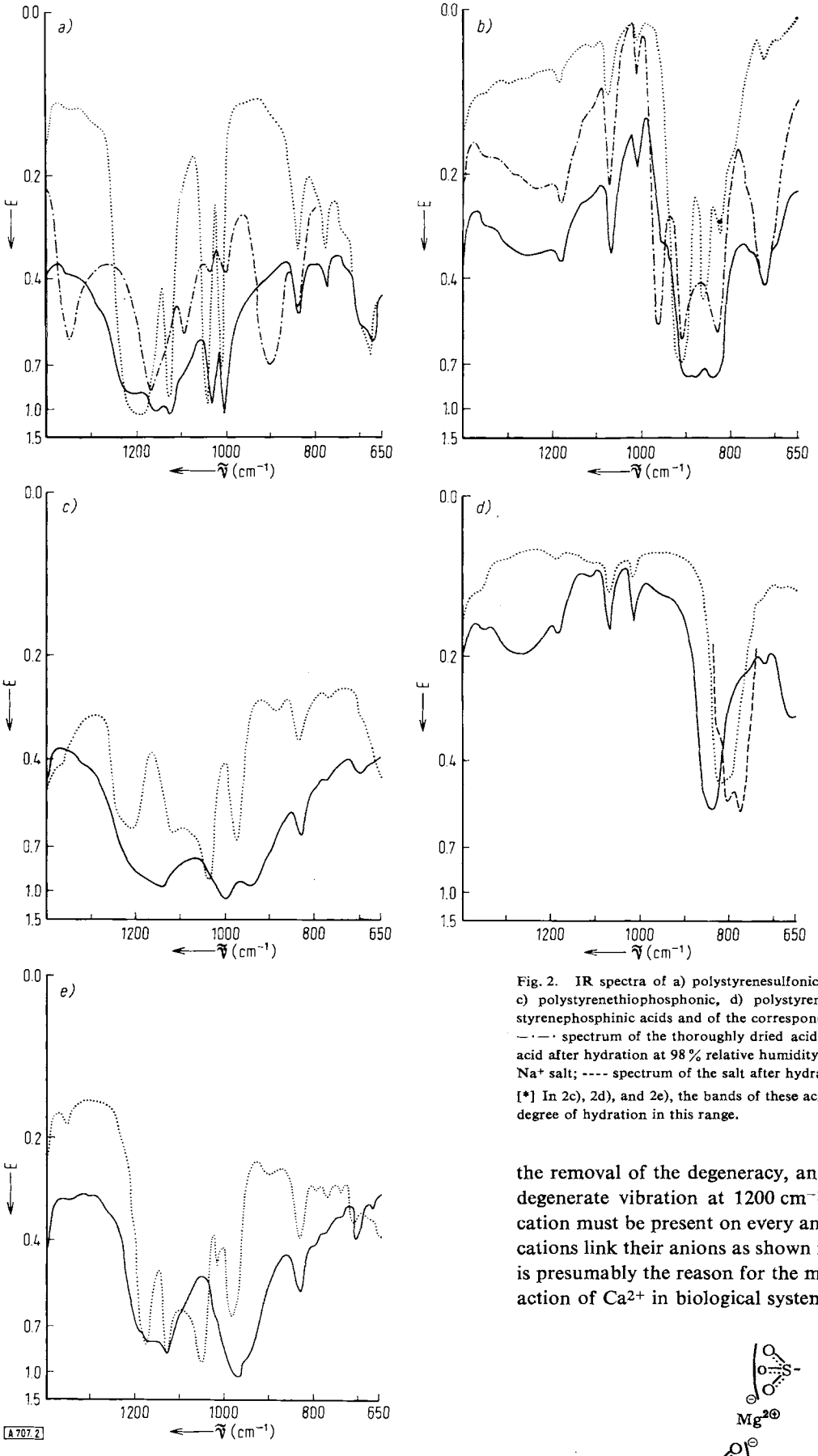
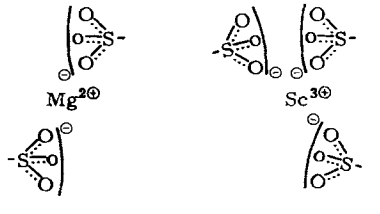


Fig. 2. IR spectra of a) polystyrenesulfonic, b) polystyreneselenonic, c) polystyrenethiophosphonic, d) polystyreneseleninic, and e) polystyrenephosphinic acids and of the corresponding Na^+ salts.
— · — · spectrum of the thoroughly dried acid [*]; —— spectrum of the acid after hydration at 98% relative humidity [*]; . . . . spectrum of the Na^+ salt; ---- spectrum of the salt after hydration with D_2O.
[*] In 2c), 2d), and 2e), the bands of these acids are independent of the degree of hydration in this range.

that the cation must be associated with a certain one of the three O atoms, in the direction of one of the SO bonds. One finds only the two bands that result from the removal of the degeneracy, and no band due to a degenerate vibration at 1200 cm^{-1}. It follows that a cation must be present on every anion. The polyvalent cations link their anions as shown in the formula. This is presumably the reason for the membrane-tightening action of Ca^{2+} in biological systems [9].



[9] *H. Schmidt* and *R. Staempfli*, Helv. physiol. pharmacol. Acta *15*, 200 (1957).

Table 1. Bands of the anions in polystyrene derivatives and assignment of the bands (st = stretching vibration).

Substance	Na^+ salt, bands	Acid, bands	
		At high degree of hydration	After thorough drying
Polystyrenesulfonic acid or Na^+ salt	at ~1200 cm^{-1}, antisymm. st [a]; 1040 cm^{-1}, symm. st of $-SO_3^-$ *(1)*	~1200 cm^{-1}, antisymm. st [a]; 1034 cm^{-1}, symm. st of $-SO_3^-$ *(1)*	1350 and 1172 cm^{-1}, antisymm. and symm. st of the double bonds; 907 cm^{-1}, st of the single bond of $-SO_2OH$ *(6)*
Polystyreneselenonic acid or Na^+ salt	909 cm^{-1}, antisymm. st; 860 cm^{-1}, symm. st of $-SeO_3^-$ *(2)*	879 cm^{-1}, antisymm. st; 847 cm^{-1}, symm. st of $-SeO_3^-$ *(2)* [b]	965 and 911 cm^{-1}, antisymm. and symm. st of the double bonds; 725 cm^{-1} st of the single bond of $-SeO_2OH$ *(7)*
Polystyrenethiophosphonic acid or Na^+ salt	1218 cm^{-1}, antisymm. PO—st; 1037 cm^{-1}, symm. PO—st of $-PSO_2^{2-}$ *(3)*	1170 cm^{-1}, st of the PO double bond of —POSHOH *(8)*, independent of degree of hydration [c]	
Polystyreneseleninic acid or Na^+ salt	803 cm^{-1} [a], symm. st; 776 cm^{-1} [a], antisymm. st of $-SeO_2^-$ *(4)*	839 cm^{-1}, st of the SeO double bond, shifts slightly to higher wavelengths on drying; 658 cm^{-1}, st of the SeO single bond of —SeOOH *(9)* independent of degree of hydration	
Polystyrenephosphinic acid or Na^+ salt	1183 cm^{-1}, antisymm. PO—st; 1056 cm^{-1}, symm. PO—st of $-PHO_2^-$ *(5)*	1170 cm^{-1}, st of the PO double bond; 965 cm^{-1}, st of the PO single bond of —PHOOH *(10)*, independent of degree of hydration	

[a] Doublet due to removal of degeneracy. [b] Also (but only weakly) the bands observed on thorough drying.
[c] Position of the band of the single bond, see [1]. [d] Measured for high degree of hydration with D_2O.

2.3. The Dissociation Process in Salts and the Nature of the Ion Pairs [10]

The splitting of the bands decreases with increasing degree of hydration [*] (see Fig. 3b) but is still present at a degree of hydration >5, as is shown by comparison with the water adsorption isotherms of these substances [11–15]. The bonds between the cations and anions therefore become progressively weaker as the degree of hydration increases; however, the cations remain with their corresponding anions even at very appreciable degrees of hydration. These processes in the dissociation of the salts are illustrated in Graph 1. The cations lie in a potential well at the O atom of their corresponding anions. This potential well is influenced by the fields of the hydration water molecules

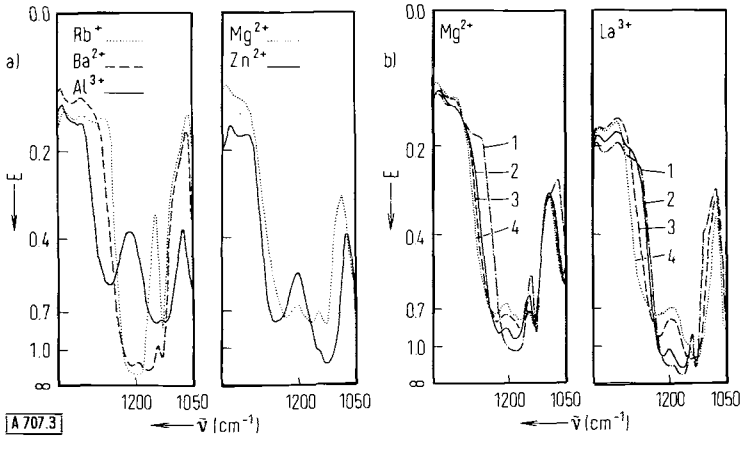
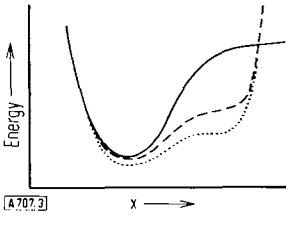


Fig. 3. Band doublets of the antisymmetric stretching vibrations of $-SO_3^-$ ions a) in the presence of Rb^+, Ba^{2+}, Mg^{2+}, Al^{3+}, and Zn^{2+}; spectra of dried membranes b) as a function of the degree of hydration; 1 to 4 in decreasing order of degree of hydration.

in such a way as to favor the temporary release of a cation from an anion. The strength of the bonding in ion pairs is thus a function of the degree of solvation and of the solvating medium. The temporary removal of the ion is the source of the electric conductivity. A cation "jumps" to the neighboring anion and forces



Graph 1. Schematic representation of the potential well on dissociation of the salts.

[10] *G. Zundel* and *A. Murr*, Electrochim. Acta (London) *12*, 1147 (1967).

[*] The degree of hydration is defined as the number of water molecules per cation.

[11] *E. Glueckauf* and *G. P. Kitt*, Proc. Roy. Soc. (London), Ser. A *228*, 322 (1955).

[12] *G. Dickel*, Chem. Techn. *1958*, 449.

[13] *G. Dickel, H. Degenhart, K. Haas*, and *J. W. Hartmann*, Z. physik. Chem. N.F. *20*, 121 (1959).

[14] *G. Dickel* and *J. W. Hartmann*, Z. physik. Chem. N.F. *23*, 1 (1960).

[15] *D. Dolar, S. Lapanje*, and *S. Paljk*, Z. physik. Chem. N.F. *34*, 360 (1962).

the cation already there to execute a similar jump. These jumping cations carry some of their water of hydration with them.

2.4. Hydration at Low Degrees of Hydration

2.4.1. Consequences of the Cation-Water Interaction

Table 2 gives the maxima of the wide bands of the OH stretching vibration of the hydration water molecules in salts of polystyrenesulfonic acid, as well as E_{KH}

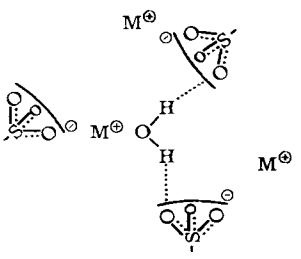
Table 2. Maximum of the OH stretching band of hydration water molecules for salts of polystyrenesulfonic acid (low degree of hydration).

Ion	ν_{max} (OH) (cm^{-1}) [a]	Ionic radius (Å) according to [16]	E_{KH} [electrostatically L.E. $cm^{-2}] \cdot 10^6$
Li^+	3458 ± 2	0.68	1.491
Na^+	3459 ± 2	0.97	1.078
K^+	3460 ± 2	1.33	0.762
Rb^+	3462 ± 2	1.47	0.670
Cs^+	3459 ± 2	1.67	0.568
$(CH_3)_4N^+$	3449 ± 5		
$(C_2H_5)_4N^+$	3430 ± 5		
Be^{2+}	3201 ± 8	0.35	4.46
Mg^{2+}	3394 ± 5	0.66	3.07
Ca^{2+}	3406 ± 10	0.99	2.11
Sr^{2+}	3412 ± 10	1.12	1.85
Ba^{2+}	3440 ± 10	1.34	1.51
Al^{3+}	3195 ± 8	0.51	5.53
Ga^{3+}	3315 ± 6	0.62	4.78
In^{3+}	3338 ± 6	0.81	3.83
Tl^{3+}	(3400 ± 10) [b]	0.95	3.32
Sc^{3+}	3350 ± 5	0.81	3.83
Y^{3+}	3364 ± 6	0.93	3.40
La^{3+}	3373 ± 6	1.14	2.73
Ce^{3+}	3369 ± 6	1.07	2.93
Gd^{3+}	3372 ± 6	0.94 [1]	3.34
Zr^{4+}	3285 ± 8	0.79	5.29
Hf^{4+}	3280 ± 8	0.78	5.33
Mn^{2+}	3406 ± 6	0.80	2.59
Co^{2+}	3381 ± 6	0.72	2.87
Ni^{2+}	3373 ± 6	0.69	2.94
Cu^{2+}	3314 ± 8	0.72	2.87
Zn^{2+}	3317 ± 8	0.74	2.80
Fe^{3+}	3310 ± 8	0.64	4.71

[a] Maximum error estimated from: number of measurements, superposition of interferences, superposition with other bands, and width of the bands in question.

[b] The membrane contains $Tl(OH)_2^+$ as well as Tl^{3+} [1].

values [17], which provide a relative measure of the strength of the cation field at the H nuclei of the water molecules. In the cation groups, this band moves toward lower wave numbers with increasing cation field. The monovalent cations and the ions of the transition elements are exceptions to this rule. The shift shows that the strength of the hydrogen bonds linking the water molecules to neighboring groups increases with increasing cation field, since the cation field polarizes the OH groups of the water molecules. The dipole moment becomes stronger and the H atoms become more increasingly positively charged. The hydrogen bond donor property of these groups increases [17]. In addition the hydrogen bond acceptor property of the O atoms of the neighboring anions also becomes stronger with increasing cation field, since these are also polarized by the cation. This polarization involves rearrangement of the electrons in the anions in such a way that two of the three O atoms become stronger acceptors, as is shown by the findings with acids. In the presence of transition element ions, the bands show much larger shifts to lower wave numbers than would be expected from the cation fields (comparison of values for transition element ions and Mg^{2+} in Table 2). Thus the water molecules are also polarized by covalent interaction of their lone electron pairs with incompletely occupied d orbitals of the cations [18].



2.4.2. Anion-Water Interaction

At low degrees of hydration the stretching vibrations of the OH groups of the hydration water molecules in the hydrogen bonds are shifted toward lower wave numbers in the series of the Na^+ salts with the anions *(1)–(5)* (Fig. 4).

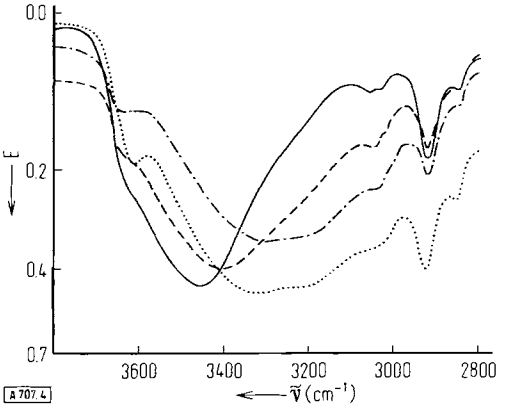


Fig. 4. IR spectra of the Na^+ salt of —— polystyrenesulfonic, ---- polystyreneselenonic, —·—· polystyreneseleninic, ... polystyrenephosphinic acids hydrated with H_2O, all membranes at a relative humidity of 11%. [Anions *(1)*, *(2)*, *(4)*, and *(5)*].

The strength of the hydrogen bonds linking the OH groups of the water molecules to the O atoms of these anions thus increases in the same order. Since the proton acceptor property of the anions also increases in this order [19], it is not surprising that the hydrogen bond acceptor property of the O atoms in the anions shows a similar tendency [20].

[16] *C. D. Hodgman*: Handbook of Chemistry and Physics. 44th Edit., Chemical Rubber Publishing Co., Cleveland/Ohio 1961.

[17] *G. Zundel* and *A. Murr*, Z. physik. Chem. N.F. *54*, 49 (1967).

[18] *G. Zundel* and *A. Murr*, Z. physik. Chem. N.F. *54*, 59 (1967).

[19] *G. Zundel*, Z. Naturforsch. *22a*, 199 (1967).

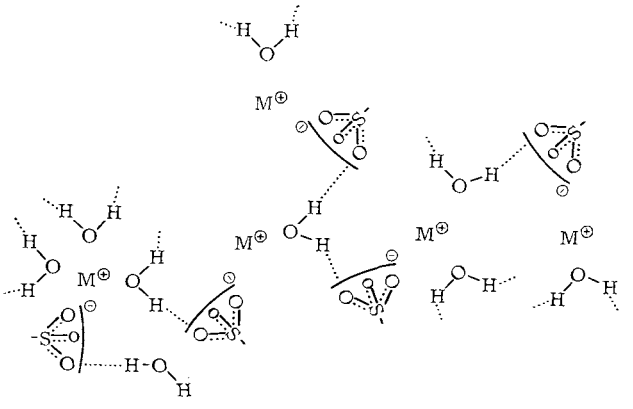
[20] *G. Zundel*, Ž. strukturnoj Chim. *6*, 384 (1965).

The magnitude of the dipole moment μ of the water, which is of fundamental importance to both the cation-water and the anion-water interactions, thus depends not only on the dipole moment of the free water molecule, but also contains a component due to the interaction with the cation and the anions. The cation-water and anion-water interactions are accordingly not independent at low degrees of hydration, but reinforce each other.

2.5. Position of the Water Molecules with respect to the Ions

At low degrees of hydration the water molecules are located between the cation and the neighboring anions as shown by the formula (this page). This is deduced from the fact that the water molecules interact with both the anions and the cation. It must, however, be remembered in considering the pictures of the hydration structure obtained by IR investigation, that the absorption of an IR quantum takes place extremely rapidly. One obtains a picture of the temporary equilibrium position, for, as is known, the hydration structures undergo frequent rearrangements as a result of thermal motion of the hydration water molecules [21–26]. IR-spectroscopy of electrolyte solutions thus affords data about structures which exist for only a short time in dynamic equilibrium with analogous structures.

The stretching vibrations of the free OH groups (*i.e.* those that are not involved in hydrogen bonding) of the hydration water molecules can be observed for some salts as a weak but sharp band at 3615 cm^{-1} (Fig. 4) [*]. Since this band is frequently absent, however, it must be concluded that disintegration of the network of ion pairs and hydration water molecules is only slight. The intensity of the shoulder increases from the Sc^{3+} to the La^{3+} salt. The hydrogen bond donor property of the OH groups of the hydration water molecules decreases in the same order, *i.e.* the number of free OH groups increases as the hydrogen bond donor property of the OH groups of the hydration water molecules decreases [28]. The number of free OH groups in the series of anions *(1)* to *(5)* investigated should decrease from $-SO_3^-$ to $-PHO_2^-$, since the hydrogen bond acceptor property of the O atoms increases in this order. This is not, however, in agreement with observations. The reason is that the number of free OH groups of the water molecules depends not only on the hydrogen bond acceptor property of the O atoms of the anions, but also in particular on the number of O atoms available on the anions to act as acceptors [28].



There is thus a usually only slightly disintegrated network of hydration water molecules and ions. The hydrogen bonds in this network are often strongly bent, and vary slightly in their length [29]. As has been shown by *Luck* [30], bending can occur if it allows the formation of more hydrogen bonds. The H_2O molecules should give an antisymmetric and a symmetric stretching vibration, *i.e.* a doublet; instead of this a wide OH stretching band is observed. Due to the fact that the hydrogen bonds are of different strengths, the two OH groups of each water molecule have become so different that they no longer vibrate together [**]. This results from the differences in stretching and bending of the hydrogen bonds.

2.6. Water Structure and Ions with Very Weak Fields

The shift of the wide OH stretching band behaves anomalously in the presence of alkali metal ions (Table 2), for which there is practically no change in the position of the band with changing cation field [33]. Now, the hydrogen bonds that link the water molecules to the O atoms of the $-SO_3^-$ ions are weaker in the presence of alkali metal ions than in liquid water; this is indicated by the OH stretching vibration band of the water molecules, which occurs at higher wave numbers in the presence of alkali metal ions than in pure liquid water [3420 cm^{-1} (25 °C)] [1]. According to the results obtained so far, the band should shift toward lower wave numbers from Cs^+ to Li^+. Since

[21] *T. J. Swift* and *R. E. Connick*, J. chem. Physics *37*, 307 (1962).

[22] *M. Eigen*, Pure appl. Chem. *6*, 97 (1963).

[23] *H. G. Hertz* and *M. D. Zeidler*, Ber. Bunsenges. physik. Chem. *67*, 774 (1963).

[24] *H. G. Hertz* and *M. D. Zeidler*, Ber. Bunsenges. physik. Chem. *68*, 821 (1964).

[25] *R. G. Pearson* and *M. M. Anderson*, Angew. Chem. *77*, 361 (1965); Angew. Chem. internat. Edit. *4*, 281 (1965).

[26] *D. G. Smith* and *J. G. Powles*, J. molecular Physics *10*, 451 (1966).

[*] The overtone of the scissor vibration of the water molecules gives rise to the shoulder observed at low degrees of hydration on the wide OH stretching band at 3250 cm^{-1}. Its intensity is increased by Fermi resonance with the stretching vibration [27].

[27] *D. F. Hornig*, J. chem. Physics *40*, 3119 (1964).

[28] *G. Zundel* and *A. Murr*, Z. Naturforsch. *21a*, 1391 (1966).

[29] *T. T. Wall* and *D. F. Hornig*, J. chem. Physics *43*, 2079 (1965).

[30] *W. Luck*, Naturwissenschaften *52*, 25, 51 (1965).

[**] The OD stretching band of the D_2O molecules usually exhibits a doublet structure (see Fig. 1a); for a discussion of this difference in the behavior of H_2O and D_2O, see [1, 31].

[31] *Th. Ackermann*, *G. Zundel*, and *K. Zwernemann*, Ber. Bunsenges. physik. Chem., in press.

[32] *G. Zundel* and *A. Murr*, Z. Naturforsch. *24b*, 375 (1969).

[33] *G. Zundel*, *A. Murr*, and *G.-M. Schwab*, Naturwissenschaften *50*, 17 (1963).

the cation-water interaction decreases from Li^+ to Cs^+, the bonding between the cations and the hydration water molecules becomes weaker in this direction. The OH groups of water molecules can displace the cations from the lone electron pairs of their hydration water molecules and form hydrogen bonds with the latter. Thus from Li^+ to Cs^+, the association of the water molecules with one another is increasingly favored in relation to the insertion of water molecules between the cation and the neighboring anions.

This discussion explains the anomalous behavior of this band in the case of the alkali metal ions, since the transition from Li^+ to Cs^+ is accompanied by increasing formation of a network of "pure" water structure. The OH stretching vibration band of these water molecules is situated, however, at lower wave numbers than that of the water molecules inserted between the cation and the neighboring $-SO_3^-$ ions, and therefore an opposing shift is superimposed. The two shifts practically cancel each other out, with the result that the position of the band is almost the same for all the alkali metal ions.

The formation of the "pure" water structure is still more noticeable in the case of the alkylammonium ions[32]. The band is situated at 3449 cm^{-1} for the $(CH_3)_4N^+$ salt and even at 3430 cm^{-1} for the $(C_2H_5)_4N^+$ salt. Thus, as expected, it has shifted much farther toward the wave number for pure liquid water than in the case of the Cs^+ salt. The position of the OH stretching vibration band is a measure of the water-structure forming action of the apolar groups in these ions.

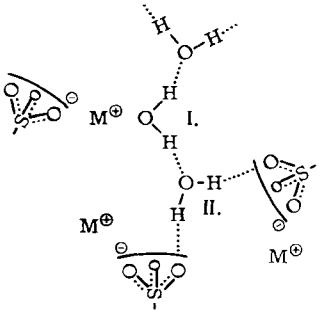
This water-structure formation is the cause of the hydrophobic interaction[34–36]. One should therefore expect a stronger interaction of the alkylammonium than of the alkali metal ions with the $-SO_3^-$ ions, and this is what is actually found, as is shown by the splitting of the antisymmetric SO stretching vibration band of the $-SO_3^-$ ion[32].

2.7. Hydration with Increasing Degree of Hydration

As the number of water molecules increases, the bonding between the cations and the anions becomes looser; this leads to two changes in the bands of the hydration water molecules.

1. If more water molecules are inserted between the cation and the anions, the polarizing effect of the cation is distributed over these water molecules, with the result that the hydrogen bonds formed by the OH groups of these water molecules become weaker[37]. The acceptor property of the O atoms of the anions also decreases somewhat, since the polarization of the anions by the cations decreases as the cation-anion bond becomes weaker. The stretching vibration band of the OH groups in hydrogen bonds of the hydration water consequently moves toward higher wave numbers with increasing hydration. In other words, the shift of the band toward smaller wave numbers decreases with increasing hydration.

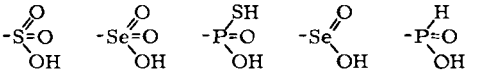
2. Two or more layers of water molecules are inserted between the cations and the neighboring anions, *i.e.* a "second hydration shell" is formed[38]. It is possible to follow this in the presence of cations



having a very strong field, *e.g.* in the Al^{3+} salt. The OH stretching vibration band of the hydration water molecules of attachment type II appears at about 3430 cm^{-1} with increasing degree of hydration. In the case of cations having strong fields, the band due to the OH stretching vibration of the hydration water molecules of attachment type I appears merely as a more or less pronounced shoulder on the low wave number flank of the hydration water band complex.

3. The Acids

When the acid proton is present on the anions, it rearranges the bonding electrons in such a way that the groupings *(6)–(10)* are formed from the fixed ions *(1)–(5)* (Fig. 2 and Table 1). The acid proton greatly reduces the mesomeric bond resonance of its anion[19].



(6) *(7)* *(8)* *(9)* *(10)*

3.1. Dissociation

The anion vibration bands of polystyrenephosphinic and polystyreneseleninic acids do not change with increasing degree of hydration. In polystyrenesulfonic and polystyreneselenonic acids, on the other hand, the rearrangement of the bonding electrons due to the acid proton disappears with increasing degree of hydration (Fig. 2). The integral extinction of these bands can be used as a measure of the removal of the proton from the anion, *i.e.* as a measure of the true degree of dissociation. According to this, the true degree of dissociation decreases from polystyrenesulfonic to polystyrenephosphinic acid in the series of acids investigat-

[34] *H. G. Hertz* and *M. D. Zeidler*, Ber. Bunsenges. physik. Chem. *68*, 821 (1964).

[35] *H. G. Hertz*, Ber. Bunsenges. physik. Chem. *68*, 907 (1964).

[36] *G. Nemethy*, Angew. Chem. *79*, 260 (1967); Angew. Chem. internat. Edit. *6*, 195 (1967).

[37] *G. Zundel* and *A. Murr*, J. Chim. et Physique, *66*, 246, (1969).

[38] *G. Zundel* and *A. Murr*, Z. physik. Chem. *233*, 415 (1966).

ed. It is understandable that the true degree of dissociation should be much lower for the –SeOOH *(9)* and –PHOOH *(10)* groups, since on dissociation of these groups the charge has only two instead of three XO bonds over which it can be distributed [19,44].

3.2. Association of the Acid Groups

After thorough drying all these acids exhibit a pair of bands (Fig. 5), which is due to the OH or OD group of the acid. When this pair of bands occurs, the acid

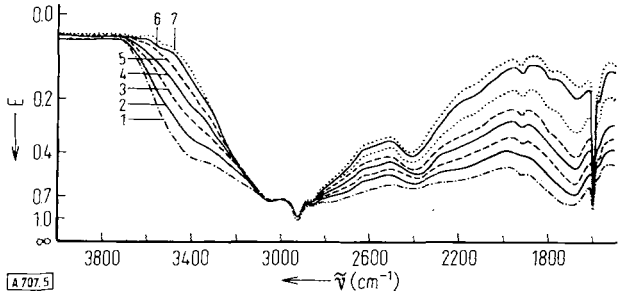
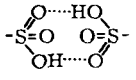


Fig. 5. IR spectra of polystyrenesulfonic acid hydrated with H_2O (two membranes superimposed on each other). The membranes were kept in the sample cell at a fixed relative humidity for about 6 hours before the spectra were recorded. The drying steps were carried out successively without interruption. 1% crosslinked [*], 1.50 acid groups/benzene ring 1 → 6 decreasing relative humidity, 7 thoroughly dried membranes; pair of bands at 2950 and 2405 cm^{-1} (OH) or at 2240 and 1805 cm^{-1} (OD) (not shown here).

[*] Crosslinking with divinylbenzene added during the polymerization.

groups are linked as shown in *(11)* [39], though not always in pairs.

According to *Hadži et al.* [40,41], the pair of bands is due to the stretching vibration and the overtone of the bending vibration of the acid OH or OD groups, these



(11)

two vibrations being coupled by Fermi resonance [*]. Such strong coupling of bands situated so far apart is possible only if a very anharmonic, *i.e.* asymmetrical, potential well exists in the hydrogen bonds formed by these groups.

These hydrogen bonds are very strong, as is shown by the position of the bands and the strong anharmonicity of the potential well. It seems at first surprising that the strong polystyrenesulfonic acid is associated *via* hydrogen bonds as strong as those formed in the weak polystyreneseleninic acid. An IR-spectroscopic and an ebullioscopic study of anhydrous *p*-toluenesulfonic acid in chlorinated hydrocarbons showed that this acid is dimeric and gives the same pair of bands [39]. How can the relatively strong polystyrenesulfonic acid form such strong hydrogen bonds? We have seen that the acid proton rearranges the electrons in these anions in such a way as to give $-SO_2OH$ groups *(6)*. Since the doubly bonded O atoms are much stronger acceptors for hydrogen bonds than the O atoms in the $-SO_3^-$ ions, the strong polystyrenesulfonic acid can form hydrogen bonds as strong as those formed by the weak polystyreneseleninic acid.

These bands are a measure of the association of the acid groups [**]. In the case of polystyrenesulfonic acid, the band at 2405 cm^{-1} appears only with increasing drying, whereas in the case of polystyreneselenonic acid the corresponding band is already faintly visible even when the membrane has been hydrated at a relative humidity of 98%; it too intensifies with increasing drying. For polystyrenethiophosphonic acid, polystyreneseleninic acid, and polystyrenephosphinic acid, the band is as intense after hydration of the membrane at 98% relative humidity as after intensive drying. The tendency to associate increases from the $-SO_2OH$ *(6)* to the –PHOOH *(10)* groups. It thus shows the opposite course from the true degree of dissociation [44].

3.3. Excess Proton, IR Continuum, and Proton Dispersion Forces

In the ion exchangers, the degree of hydration can be reduced to any desired extent without modification of the amorphous structure of the liquid state by crystallization. These substances have therefore proved particularly suitable for the investigation of the nature of the excess proton, which is hydrated with only a few water molecules [45–47,58].

Curves on the right-hand side of Figure 6 show a plot of the number of water molecules available to the excess proton against the true degree of dissociation α_t of the polystyrenesulfonic acid. α_t was determined from the integral extinction of the bands of the $-SO_2OH$ groups *(6)*. The acid proton in polystyrenesulfonic acid is released from the anion when it has two water molecules available (extrapolation of the curves on the right hand side in Fig. 6).

Polystyrenesulfonic acid gives an intense absorption continuum extending from the OH or OD stretching vibration bands toward lower wave numbers (see Figs. 1a, 1b). The extinction of this absorption continuum increases in proportion to the true degree of dissociation at low excess proton densities (curves on left-hand side in Fig. 6). Since the dissociation of poly-

[39] *G. Zundel*, *H. Metzger*, and *I. Scheuing*, Z. Naturforsch. *22b*, 127 (1967).

[40] *D. Hadži*, Pure appl. Chem. *11*, 435 (1965).

[41] *D. Hadži* and *N. Kobilarow*, J. chem. Soc. (London) *1966*, 439.

[*] The appearance of the two vibrations was earlier explained by an asymmetrical double potential minimum in these hydrogen bonds [42], on the basis of work by *Somorjai* and *Hornig* [43]. However, *Hadži et al.* [40, 41] studied this pair of bands for hydrogen bonds whose acceptors differ appreciably in their strength. They concluded that the pair of bands cannot be explained by an asymmetrical double potential minimum.

[42] *G. Zundel* and *H. Metzger*, Spectrochim. Acta, Part A *23*, 759 (1967).

[43] *R. L. Somorjai* and *D. F. Hornig*, J. chem. Physics *36*, 1980 (1962).

[**] However, the band at the higher wave number cannot be used as a measure of the degree of association, since another band becomes superimposed on it with increasing hydration [1].

[44] *G. Zundel* and *A. Metzger*, Z. physik. Chem., *240*, 50 (1969).

[45] *G. Zundel* and *H. Metzger*, Z. physik. Chem., N.F. *58*, 225 (1968).

[46] *G. Zundel* and *H. Metzger*, Z. Naturforsch. *22a*, 1412 (1967).

[47] *G. Zundel* and *H. Metzger*, Z. physik. Chem., N.F. *59*, 225 (1968).

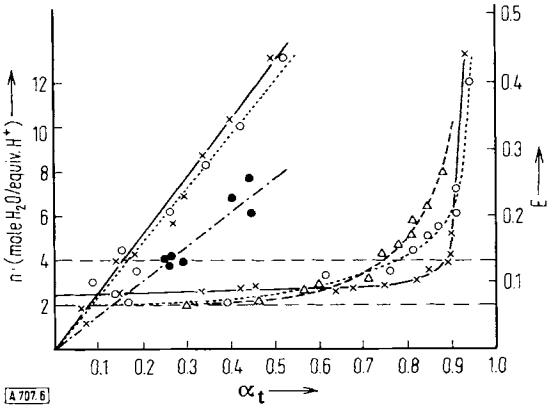


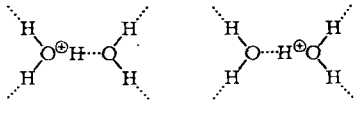
Fig. 6[*]. a) Number (n*) of water molecules available to the excess proton as a function of the true degree of dissociation α_t of polystyrenesulfonic acids (three curves on the right-hand side of the Figure; left ordinate). b) Extinction of the absorption continuum (at 2000 cm^{-1}) as a function of the true degree of dissociation α_t of polystyrenesulfonic acids (three straight lines on left-hand side of the Figure; right ordinate).

Each of the sets of three curves shows curves for membranes having different degrees of crosslinking and sulfonation.

styrenesulfonic acid occurs when there are two water molecules available to the acid proton, this result shows that the continuum arises when $H_5O_2^+$ groupings are formed.

In crystals containing the grouping H_3O^+, the symmetric bending vibration of this grouping is observed at about 1200 cm^{-1} [48–50]. When the spectrum contains a symmetric bending vibration of the grouping H_3O^+, the band of this vibration at about 1200 cm^{-1} should disappear on transition from H_2O to D_2O hydration, and should be replaced by the D_3O^+ band at about 890 cm^{-1}. However, no appreciable change is observed on transition from H_2O to D_2O hydration. The grouping H_3O^+ accordingly does not execute any vibrations as an entity in the non-crystalline medium. This can be explained only if the life-time of the H_3O^+ grouping is very short under these conditions.

The excess proton thus moves extremely rapidly between the two water molecules in $H_5O_2^+$. This grouping can therefore be represented by the two boundary structures [51]. The absorption continuum is closely connected with this mobility of the excess proton in $H_5O_2^+$.



The absorption continuum is not temperature-dependent between 292 and 85 °K [52]. Thus no activation energy is required for the movement of the excess proton in $H_5O_2^+$. The proton tunnels accordingly in the hydrogen bond of this grouping. A potential well is present, as is shown in Fig. 7.

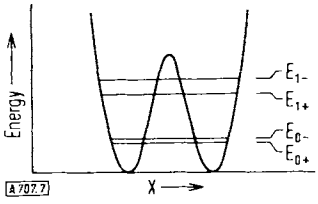


Fig. 7. Symmetrical double minimum potential well in a symmetrical hydrogen bond (spatial coordinate x in arbitrary units).

Do the two water molecules of the $H_5O_2^+$ retain their individuality as vibrating groups while the excess proton is tunneling between them? At low degrees of hydration, *i.e.* when the $H_5O_2^+$ groupings are being formed, the extinction of the absorption continuum increases linearly with the integral extinction of the scissor vibration. This is possible only if the water molecules in $H_5O_2^+$ vibrate as individuals [45].

Many authors have studied and discussed the special stability of the $H_9O_4^+$ grouping. (For reviews see [1, 53, 54].) The integral extinction of the scissor vibration increases strongly while the first four water molecules are adding to the proton that has been removed from the anion. Hence the extinction coefficient of the scissor vibration of the outer water molecules in the grouping $H_9O_4^+$ is very much higher than that of the water molecules in pure liquid water [1, 46].

All this shows the special position of this grouping in the network of the hydration structure. The extinction of the continuum does not change on transition from $H_5O_2^+$ to $H_9O_4^+$. Owing to the symmetry of the grouping $H_9O_4^+$, however, none of the three hydrogen bonds can be favored, *i.e.* they must all have a potential well with a low barrier, the potential being so symmetrical that the protons can tunnel. Thus the three inner protons in $H_9O_4^+$ act as the excess proton.

The continuum is due to the tunneling excess protons, which have a continuous energy distribution, *i.e.* are in energy bands. How do these energy bands arise? The tunneling of a particle in a potential well, as shown in Figure 7, always causes splitting of the energy levels, but never broadening. The continuum must therefore be due to some other factor. The transition of an excess proton from one boundary position to the other is associated with a fluctuation of the electromagnetic field in the neighborhood. This field fluctuation changes the potential at the position of a neighboring excess proton. It is very large, since the center of the charge is displaced much more on tunneling of a proton than the tunneling H nucleus itself. This is because the transition of the H nucleus causes a considerable displacement of the electrons, *i.e.* of the negative charge, in the opposite direction, and the field fluctuation depends on the amount of displacement, not of the H nucleus alone, but of the center of the charge. Neighboring tunneling protons are coupled *via* this fluctuating field, and this coupling leads to a shift of the energy levels. Estimation of the shift of the levels by these coupling forces for pairs of tunneling protons with the

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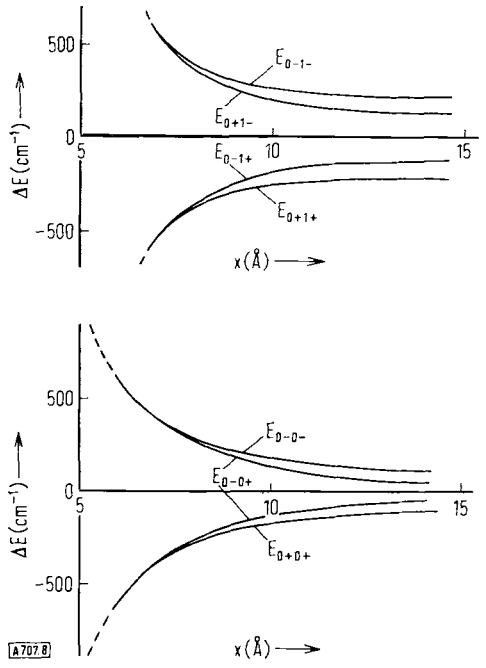


Fig. 8. Shift and splitting ΔE of the energy terms of the tunneling protons as a function of the distance from the center of the hydrogen bonds.

perturbation calculation for nearly degenerate states [55] gives the energy terms of the tunneling protons as a function of the distance between the centers of the two hydrogen bonds Fig. 8 [56].

The shift of the lowest level by the fluctuating fields associated with the tunneling of the proton is

$$\Delta E_{0+0+} = h\nu_0 \left[1 - \sqrt{1 + \left(\frac{p^2}{\varepsilon h\nu_0}\frac{g}{R^3}\right)^2}\right]$$

where ν_0 is the tunneling frequency in the ground state, p is the dipole moment of the grouping $H_5O_2^+$ when the proton is in one of the boundary positions, ε is the dielectric constant of the medium between the tunneling protons, and g is a factor that takes into account the orientation of the two hydrogen bonds with respect to each other. It passes through values from -2 to $+2$. R is the distance between the hydrogen bonds with the tunneling protons. Similar relations exist for the shifts of the other levels.

If we consider many pairs of tunneling excess protons in a liquid, the orientation factor g and the distance R pass through a random statistical multiplicity of values. The shifts of the energy levels consequently pass through a continuous range of values. This is the cause of the energy bands of the tunneling protons, and hence of the absorption continuum.

The lowest energy level, which is preferentially occupied by the tunneling protons, is lowered. The tunneling protons thus attract one another. The term "proton dispersion forces" is suggested by the processes involved in their occurrence. These forces are as strong as the other intermolecular forces.

When the concentration of tunneling protons in polystyrenesulfonic acid exceeds 1.5 mequiv. of H^+/g, the extinction of the continuum no longer increases appreciably with increasing concentration [*]. The extinction of the continuum per tunneling proton thus decreases at approximately the same rate as the concentration is being increased at high concentrations of tunneling protons. The extinction of the continuum shows a saturation effect, which presumably corresponds to the transition from coupling in pairs to coupling of all the tunneling protons [58].

This absorption continuum is not confined to dissociated polystyrenesulfonic acid. It was observed by *Suhrmann* and *Breyer* [59] as early as 1933 in the investigation of aqueous acid and base solutions in the overtone region, and later by *Ackermann* [60,61] in the fundamental vibration region. It occurs with all polyelectrolytes having dissociated acidic and basic (Fig. 9a) groups [1]. It is observed when an excess proton

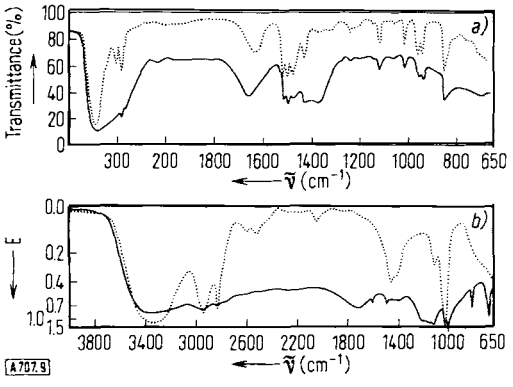


Fig. 9. IR spectra. a) —— poly-*p*-trimethylammoniumstyrene hydroxide [31, 62], hydrated; .... poly-*p*-trimethylammoniumstyrene iodide [31, 62], hydrated; b) —— saturated solution of *p*-toluenesulfonic acid monohydrate in CH_3OH; .... CH_3OH.

tunnels between molecules such as methanol (Fig. 9b) and dimethyl sulfoxide [1], and has recently also been discovered in biopolymers [1]. Energy bands of tunneling protons and proton dispersion forces thus play a part in many systems.

The rate-determining step in the anomalous conductivity of protons is the structure migration (or structure diffusion), as discussed in particular by *Eigen et al.* [63]; the structure migration of a grouping of the size $H_5O_2^+$ is sufficient. In this process, the H nucleus can tunnel and so migrate in the field direction if the bridges formed by the outer water molecules in $H_5O_2^+$ or $H_9O_4^+$ are linearized during thermal motion [1]. This H nucleus then assumes the role of the excess proton.

[*] The concentration of the tunneling protons cannot be varied directly *via* the concentration of fixed ions incorporated, since the latter are no longer uniformly distributed in the membrane at low concentrations, as is shown by the kinetics of the sulfonation reaction [57].

[55] *A. Dalgarno* in *D. R. Bates*: Quantum Theory. Academic Press, New York 1961, Vol. 1, p. 202ff.

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[59] *R. Suhrmann* and *F. Breyer*, Z. physik. Chem., Abt. B *23*, 193 (1933).

[60] *Th. Ackermann*, Z. physik. Chem. N.F. *27*, 253 (1961).

[61] *Th. Ackermann*, Z. physik. Chem. N.F. *41*, 113 (1964).

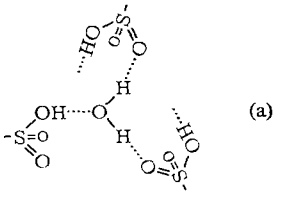
[62] *Th. Ackermann*, *G. Zundel*, and *K. Zwernemann*, Z. physik. Chem. N.F. *49*, 331 (1966).

[63] *M. Eigen* and *L. DeMaeyer*, Proc. Roy. Soc. (London), Ser. A *247*, 505 (1958).

3.4. The Hydration Structure of the Acids

3.4.1. Polystyrenesulfonic Acid[47]

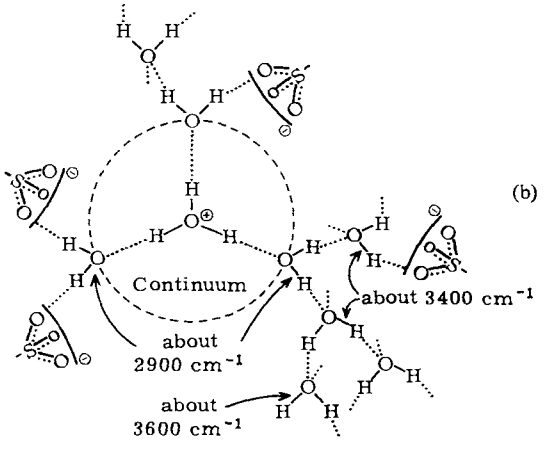
The $-SO_2OH$ groups of polystyrenesulfonic acid dissociate only when two water molecules are available per acid group. If this acid is slowly dried, the last water molecule per acid group is attached as shown in (a).



(a)

This water molecule is presumably often bound, not merely to one acid OH group, but to two, *i.e.* by one on each lone electron pair. The OH stretching vibration bands of the OH groups in the two different hydrogen bonds are found at 3210 and 3050 cm^{-1}. If two water molecules are present, the acid proton is removed from the anion. However, the number of water molecules on the excess proton increases only slowly at first with increasing degree of dissociation (curves on right-hand side in Fig. 6). This situation changes only when most of the $-SO_2OH$ groups have dissociated.

If no further water molecules are available, the $H_5O_2^+$ or $H_9O_4^+$ groupings formed are linked to the O atoms of the $-SO_3^-$ ions *(1) via* hydrogen bonds, as is shown by the following findings: 1. A stretching vibration band due to free OH groups at about 3600 cm^{-1} is at best indistinct. 2. The degeneracy of the antisymmetric stretching vibration band at about 1200 cm^{-1} is removed (cf. the doublet in Fig. 1a). The stretching vibration band of the OH groups in the hydrogen bonds formed by the outer water molecules of $H_5O_2^+$ or $H_9O_4^+$ is very broad and is situated at about 2900 cm^{-1}, while that of the OD groups occurs at

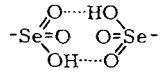


(b)

2100 cm^{-1}. The stretching vibration band of the OH groups of the water molecules attached to the $H_9O_4^+$ grouping appears at about 3400 (H_2O) or 2500 cm^{-1} (D_2O) with increasing degree of hydration. The resulting network of the hydration structure is shown schematically in (b). For the sake of clarity only one excess proton is shown.

3.4.2. Polystyreneselenonic Acid

The hydration structure of polystyreneselenonic acid does not differ very greatly from that of polystyrenesulfonic acid, except that the true degree of dissociation of the $-SeO_2OH$ groups *(7)* is smaller than that of the $-SO_2OH$ groups *(6)*. Thus the $-SeO_2OH$ groups are mostly not yet dissociated when they have two water molecules available. Moreover, the groupings *(12)* are

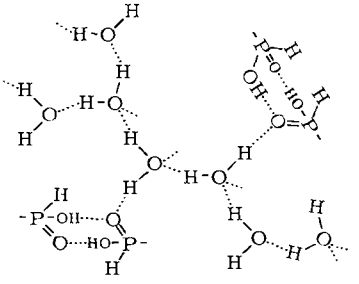


(12)

not yet all dissociated even when the membranes have been hydrated at 98% relative humidity. Therefore, hydrated $-SeO_2OH$ groups, which are probably mostly still associated even at relatively high degrees of hydration, are situated between the hydration structures around the dissociated acid proton[44].

3.4.3. Polystyreneseleninic and Polystyrenephosphinic Acids

Quite different hydration is found in polystyreneseleninic and polystyrenephosphinic acids[44]. The $-SeOOH$ *(9)* and $-PHOOH$ *(10)* groups dissociate only to an extremely small extent, and they remain associated even when these membranes are considerably hydrated. The band that arises at 3390 (H_2O) or 2490 cm^{-1} (D_2O) with increasing hydration thus corresponds to the stretching vibration of the OH or OD groups in the hydrogen bonds of the water molecules by which the latter are linked to O atoms of the acid groups or to one another. Finally, the shoulder at about 3640 (H_2O) or 2680 cm^{-1} (D_2O) shows that there are a considerable number of free OH or OD groups in the network of the hydration structure, which consequently shows appreciable disintegration, particularly in polystyrenephosphinic acid. This is understandable in view of the strong hydrogen bonds between the associated acid groups, which strain the structure. A hydration structure is thus present in these two acids, as is shown schematically in (c).



(c)

Received: January 25, 1968 [A 707 IE]
Revised: September 23, 1968
German version: Angew. Chem. *81*, 507 (1969)
Translated by Express Translation Service, London

Bis(*N*-fluorosulfonylimido)sulfur and Bis(*N*-fluorosulfonylimido)sulfur Difluoride[1]

By *H. W. Roesky* and *D. P. Babb* [*]

UV irradiation of *N*-(fluorosulfonyl)sulfur oxide imide[2] *(1)* leads to bis(*N*-fluorosulfonylimido)sulfur *(2)*.

$$2\,FSO_2-N=S=O \rightarrow FO_2S-N=S=N-SO_2F + SO_2$$
(1) *(2)*

Compound *(2)* (molecular weight 226; cryoscopic in benzene 226) is a yellow liquid having an unpleasant odor: b.p. 42 to 43 °C/0.01 torr, $d_4^{20} = 1.9104$, $n_D^{20} = 1.4802$. The IR spectrum (capillary film) shows bands at 1450 vs, 1390 vs, 1220 vs, 1180 vs, 1090 vs, 1020 vs 770–850 vs, 680 m cm^{-1} in the NaCl region. The ^{19}F-NMR spectrum (in substance) contains a singlet at −58.5 ppm measured against CCl_3F as external reference.

Compound *(2)* reacts with fluorine when exposed to UV radiation to give bis(*N*-fluorosulfonylimido)sulfur difluoride *(3)*.

$$(2) + F_2 \rightarrow FO_2S-N=S=N-SO_2F \quad (3)$$
(F on the S atom)

Compound *(3)* (molecular weight 264; cryoscopic in benzene 259) is a water-clear liquid: b.p. 53 °C/12–14 torr; as expected, it is more volatile than *(2)*. The IR spectrum (capillary film) contains bands at 1460 vs, 1330 vs, 1220 vs, 1120 w, 1030 w, 930 w, 780–900 vs, 740 m, 675 m cm^{-1} in the NaCl region. The ^{19}F-NMR spectrum (in substance) consists of two triplets of equal area at −45.3 and −62.0 ppm measured against CCl_3F as external reference. The signal at −45.3 ppm is tentatively assigned to the fluorine atoms of the SF_2 group, and that at −62.0 ppm to the fluorine atoms in the FSO_2 groups. $J_{FF} = 6.9$ Hz.

Bis(N-fluorosulfonylimido)sulfur (2)

50 g of compound *(1)* is placed in a quartz vessel and subjected to UV irradiation[3] for 48 h. The SO_2 liberated is collected in a cold trap (acetone/Dry Ice). After removal of unreacted *(1)* under oil-pump vacuum, the residue is distilled twice under reduced pressure. Yield 26 g (65%).

Bis(N-fluorosulfonylimido)sulfur difluoride (3)

Fluorine is passed at a rate of 60 bubbles per minute through a quartz vessel with 50 g of *(2)* that is exposed to UV irradiation. During the reaction gaseous products collect in a condensation trap (acetone/Dry Ice). [Caution! The gas mixture is explosive. During experiments a violent explosion occurred in the gas phase.] After 36 hours the liquid remaining in the reaction vessel is distilled at water-pump vacuum. Yield: 9 g (15%).

Received: March 26; revised May 28, 1969 [Z 984 IE]
German version: Angew. Chem. *81*, 494 (1969)

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[1] Part 18 of Sulfur-Nitrogen Compounds. – Part 17: *H. W. Roesky* and *D. P. Babb*, Inorg. Chem., in press.

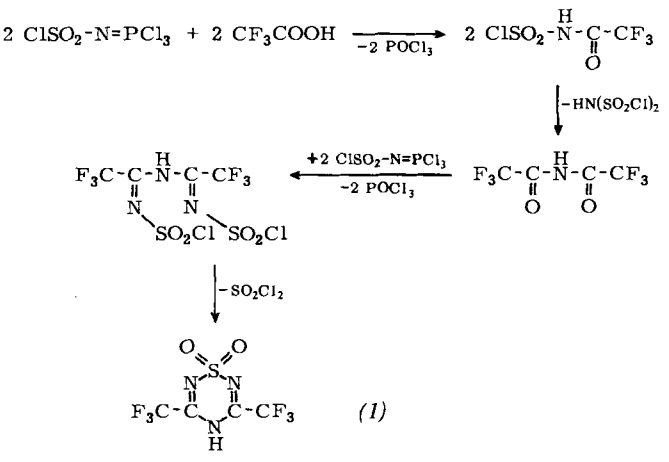
[2] *H. W. Roesky*, Angew. Chem. *79*, 724 (1967); Angew. Chem. internat. Edit. *6*, 711 (1967).

[3] UV lamp produced by Philips, 500 W, Type 57300 ZB.

3,5-Bis(trifluoromethyl)-1,2,4,6-thiatriaza-2,5-cyclohexadiene-1,1-dione[1]

By *H. W. Roesky* [*]

N-Chlorosulfonyliminotrichlorophosphorane $ClSO_2-N=PCl_3$, prepared from amidosulfuric acid and phosphorus pentachloride[2], reacts with trifluoroacetic acid to give 3,5-bis(trifluoromethyl)-1,2,4,6-thiatriaza-2,5-cyclohexadiene-1,1-dione *(1)*. The formation of $POCl_3$, SO_2Cl_2, and $HN(SO_2Cl)_2$ as additional products was established by IR spectroscopy, thus suggesting the following reaction scheme:



The structure of *(1)* is indicated by elemental analysis, ^{19}F- and ^1H-NMR data, and its mass and IR spectra. Compound *(1)* is a solid at room temperature, can be sublimed in a sealed tube, and is readily soluble in water. Addition of tetraphenylphosphonium and tetraphenylarsonium chloride to an aqueous solution of *(1)* leads to the precipitation of the corresponding salts:

$[(C_6H_5)_4P]^+[C_4F_6N_3O_2S]^-$, m.p. 160 °C

$[(C_6H_5)_4As]^+[C_4F_6N_3O_2S]^-$, m.p. 158 °C

The mass spectrum of *(1)* contains the molecular ion at *m/e* 269 (25.5%) in addition to the fragments *m/e* 250 (4.5%; *(1)* − F) and 205 (75.8%; *(1)* − SO_2), and a large number having smaller masses.

The ^{19}F-NMR spectrum (CD_3CN) shows a singlet at +73.0 ppm measured against CCl_3F as external reference. A singlet is observed in the ^1H-NMR spectrum at −11.5 ppm (TMS as external reference).

IR spectrum (NaCl and KBr regions): ≈ 3200 m, ≈ 3100 m, 1690 s, 1515 s, 1385 m, 1375 vs, 1325 m, 1250 vs, 1170 vs, 792 vs, 758 m, 736 w, 682 vs, 597 vs, 568 s cm^{-1}.

Procedure:

A mixture of *N*-chlorosulfonyliminotrichlorophosphorane (1 mole) and trifluoroacetic acid (1 mole) is heated to 60–70 °C for 24 h. Compound *(1)* can be isolated from the semi-solid reaction mixture in a distillation-sublimation apparatus (oil-pump vacuum); it was purified by subliming twice at 175–180 °C/0.05 torr. Yield: 33.5 g (50%).

Received: March 20; revised: May 28, 1969 [Z 985 IE]
German version: Angew. Chem. *81*, 493 (1969)

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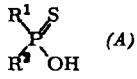
[1] Part 20 of Sulfur-Nitrogen Compounds. – Part 19: *H. W. Roesky* and *W. Grosse-Böwing*, Inorg. nuclear Chem. Letters, in press.

[2] *A. Kirsanov*, Izvest. Akad. Nauk SSSR, Otdel chim. Nauk *1950*, 426; Chem. Abstr. *45*, 1503 (1951); Inorg. Syntheses *8*, 105 (1966).

Geometric Isomerism in Cyclic Five- and Six-Membered Monothiophosphoric Acid Derivatives[**]

By *M. Mikolajczyk* and *H. M. Schiebel*[*]

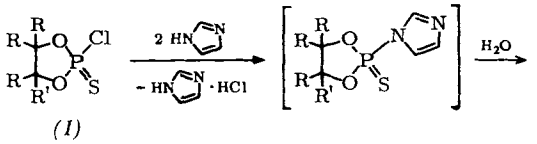
Monothiophosphoric acids (*A*) are chiralic compounds with the phosphorus atom as asymmetric center[1]. Because of their high reactivity they prove most suitable as starting



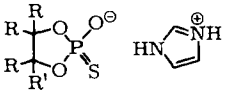
(A)

materials for the synthesis of other optically active phosphorus compounds containing P=O- or P=S-groupings[1,2].

We report here on the geometric isomerism of cyclic monothiophosphoric acid derivatives[3] which occurs when the molecule contains at least one asymmetric center at a ring carbon atom.



(1)



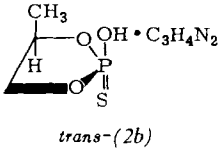
(2)

	R	R'	(2) M.p. (°C) [a]	Yield (%)	$\delta_{31}P$ (ppm) [b]
(a)	H	H	119–123.5	72	−154.3
(b) [c]	H	CH_3	74–99	88	−160 [d]
(c)	CH_3	CH_3	177–180	68	−144.3

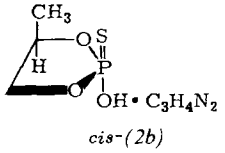
[a] From *n*-propanol/ether. [b] Measured in H_2O.
[c] Mixture of *cis* and *trans* forms. [d] Two signals.

By reaction of the cyclic thiophosphoryl chlorides *(1)*[4] with imidazole in tetrahydrofuran, we were able to prepare the corresponding imidazolides, which, on account of their instability, were converted without isolation into the imidazolium salts *(2)* of thiophosphoric acids by reaction with water.

As is to be expected, the imidazolium propylenethionophosphate *(2b)* prepared in this way is a mixture of the *cis* and *trans* isomers[5].



trans-(2b)

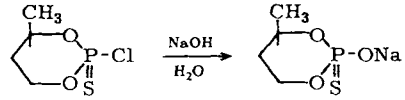


cis-(2b)

The ^{1}H-NMR spectrum at 100 MHz shows two doublets of equal intensity at 1.40 and 1.41 ppm (J_{H-CH_3} = 6.1 Hz) (measured in D_2O with sodium 2-trimethylsilylpropanesulfonate as internal standard), which can be ascribed to the protons of the methyl group.

In the ^{31}P-NMR spectrum (measured in H_2O with 80% phosphoric acid as external standard), two signals appear at −160.0 ppm which are separated by about 22 Hz. We have been able to obtain one isomer in the pure state [m.p. 122 to 125 °C, δ = 1.41 ppm (CH_3)] by repeated recrystallization of the mixture from *n*-propanol/ether. The other isomer can be isolated from the mother liquor in about 90% purity (m.p. 78.5–83 °C). Assignment of the *cis* and *trans* forms has not, as yet, been possible.

The sodium salt of 2-hydroxy-4-methyl-1,3,2-dioxaphosphor^V-inane-2-thione *(3)* (sodium 1-methyltrimethylenethionophosphate) was prepared in 92% yield by alkaline hydrolysis of the chloride, according to the method of *Edmundson*[6]. The isomers were separated by fractional crystallization.



(3)

The *cis* and *trans* isomers of compound *(3)* are likewise distinguishable from each other in their ^{1}H- and ^{31}P-NMR spectra.

δ = 1.27 ppm (CH_3, q)	δ = 1.28 ppm (CH_3, q)

(measured in D_2O with DSS as internal standard)

J_{H-CH_3} = 6.2 Hz	J_{H-CH_3} = 6.2 Hz
$J_{P-O-CH-CH_3}$ = 2 Hz	$J_{P-O-CH-CH_3}$ = 1.7 Hz
δ_{31P} = −112.9 ppm	δ_{31P} = −120 ppm

(measured in H_2O with 80% H_3PO_4 as external standard)

(Two signals, separated by 60 Hz)	(Two signals, separated by 48 Hz)

(For assignment of data to the *cis* and *trans* forms see [7].)

Good results were obtained in the elemental analyses of all the compounds investigated. The ^{31}P-NMR measurements were carried out with a Perkin Elmer R 10 spectrometer in combination with a Northern Scientific NS 544 Digital Memory Oscilloscope.

Received: April 2, 1969 [Z 992a IE]
German version: Angew. Chem. *81*, 494 (1969)

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[**] M. M. thanks the Max-Planck-Institut für experimentelle Medizin (Göttingen) for a one-year stipend.

[1] *R. F. Hudson* and *M. Green*, Angew. Chem. *75*, 47 (1963); Angew. Chem. internat. Edit. *2*, 11 (1963); *H. E. McEwen*, Topics in Phosphorus Chemistry *2*, 1 (1965); *J. Michalski*, Bull. Soc. chim. France *4*, 1109 (1967).

[2] *J. Michalski*, *M. Mikolajczyk*, and *J. Omelanczuk*, Tetrahedron Letters *1965*, 1779; *J. Michalski*, *M. Mikołajczyk*, *B. Mlotkowska*, and *J. Omelanczuk*, Tetrahedron *25*, 1743 (1969).

[3] *F. Eckstein* and *H. Gindl*, Chem. Ber. *101*, 1670 (1968); *F. Eckstein*, FEBS-Letters *2*, 85 (1968).

[4] *Houben-Weyl*: Methoden der organischen Chemie Vol. XII/2. Thieme-Verlag, Stuttgart 1964, p. 610. The chloride *(1c)*, m.p. 62–65 °C, was obtained from 2-mercapto-4,4,5,5-tetramethyl-1,3,2-dioxaphospholane-2-thione and phosphorus pentachloride.

[5] We designate the thiophosphoric acid having methyl group and sulfur atom *cis* to each other as the *cis*-acid.

[6] *R. S. Edmundson* and *A. J. Lambie*, J. chem. Soc. (London) *B 1967*, 577.

[7] *M. Mikolajczyk*, Angew. Chem. *81*, 495 (1969); Angew. Chem. internat. Edit. *8*, 511 (1969).

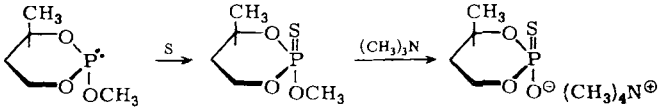
Stereospecific Synthesis of *cis*-2-Hydroxy-4-methyl-1,3,2-dioxaphosphor^V-inane-2-thione[**]

By *M. Mikolajczyk*[*]

The sodium salt of 2-hydroxy-4-methyl-1,3,2-dioxaphosphor^V-inane-2-thione (sodium 1-methyltrimethylenethionophosphate)[1] can exist in two geometrical forms, which are distinguishable from each other in their ^{1}H- and their ^{31}P-NMR spectra. In oder to assign the NMR data to the isomers

and to avoid fractional crystallization of the mixture of *cis* and *trans* compounds – which leads to very low yields – we synthesized the tetramethylammonium salt of the *cis*-thiophosphoric acid *(3)* [1a].

The more stable form [1a] of 2-methoxy-4-methyl-1,3,2-dioxaphosphorV-inane *(1)* [2, 3b] ($\delta_{31P} = -301.4$ ppm), which was contaminated with up to 10% of the other isomer ($\delta_{31P} = -292.8$ ppm; measured in ether with 80% H_3PO_4 as external standard), served as starting material. Compound *(1)* adds on sulfur in a strongly exothermic reaction and is thus converted into 2-methoxy-4-methyl-1,3,2-dioxaphosphorV-inane-2-thione *(2)* (b.p. 78–80 °C/0.3 torr; $n_D^{20} = 1.4922$; yield 80%). The ratio of the two isomeric thiophosphates is unchanged after the addition. The last step in the synthesis is the reaction of *(2)* with trimethylamine in benzene at room temperature, which leads to formation of the tetramethylammonium salt of the thiophosphoric acid *(3)* (m.p. 205–208 °C, yield 75%; NMR spectra: $\delta = 1.27$ ppm (CH_3), (measured in D_2O with sodium 2-trimethylsilylpropanesulfonate (DSS) as internal standard); $J_{H-CH_3} = 6.2$ Hz; $J_{P-O-CH-CH_3} = 2$ Hz; $\delta_{31p} = -112.8$ ppm (measured in H_2O with 80% H_3PO_4 as external standard).



(1) *cis*-*(2)* *cis*-*(3)*

Since the configuration at the phosphorus atom is unchanged during the demethylation, and addition of sulfur proceeds stereospecifically with retention of configuration [3], the thiophosphate *(3)* obtained is the *cis* isomer.

Further, we have found that the tetramethylammonium salt of the *cis* acid *(3)* can also be prepared by reaction of trimethylamine in benzene with the 1:1 mixture of the isomeric thiophosphates *(2)* [4]. Practically only *cis*-*(3)* precipitates from the reaction solution after *ca.* 8–10 hours at room temperature; it can be purified by a single recrystallization from *n*-propanol/acetone. Unreacted *trans*-*(2)* can be isolated from the filtrate by evaporation and subsequent distillation.

As a result of this investigation we have been able to assign the NMR values of the *cis* and *trans* forms of compounds *(2)*. *cis*-*(2)*: $\delta_{CH_3} = 1.41$ ppm; $\delta_{OCH_3} = 3.82$ ppm (at 100 MHz, measured in $CDCl_3$ with TMS); $\delta_{31P} = -148.6$ ppm (measured in ether). *trans*-*(2)*: $\delta_{CH_3} = 1.39$ ppm; $\delta_{OCH_3} = 3.75$ ppm (at 100 MHz, measured in $CDCl_3$ with TMS); $\delta_{31p} = 141.4$ ppm (measured in ether).

The difference in the reactivity of the two isomeric forms of *(2)* toward trimethylamine is probably due to the presence of the methyl group on C-4, which sterically hinders attack of the amine on the methoxy group of the *trans*-thiophosphate *(2)*.

Received: April 2, 1969 [Z 992b IE]
German version: Angew. Chem. *81*, 495 (1969)

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[**] Geometric Isomerism in Cyclic Monothiophosphoric Acids, Part 2. – Part 1: [1].

[1] *M. Mikołajczyk* and *H. M. Schiebel*, Angew. Chem. *81*, 494 (1969); Angew. Chem. internat. Edit. *8*, 511 (1969).

[1a] We designate the thiophosphoric acid having the methyl group and sulfur atom *cis* to each other as the *cis* acid. The more stable form of *(1)* has the "cisoid" conformation.

[2] *D. Z. Denney* and *D. B. Denney*, J. Amer. chem. Soc. *88*, 1830 (1966).

[3] a) *W. E. McEwen*, Topics in Phosphorus Chemistry *2*, 1 (1965); b) *G. Aksnes*, *R. Eriksen*, and *K. Mellingen*, Acta chem. scand. *21*, 1028 (1967); c) *G. Bentrude*, *J. H. Hargis*, and *P. E. Rusek*, Chem. Commun. *1969*, 296.

[4] This mixture occurs in the reaction of 2-chloro-4-methyl-1,3,2-dioxaphosphorV-inane-2-thione with sodium methoxide in methanol.

Pulse Radiolysis at High Pressure: Pressure Dependence of the Absorption Spectrum and the Lifetime of Hydrated Electrons [**]

By *U. Schindewolf*, *H. Kohrmann*, and *G. Lang* [*]

The physical and chemical properties of solvated electrons in liquid ammonia [1] (electrical conductivity [2], absorption [3], reflection [4], and ESR spectrum [5], physical [6] and chemical equilibria [7]) show a marked dependence upon pressure. Solvated electrons produced in metal-ammonia solutions by dissociation of the metal react only slowly with the solvent and have a long lifetime (months).

In order to carry out comparative studies of the influence of pressure on hydrated electrons [8], *i.e.* electrons dissolved in water, these electrons must be produced under pressure and fast-registering methods must be available for their detection owing to their fast reaction with water (lifetime <1 ms).

We have now succeeded in measuring the pressure dependence of the absorption spectrum and the lifetime of hydrated electrons produced by radiolysis of aqueous solutions by high-energy electrons from a pulsed linear electron accelerator (up to 300 pulses of 5-μs duration per second; 15 MeV, 0.5 A). Irradiation was performed in a high-pressure cell [9] (wall thickness 2.5 mm) placed in the crossed beam paths of the accelerator and of a spectrophotometer having a photocathode detector.

The radiation-induced ionization of water gives rise to hydrated electrons,

$$H_2O \rightarrow H_2O^+ + e^- \qquad (1)$$

which react with added substrates, with other radiolysis products (H^+, OH, H, *etc.*), and with water itself. The "bimolecular" reaction with water yields hydrogen ($k \approx 10^{10}$ l/mole sec) [8]

$$2\,e^- + 2\,H_2O \rightarrow H_2 + 2\,OH^- \qquad (2)$$

and limits the lifetime of the electrons, even in the absence of any other reactive substances. To study this reaction alone, the other radiolysis products are intercepted with hydrogen and hydroxide ions [8] (stock solution: 0.01 M NaOH, saturated with hydrogen under normal pressure):

$$H_2O^+ \rightarrow H^+ + OH \qquad (3)$$

$$H^+ + OH^- \rightarrow H_2O \qquad (4)$$

$$OH + H_2 \rightarrow H_2O + H \qquad (5)$$

$$H + OH^- \rightarrow H_2O + e^- \qquad (6)$$

The yield of hydrated electrons is actually doubled by reaction (6). Since the electrons in solution only react with water according to reaction (2) – provided that no impurities are present – and the reactions (1) to (6) balance one another, the solution undergoes no permanent change on irradiation.

Following a pulse of electrons, the transmittance of the solution in the range of about 0.4 to 1.0 μm is reduced, owing to the direct and delayed formation of hydrated electrons, for a period of up to 50 μs, after which it returns to the value for the non-irradiated solution within 1 ms as a result of reaction (2) (in all previous experiments performed in steel autoclaves, a first order reaction involving an undefined impurity was superposed upon reaction (2), which is second order with respect to the electrons).

The variation with wavelength of the optical density of the solution (proportional to $\varepsilon \times c_{e^-}$) yields the absorption spectrum of the hydrated electrons. The time dependence of the concentration of electrons, and thus their rate of reaction, can be deduced from the time-dependence of the optical density.

a) *Pressure dependence of the absorption spectrum*

In Fig. 1, the relative optical density of the solutions, extrapolated back to the time of pulse termination, at 1 and at 1000 atm pressure is plotted against the wavelength. The

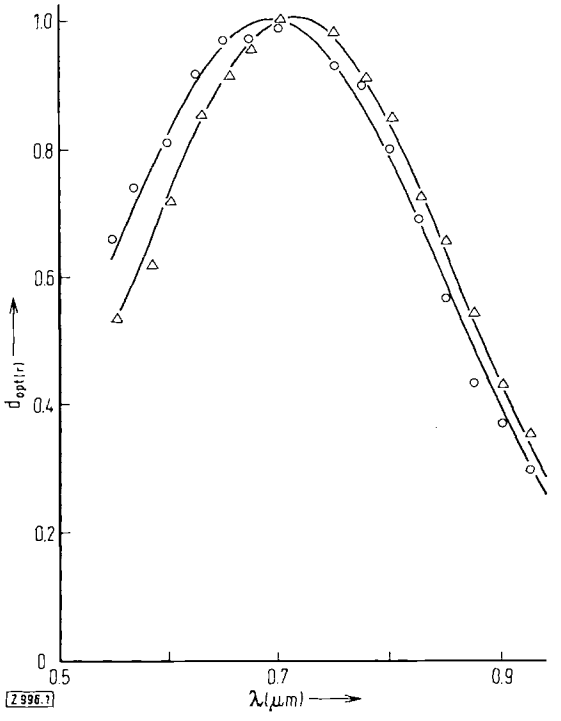


Fig. 1. Absorption spectrum of hydrated electrons at 24 °C and 1 atm (Δ) and 1000 atm (○). The points shown are mean values of five individual measurements.

1000-atm curve is normalized to the 1-atm curve. Both curves were calculated from the measured points by the method of least squares, assuming a Gaussian form.

In agreement with the data given in the literature[8] the absorption maximum of the 1-atm spectrum lies at 0.72 μm; that of the 1000-atm curve is shifted by 200 ± 50 Å towards the blue end of the spectrum. According to *Jortner*'s cavity model[10], this blue shift, which we have also found for solvated electrons in ammonia[3,4] and which must be considered in conjunction with the red shift with increasing temperature[1,3,4,8], can be interpreted as a compression of the space occupied by the dissolved electrons.

Fig. 1 shows that the product of ε_{max} and c_{e^-} is independent of pressure within the limits of experimental accuracy. Since the investigations by *Hentz et al.*[11], who studied the yield of stable radiolysis products on γ-irradiation of aqueous solutions under pressure, show the radiolysis yield of hydrated electrons to be independent of pressure, it follows that their maximum extinction coefficient must also be independent of pressure.

b) *Pressure dependence of the rate of reaction*

Fig. 2 shows the variation with time of the relative optical density (proportional to c_{e^-}) at 1 and 1000 atm, in each case for the wavelength of maximum absorption. Within the limits of experimental accuracy, the measured points for both pressures lie on one curve, thus demonstrating that the rate of reaction, or the mean lifetime of the hydrated electrons, with regard to reaction (2) – and with regard to the reaction with the unidentified impurity – is independent of pressure, *i.e.* that the activation volume of these reactions is vanishingly small. These direct measurements of the rate of reaction under pressure confirm the results obtained by *Hentz*[11] by indirect methods.

In a number of preliminary measurements[12] on the extremely slow reaction between solvated electrons and water in liquid ammonia (20% H_2O, 80% NH_3; lifetime of electrons in the order of 10 s to 1 min; activation energy <3 kcal/mole) we have found that an increase in pressure of 1000 atm causes a three- to fourfold acceleration of the reaction, corresponding to an activation volume of about −25 ml/mole. The difference in the pressure dependence of the reaction rate in water and

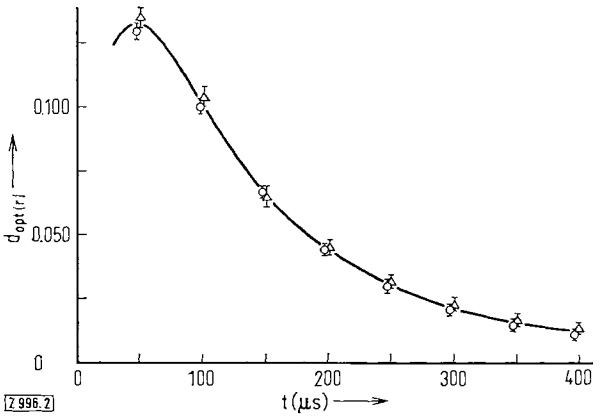


Fig. 2. Variation of the optical density of an aqueous solution with time after irradiation with a pulse of electrons at 24 °C and 1 atm (Δ) and 1000 atm (○). The points shown are mean values of five individual measurements.

in ammonia reflect the different space requirements of solvated electrons in these two solvents (<20 ml/mole in water, 60 to 90 ml/mole in ammonia).

Received: May 12, 1969 [Z 996 IE]
German version: Angew. Chem. *81*, 496 (1969)

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We wish to thank the Institut für Strahlentechnologie of the Bundesanstalt für Lebensmittelfrischhaltung for placing the linear accelerator at our disposal and *M. Rudolf* for operating it.

[1] For a review see *U. Schindewolf*, Angew. Chem. *80*, 165 (1968); Angew. Chem. internat. Edit. *7*, 190 (1968), and further literature cited there.

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[9] *U. Schindewolf, G. Lang*, and *H. Kohrmann*, Chemie-Ing.-Techn., in press.

[10] *J. Jortner*, J. chem. Physics *30*, 839 (1959); Radiat. Res. Suppl. *4*, 24 (1964); *J. Jortner, S. A. Rice*, and *E. G. Wilson* in *G. Lepoutre* and *M. J. Sienko*: Solutions Métal-Ammoniac. Benjamin, New York 1964, p. 222.

[11] *R. R. Hentz, Farhataziz*, and *D. J. Milner*, J. chem. Physics *47*, 4865 (1967).

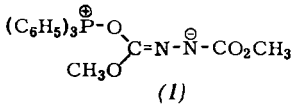
[12] *U. Schindewolf* and *R. Olinger*, Paper read to the 68th Meeting of the Bunsen Gesellschaft at Frankfurt, 1969.

Structure and Reactivity of the Betaine Derived from Triphenylphosphine and Dimethyl Azodicarboxylate[**]

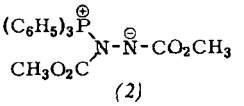
By *E. Brunn* and *R. Huisgen*[*]

The reaction of triphenylphosphine with dimethyl azodicarboxylate has repeatedly been interpreted[1–3] as a nucleophilic attack on the carbonyl oxygen of the ester as shown in

(1). We consider that the chemical properties of the labile adduct, which is usually subjected to further reaction *in situ*, are more nearly consistent with the original formulation *(2)*[4]; moreover, such a formulation corresponds to the known high electrophilic activity of the nitrogen of dimethyl azodicarboxylate[5]. The quasi-1,3-dipole *(2)* can be intercepted by cycloaddition processes. The fact that only strongly electrophilic dipolarophiles prove suitable for this reaction suggests a multi-step mechanism initiated by attack on the anionic nitrogen atom of *(2)*.

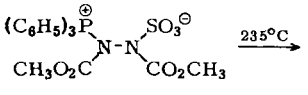


(1)

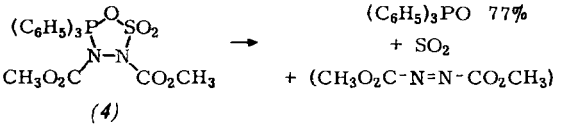


(2)

Distillation of sulfur trioxide into a solution of *(2)* in 1,2-dichloroethane affords the adduct *(3)*, m.p. 195.5–197 °C (decomp.), in 82% yield; IR (KBr): ester carbonyl = 1740 and 1721 cm^{-1}; ^{31}P-NMR ($CDCl_3$): −53 ppm. Thermolysis is in accord with the following scheme involving *(4)* as intermediate. Cleavage of *(3)* by boiling water gives triphenylphosphine oxide and sulfate ion.

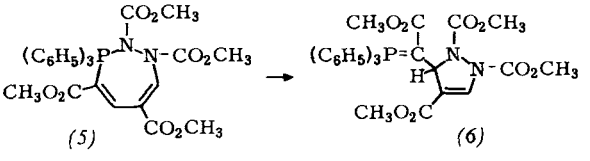


(3)



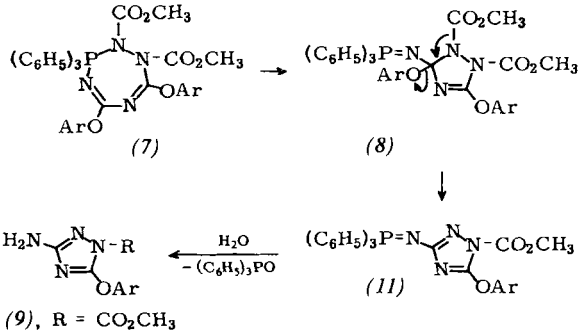
(4)

The quasi-1,3-dipole *(2)* reacts with 2 equivalents of methyl propiolate to give the heterocyclic methylenephosphorane *(6)* in 58% yield, which is presumably formed *via* ring contraction from a cycloadduct *(5)* having a seven-membered ring. The ^{31}P resonance signal at −21.5 ppm ($CHCl_3$) and the broadening of the OCH_3 signal (τ = 6.74) of the ester group attached to the ylide carbon atom (slow interconversion of *cis-trans* isomeric forms[6]) provide support for *(6)*; m.p. 201–202 °C (decomp.); the ^{1}H-NMR signal of the

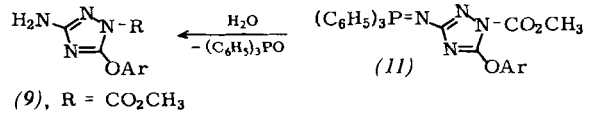


(5) *(6)*

proton in the β position to the phosphorus at τ = 4.91 shows J_{PH} = 12.0 Hz and an allylic coupling of J_{HH} <1 Hz. Acetolysis of *(6)* at 100 °C proceeded *via* elimination of CO_2 to give methoxycarbonylmethylenetriphenylphosphorane (81%) and dimethyl 1,4-pyrazoledicarboxylate (m.p. 122.5–124 °C,



(7) *(8)*



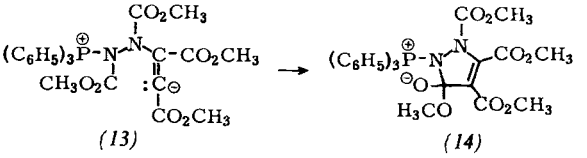
(9), R = CO_2CH_3
(10), R = H

+ ArO-CO_2CH_3 *(12)*

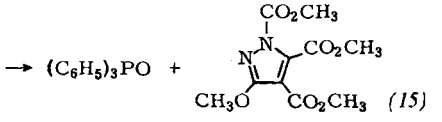
Ar = 2,4-Dimethyl-phenyl

68%), which was identified by alkaline degradation to 4-pyrazolecarboxylic acid.

Reaction of *(2)* with 2,4-dimethylphenyl cyanate[7] also resulted in consumption of two equivalents of the latter. We suppose that an analogous initial addition to *(7)* occurs. The ring-contraction product *(8)* is not isolable but eliminates the methyl aryl carbonate *(12)* (66%, b.p. 120–130 °C (bath temp.)/10 torr) to give the triazolyliminophosphorane *(11)*; 72%, m.p. 164–165 °C; IR (KBr): CO_2CH_3 = 1754 cm^{-1}; ^{31}P-NMR ($CDCl_3$): −18.5 ppm. Treatment with hot 90% acetic acid converts *(11)* into triphenylphosphine oxide and *(9)* [76%, m.p. 177–178.5 °C (decomp.)]. Compound *(10)* (m.p. 140.5–142 °C), produced on alkaline hydrolysis of *(9)*, was synthesized by an independent route.

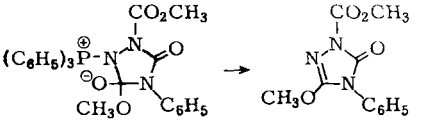


(13) *(14)*

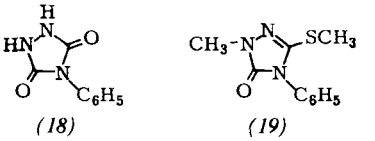


(15)

Surprisingly, *(2)* reacted with only one equivalent of dimethyl acetylenedicarboxylate. We isolated a 71% yield of trimethyl 3-methoxy-1,4,5-pyrazoletricarboxylate *(15)* (m.p. 141 to 142 °C), which may possibly be formed *via* elimination of phosphine oxide from *(13)*. The magnetic non-equivalence of the *O*-methyl groups (in $CDCl_3$, τ = 5.89, 5.91, 5.96, 6.13) supports the chemical evidence obtained by *Cookson* and *Locke*[2] for the analogous pyrazole derivative obtained from *(2)*, C_2H_5 instead of CH_3, and dimethyl acetylenedicarboxylate.



(16) *(17)*

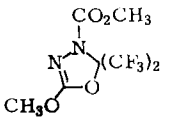


(18) *(19)*

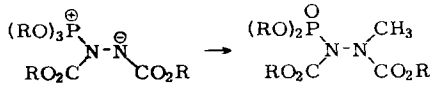
Like dimethyl acetylenedicarboxylate, isocyanates and isothiocyanates react with one equivalent of *(2)* at room temperature. From the reaction with phenyl isocyanate we obtained 1,2,4-triazolone *(17)* (80%) along with triphenylphosphine oxide. The structure of *(17)* (m.p. 168–170 °C; ^{1}H-NMR ($CDCl_3$): OCH_3 s τ = 5.90, 5.97) was established by conversion into 4-phenylurazole *(18)*. Methyl isocyanate and *p*-phenylene diisocyanate gave products analogous to *(17)* in yields of 73 and 68%, respectively.

Phenyl isothiocyanate combined with *(2)* to give 1,2,4-triazolinethione [*(17)*, =S in place of =O] in 71% yield; m.p. 152–153 °C, ^{1}H-NMR ($CDCl_3$): OCH_3 s τ = 5.93, 5.88. Alkaline hydrolysis afforded 5-methoxy-4-phenyl-1,2,4-triazoline-3-thione, whose composition was proved by synthesis of a degradation product. Thermolysis at 200 °C yielded *(19)* *via* elimination of CO_2 and a shift of two methyl groups. In a similar manner, reaction of methyl isothiocyanate and allyl isothiocyanate with *(2)* proceeded by way of phosphine-oxide elimination to give adducts.

Hexafluoroacetone reacted with *(2)* at −40 °C to give triphenylphosphine oxide (86%) and an adduct of probable structure *(20)* (75%).



(20)



(21) (22)

An oily adduct obtained from triethyl phosphite and diethyl azodicarboxylate was regarded by *Morrison*[4] as *(22)*, whereas *Ginsburg et al.*[1] suggested an alternative structure. Interception of the precursor *(21)* by a cycloaddition process provides evidence in favor of *(22)*. On slow addition of dimethyl azodicarboxylate to trimethyl phosphite and phenyl isocyanate in benzene, we were able to isolate *(17)* in 84% yield; the reaction probably proceeds *via* an intermediate analogous to *(16)* having OCH_3 instead of C_6H_5 attached to the phosphorus.

Received: May 23, 1969 [Z 1 IE]
German version: Angew. Chem. *81*, 534 (1969)

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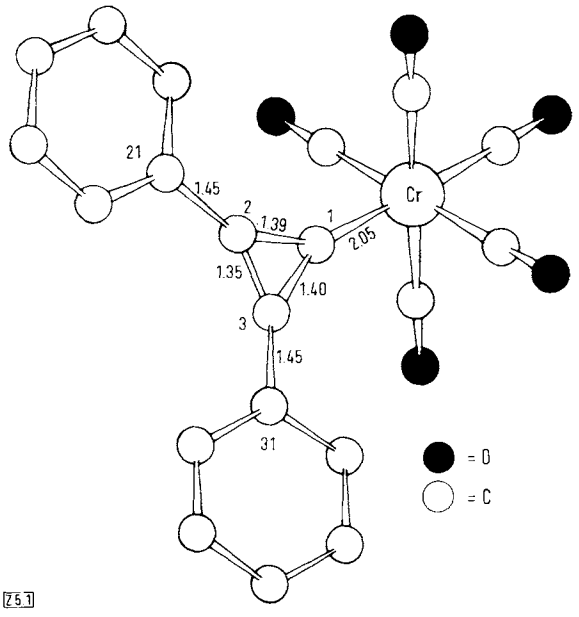
The Crystal Structure of Pentacarbonyl-(2,3-diphenylcyclopropenylidene)chromium(0) [**]

By *G. Huttner, S. Schelle*, and *O. S. Mills*[*]

We have determined the crystal structure of pentacarbonyl-(2,3-diphenylcyclopropenylidene)chromium(0), recently prepared by *Öfele*[1], in an attempt to understand the unusual bonding in this remarkably stable complex.

The compound crystallizes in the triclinic system, space-group $P\bar{1}$ (C_i^1, No. 2) with $a = 13.31$, $b = 9.25$, $c = 9.93$ Å, $\alpha = 91.3$, $\beta = 104.2$, and $\gamma = 129.2°$, $d_m = 1.427$, $d_c = 1.423$ gcm^{-3}, $Z = 2$. The intensities of 1976 reflexions were measured, with molybdenum radiation ($\lambda = 0.71069$ Å), on a Stoé automatic Weissenberg diffractometer. The structure was solved by conventional Patterson and Fourier methods. At present, the agreement index, after partial refinement of anisotropic temperature factors, is R = 0.086.

Pentacarbonyl(2,3-diphenylcyclopropenylidene)chromium(0) is the first mononuclear carbene complex in which the carbene ligand is not stabilized by heteroatom substitution. The chromium atom is coordinated octahedrally (Fig. 1). Five of the positions are occupied by CO groups ($Cr-C_{CO}$ 1.88–1.92 Å, C–O 1.10–1.15 Å) and the sixth by the 2,3-diphenylcyclopropenylidene fragment. The Cr–C distance, 2.05 ± 0.01 Å, is appreciably shorter than that expected for a single bond between Cr^0 and a sp^2-hybridized carbon (2.21 Å)[2] and indicates appreciable double-bonding.



Z 5.1

Fig. 1. Crystal structure of pentacarbonyl(2,3-diphenylcyclopropenylidene)chromium(0).

The distances C^2-C^{21} and C^3-C^{31} (Fig. 1) are somewhat shorter than the single-bond separation between two sp^2-hybridized carbon atoms (1.48 Å)[3]. One of the phenyl rings lies in the plane of the three-membered ring whilst the other is twisted out of this plane by 7.5°, presumably by repulsions of the phenyl *ortho*-hydrogens.

The mean C–C distance in the three-membered ring is not significantly different from that found for the aromatic triphenylcyclopropenylium cation (1.37 Å)[4]. However, whereas all the distances in the aromatic three-membered ring are equal within experimental error, in the complex the C^1-C^2 and C^1-C^3 separations are somewhat different from C^2-C^3. This difference is probably significant and points to a small distortion of the ring towards a cyclopropene system. This observation is also in accord with the suggestion of double-bond character in the $Cr-C^1$ bond.

Received: April 15, 1969 [Z 5 IE]
German version: Angew. Chem. *81*, 536 (1969)

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[**] We wish to thank the Bayerische Akademie der Wissenschaften for permission to use the computer installations at the Leibniz Rechenzentrum, München.

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Diphenylborane Derivatives Containing Boron-Tin Bonds

By *H. Nöth, H. Schäfer*, and *G. Schmid*[*]

Whereas bis(dimethylamino)trialkylstannylboranes are accessible from R_3SnLi (R = alkyl) and $ClB[N(CH_3)_2]_2$[1], the synthesis of dialkyl- and diphenyl-trialkylstannylboranes

could not be accomplished by this method. No boron-tin compounds could be detected on reaction of $(C_6H_5)_3SnLi$ with BCl_3, $RBCl_2$, and R_2BCl; instead, hexaphenyldistannane was identified as the main reaction product.

Bis(diphenylboro)bis(tetraphenyldiphosphinoethane)-cobalt(II) [2, 3] has proved a suitable reagent for the introduction of diphenylboryl groups into inorganic and organic compounds. It reacts with methyltin chlorides or bromides according to equation (1) to give the methylstannyldiphenylboranes *(1)–(3)* (see Table) in 60–80% yield and thus permits the formation of several Sn–B bonds in one molecule. Reaction with $SnBr_4$ affords tetrakis(diphenylboryl)stannane *(4)*.

$$\frac{n}{2}\ Ph_2B\text{–}[Co]\text{–}BPh_2 + (CH_3)_{4-n}SnX_n \rightarrow \frac{n}{2}\ [Co]X_2 + (CH_3)_{4-n}Sn(BPh_2)_n \quad (1)$$

X = Cl, Br; Ph = C_6H_5;
[Co] = $[(C_6H_5)_2P\text{–}CH_2\text{–}CH_2\text{–}P(C_6H_5)_2]_2Co$

The colorless crystalline compounds are of low thermal stability and are extremely sensitive to oxygen. They react rapidly even with traces of oxygen to give tetraphenyldiboron oxide and the corresponding stannoxanes *via* intermediates containing Sn–O–B bonds. Degradation with bromine yields diphenylboron bromide and $(CH_3)_{4-n}SnBr_n$.

The magnetic equivalence of all the B atoms in the molecules *(1)–(4)* can be deduced from the single broad ^{11}B resonance signal, whose almost constant position shows that the boron atoms are exposed to a similar shielding in all four compounds, which is determined mainly by the phenyl groups. The area ratio of the proton resonance signals are in good agreement with the calculated intensities. The signals of the CH_3 groups in *(1)–(3)* are shifted upfield compared to the corresponding signals of the methyltin chlorides.

Table: Characteristic data for diphenylborylstannanes.

	M.p. (°C)	$\delta^{11}B$ (ppm) [a]	δCH_3Sn (ppm) [b]	δC_6H_5 (ppm) [b]	Yield (%)
$(CH_3)_3SnB(C_6H_5)_2$ *(1)*	110–115 (decomp.)	−66	−0.22	−7.28	61
$(CH_3)_2Sn[B(C_6H_5)_2]_2$ *(2)*	118–121 (decomp.)	−67	−0.57	−7.26	79
$CH_3Sn[B(C_6H_5)_2]_3$ *(3)*	112–118	−68	−1.15	−7.38	69
$Sn[B(C_6H_5)_2]_4$ *(4)*	119–124	−66	–	−7.19	76

[a] In benzene, $BF_3{\cdot}OR_2$ as external standard.
[b] In cyclohexane, $Si(CH_3)_4$ as external standard.

Tetrakis(diphenylboryl)stannane (4):

$[(C_6H_5)_2PCH_2CH_2P(C_6H_5)_2]_2Co[B(C_6H_5)_2]_2$ (6.41 g) is treated with $SnBr_4$ (1.18 g) in 100 ml of anhydrous benzene under highly pure nitrogen or argon for four hours with stirring; $[(C_6H_5)_2PCH_2CH_2P(C_6H_5)_2]_2CoBr_2$ (5.3 g) is then filtered off and the solvent removed under vacuum. Compound *(4)* is extracted from the residue by stirring for eight hours with cyclohexane (50 ml). The product is recrystallized from the same solvent.

Received: April 15, 1969 [Z 4 IE]
German version: Angew. Chem. *81*, 530 (1969)

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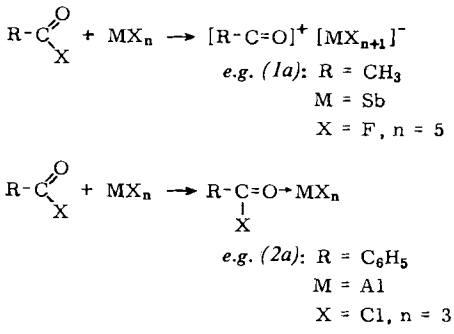
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Existence of the Oxalyl Dication $[C_2O_2]^{2+}$ [1]

By *M. Adelhelm* [*]

Reaction of acyl halides RCOX with Lewis acids MX_n can lead to two different products [2–4]:



X-ray analysis has established the structures of the representatives *(1a)* and *(2a)* [5] of both types of compounds, *i.e.* of the oxocarbonium (or acylium) salt *(1)* and the adduct *(2)*. Compounds *(1)* and *(2)* can also be distinguished by means of their CO bands in the vibrational spectra, which show a characteristic shift compared to the free acyl halide [3,4,6]. Thus the CO stretching vibration of *(1a)* is observed at 2294 cm^{-1} [7] and that of *(2a)* at 1548 cm^{-1} [4], corresponding to an increase and a decrease of the CO bond order, respectively.

We have attempted to prepare the oxalyl dication, an interesting species owing to its bonding, and to examine it by vibrational spectroscopy. It is the simplest representative of the "acyl dications", which were first described by *Olah* and *Comisarow* [8].

It proved expedient to carry out the reaction between oxalyl chloride and antimony pentafluoride directly in an IR low-temperature cell of the usual type [9]. Thin films of $C_2O_2Cl_2$ and an excess of SbF_5 were condensed onto the inner cell plate (AgCl) [10], which was cooled with liquid air. The dotted curve in Figure 1 reproduces the infrared spectrum measured at this stage [11]: it arises by superposition of the individual spectra of the unchanged starting materials. Gradual increase of the temperature to −35 °C initiates the reaction, as is evidenced by the appearance of small gas bubbles on the plate. After cooling to about −50 °C (to avoid decomposition), the spectrum represented by the continuous line in Figure 1 was recorded. By turning the AgCl plate out of the beam path the gaseous product could be identified spectroscopically as COFCl with traces of CO (and COF_2?) (see dashed curve in Figure 1). After the gases had been pumped off, the spectrum of the solid, colorless reaction product was recorded at −78 °C (Figure 2).

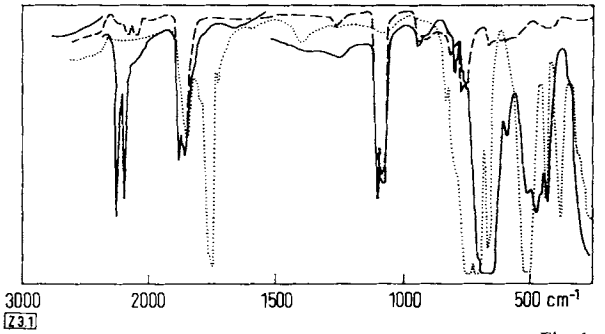


Fig. 1.

The absorptions in the CO-triple bond region at 2235 and 2182 cm^{-1} indicate an oxocarbonium structure *(1)*. On warming, both bands decreased irreversibly in intensity – that at 2235 cm^{-1} particularly rapidly – owing to formation of COFCl. The varying intensity ratio of these two bands indicated two species of different stability in the solid. Since

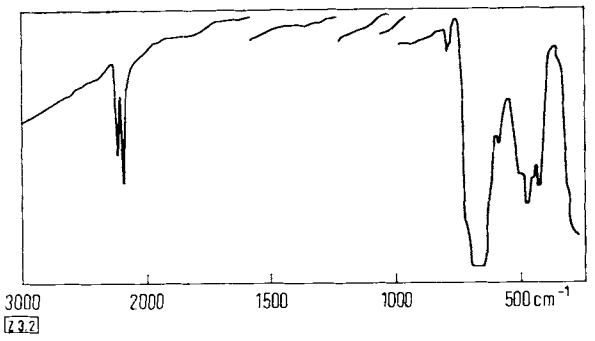


Fig. 2.

only one CO band can be attributed to each one of these species, they must be highly symmetrical ions that form COFCl with the counter-ions at elevated temperatures. The spectra can be interpreted in terms of the following reaction scheme:

$$C_2O_2Cl_2 + 2\,SbF_5 \rightarrow [C_2O_2]^{2+}\,2\,[SbF_5Cl]^-$$
$$\nu_{as}CO = 2235\ cm^{-1}$$

$$[C_2O_2]^{2+} \longrightarrow 2\,[CO]^+$$
$$\nu_{as}CO = 2235\ cm^{-1} \qquad \nu CO = 2182\ cm^{-1}$$

$$[C_2O_2]^{2+}\ 2[SbF_5Cl]^- \searrow$$
$$2\,COFCl + [SbF_3 \cdot SbF_5]$$
$$2\,[CO]^+[SbF_5Cl]^- \nearrow$$

The initially formed oxalyl dication $[C_2O_2]^{2+}$ is stable at low temperature ($< -50\,°C$). It decomposes with cleavage of the CC bond into radical ions $[CO]^+$, and COFCl is formed *via* a redox reaction with the anionic component.

The surprising dissociation of *(3)* into radical ions

$$:\overset{+}{O}\equiv C-C\equiv\overset{+}{O}: \leftrightarrow \ddot{O}=\overset{+}{C}-\overset{+}{C}=\ddot{O}$$

(3)

is probably a result of the double positive charge and is paralleled in the pseudohalogen character of the isoelectronic cyanogen. The wave number of the free $[CO]^+$ is known from the band spectrum to be 2183.9 cm^{-1} [12].

The existence of the anion formulated as $[SbF_5Cl]^-$ and its reaction products have not yet been proved because no suitable spectra are available for comparison; the situation is also complicated by the presence of an excess of SbF_6.

The antisymmetric stretching vibration of the linear $[C_2O_2]^{2+}$ is consistent with those of comparable molecules. $\nu_{as}C\equiv X$ (cm^{-1}): $HC\equiv C-C\equiv CH$, 2020; $N\equiv C-C\equiv N$, 2149; $[O\equiv C-C\equiv O]^{2+}$, 2235.

Received: April 2, 1969 [Z 3 IE]
German version: Angew. Chem. *81*, 530 (1969)

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The Tribromine Cation in $[Br_3]^+[AsF_6]^-$

By *O. Glemser* and *A. Šmalc* [*]

The dibromine cation $[Br_2]^+$ has recently been produced by reaction of bromine pentafluoride, bromine, and antimony pentafluoride, and isolated in the form of $[Br_2]^+[Sb_3F_{16}]^-$ [1]. In contrast, the tribromine cation $[Br_3]^+$ has hitherto only been detected in solution [2]. By reaction of dioxygenyl hexafluoroarsenate(v) with bromine

$$[O_2]^+[AsF_6]^- + 3/2\ Br_2 \rightarrow [Br_3]^+[AsF_6]^- + O_2$$

and by reaction of bromine trifluoride or pentafluoride, bromine, and arsenic pentafluoride we have now succeeded for the first time in obtaining $[Br_3]^+$ as $[Br_3]^+[AsF_6]^-$. The composition of the compound, which is chocolate brown at room temperature and carmine red at the temperature of liquid nitrogen, was determined as the mean value of ten analyses. The substance sublimes at +30 to +50 °C; under nitrogen (1 atm) it decomposes above 70 °C with evolution of bromine.

The mass spectrum exhibits the following fragments: (*m/e*): 162, 160, 158 Br_2^+ (49.4, 100.0, 52.7%); 151 AsF_4^+ (59.3%); 132 AsF_3^+ (10.4%); 113 AsF_2^+ (13.2%); 100, 98 BrF^+ (11.5, 12.1%); 94 AsF^+ (6.6%); 81, 79 Br^+ (38.5, 39.6%); 75 As^+ (5%); 40.5, 39.5 Br^{2+} (3.3, 3.3%) [3].

IR spectrum (film of substance condensed directly onto the AgCl plates of a low temperature cell): In the 4000–400 cm^{-1} region, the strong band characteristic of $[AsF_6]^-$ was observed at 709 cm^{-1} (ν_3).

^{19}F-NMR spectrum (solution in BrF_5, CCl_3F as external standard): A broad signal at 62.5 ppm that is assigned to the $[AsF_6]^-$ ion (unresolved quadruplet; strong line broadening due to the quadrupole moment of As).

UV spectrum (solution in HSO_3F): Two bands are observed at 310 and 375 nm, which are ascribed to the $[Br_3]^+$ cation in solution [2].

Magnetic measurements: The expected diamagnetism was confirmed on a magnetic balance; solid Br_3AsF_6 did not give an ESR spectrum.

Procedure:

BrF_5 (19 g) and Br_2 (4.7 g) are condensed into a quartz vessel together with AsF_5 (5 g, 29% excess) at −196 °C. After permitting the reaction mixture to reach a temperature of −50 °C, the excess of BrF_5 and AsF_5 is pumped off, first for 1/2 h at −50 °C and then for 1–2 h at 0 °C. The reaction proceeds almost quantitatively to give 9.0 g of $[Br_3]^+[AsF_6]^-$.

Received: April 23, 1969 [Z 6 IE]
German version: Angew. Chem. *81*, 531 (1969)

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Oxidative Dimerization of Olefins[1]

By *H. Schäfer* and *E. Steckhan*[*]

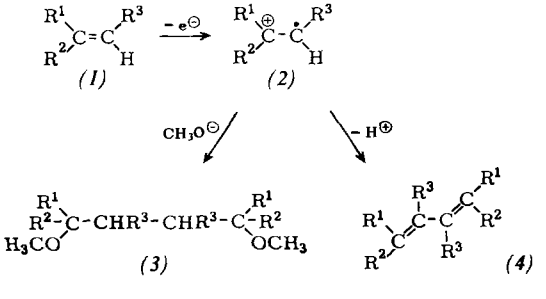
Organic anions, for example alkali metal salts of aliphatic nitro or 1,3-dicarbonyl compounds, undergo oxidative addition to non-activated double bonds at a platinum anode[2,3]. We have now found that such additions are almost completely suppressed at graphite electrodes; instead, the dimers of the olefins present are formed. Electrolysis of olefin/methanol mixtures (2:3 v/v) between graphite electrodes with sodium iodide or sodium perchlorate/sodium methoxide as conducting salt at anode potentials between +0.5 and +1.4 V (measured against Ag/AgCl) and temperatures between −20 and +20 °C we obtained the products listed in the Table[4].

Olefin	Product [a]	Yield (%) [b]
Styrene	1,4-Diphenyl-1,4-dimethoxybutane	60
Vinyl ethyl ether	1,4-Diethoxy-1,4-dimethoxybutane	51
α-Methylstyrene	1,4-Diphenyl-1,4-dimethylbutadiene	45
Butadiene	*trans,trans*-1,8-Dimethoxy-2,6-octadiene	13
	trans-1,6-Dimethoxy-2,7-octadiene	13
	3,6-Dimethoxy-1,7-octadiene	13
	trans,trans-1,10-Dimethoxy-2,6,11-dodecatriene	6.6
	all-trans-1,12-Dimethoxy-2,6,10-dodecatriene	5.5
1-Ethoxy-1-cyclohexene	2,2'-Bicyclohexanone [c]	27
Indene	1,1'-Dimethoxy-2,2'-bisindanyl [d]	38

[a] The products were characterized by IR, ^{1}H-NMR, and mass spectrometry, and C, H analyses, or by comparison with authentic material.— [b] Based on current consumption. — [c] After acid hydrolysis of the crude product. — [d] In addition to 19% of 1,2-dimethoxyindan.

By simultaneous linkage of two carbon atoms and introduction of substituents or double bonds this oxidative dimerization of olefins affords derivatives of 1,4-dimethoxybutane and butadiene in one step. Furthermore, aldehydes or ketones can be coupled *via* the enol ethers to give 1,4-dicarbonyl compounds[5].

We assume the oxidation of the olefin *(1)* to a radical cation *(2)* to be the initial step, the lone electron and the positive charge in unsymmetrical olefins being localized in such a manner that the cation experiences the greater stabilization by substituents. The butane derivatives *(3)* and *(4)* are formed from *(2)* by dimerization of two radicals and S_N1 and E_1 reaction of the carbonium ions, respectively. With butadiene the isomeric octadiene derivatives are formed by methanolysis of the allyl cations in positions 1 and 3; 1,4-addition of *(2)* to butadiene leads to the dodecatrienes.



1,4-Diethoxy-1,4-dimethoxybutane:

A solution of NaI (1.4 g) in methanol (120 ml) and vinyl ethyl ether (80 ml) is electrolyzed between graphite electrodes[6] at −5 °C, a current density of 40 mA/cm², and an anode potential of +0.6 to +0.9 V (measured against Ag/AgCl) in a cell without diaphragm until 0.232 Faraday has been consumed. After removal of the solvent by distillation, water (20 ml) is added to the residue which is then extracted with ether, the extract being worked up in the usual way. Distillation affords 1,4-diethoxy-1,4-dimethoxybutane (yield 12.3 g, b.p. 93–95 °C/14 torr). ^{1}H-NMR spectrum: δ (ppm measured against TMS): 4.3 (broadened triplet, 1 H), 3.5 and 3.45 (two q, 2 H); 3.2 (s, 3 H); 1.55 (m, 2 H); 1.18 (t, 3 H). The bisphenylhydrazone shows no lowering of melting point when mixed with the corresponding derivative of succinic dialdehyde.

Received: April 16, 1969 [Z 9 IE]
German version: Angew. Chem. *81*, 532 (1969)

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A New Method for the Formation of S–S Bonds

By *E. Lindner* and *G. Vitzthum*[*]

Reaction of mononuclear carbonyl complexes of metals of Groups VI and VIII with organosulfenyl chlorides in polar solvents yields organic disulfides:

$$M(CO)_n + 2\,RSCl \xrightarrow[THF]{<0°C} MCl_2 + RSSR + n\,CO \qquad (1)$$

[M = Cr, Fe, Ni (n = 6, 5, 4); R = alkyl, aryl, perhaloalkyl]

This new method has an advantage over all previously known techniques[1] in that it is generally applicable and proceeds under particularly mild conditions – below 0 °C – to give high yields (> 90%) of disulfide.

In the case of perchloro- or perbromoalkanesulfenyl chlorides, formation of the S–S linkage is followed by an additional partial dehalogenation of the alkyl groups:

$$2\,\underset{(1)}{CCl_3CCl_2SCl} + \underset{(2)}{Fe(CO)_5} \xrightarrow[THF]{-80°C} \underset{(3)}{Fe(CO)_4Cl_2} + CO + \underset{(4)}{(CCl_3CCl_2)_2S_2} \qquad (2)$$

$$4\,(2) + 3\,(4) \rightarrow 4\,FeCl_3 + 20\,CO + 3\,\underset{(5)}{(CCl_2{=}CCl)_2S_2} \qquad (3)$$

$$4\,(3) + (4) \rightarrow 4\,FeCl_3 + 16\,CO + (5) \qquad (4)$$

If pentacarbonyliron *(2)* is used for reduction of perchloroethanesulfenyl chloride *(1)*, tetracarbonyldichloroiron(II) *(3)* is formed as intermediate and is responsible, together

with the excess of *(2)*, for the dehalogenation of the alkyl groups. Proof that *(3)* is actually formed as intermediate is provided by the reaction of trifluoromethanesulfenyl chloride *(6)* with *(2)* in the absence of a solvent in a sealed tube:

$$(2) + 2\ (6) \xrightarrow{-20\,^{\circ}C} (3) + CF_3SSCF_3 + CO \qquad (5)$$

Owing to the considerably stronger C–F bond, the reaction does not proceed further than the saturated disulfide *(7)* so that compound *(3)* can be detected by elemental analysis and by its IR spectrum.

Bis(trichlorovinyl)disulfide *(5)*, a compound that acts as an insecticide, nematocide, and fungicide, has hitherto been prepared from $(CCl_3CHCl)_2S_2$ and triethylamine[2]; the yield is low if the unsaturated disulfide *(5)* is required in high purity. With our method, the yield of *(5)* is 40% after chromatographic purification [ν(C=C) = 1532 and 1507 cm^{-1}; ν(C–Cl) + ν(C–S) = 975, 882, 865, and 750 cm^{-1} (film)]. It is absolutely essential that polar solvents be employed; in nonpolar solvents, *e.g. n*-heptane, secondary reactions occur. Thus compound *(5)*, formed according to equations *(2)–(4)*, reacts with *(2)* or $Ni(CO)_4$ to give the high-polymeric iron and nickel complexes $[Fe(CO)_2(SCCl{=}CCl_2)_2]_n$[3] and $[Ni(SCCl{=}CCl_2)_2]_n$[4], which were characterized by their elemental analyses and their IR spectra.

Experimental:

Bis(trichlorovinyl) disulfide (5):

A solution of C_2Cl_5SCl (7.3 g, 27 mmoles) in THF (200 ml) is treated with $Fe(CO)_5$ (5.6 g, 28 mmoles) at −80 °C. After eight hours, the THF is removed under vacuum and the residue is taken up in *n*-heptane and filtered (G3). The filtrate *(5)* can be purified by column chromatography on basic Al_2O_3, Activity I (Woelm) with *n*-heptane as eluant.

Bis(trifluoromethyl) disulfide (7):

CF_3SCl (6 ml) is condensed into a solution of $Fe(CO)_5$ (7.3 g, 37.3 mmoles) in THF (75 ml) at −80 °C. After elimination of gas has ceased, the colorless precipitate ($FeCl_2 \cdot 1.5$ THF) is filtered off. Compound *(7)* (b.p. 33–34 °C) can be distilled from the filtrate.

Received: April 25, 1969 [Z 11 IE]
German version: Angew. Chem. *81*, 532 (1969)

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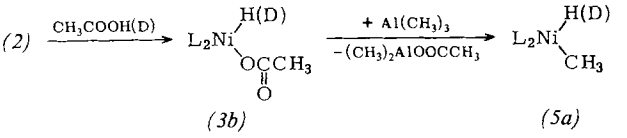
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Hydrido and Alkyl(aryl)hydrido Complexes of Nickel

By *K. Jonas* and *G. Wilke*[*]

Jolly and *Jonas*[1] recently reported on bis[bis(tricyclohexylphosphine)nickel]dinitrogen $(L_2Ni)_2N_2$ (L = $(C_6H_{11})_3P$) *(1)*, the first Ni^0 complex containing molecular nitrogen as ligand. The nitrogen molecule in *(1)* is bonded only weakly to the nucleus; when a stream of argon is passed through a solution of the complex in toluene the nitrogen is released with formation of L_2Ni *(2)*, the deep red color of the original solution changing to a yellowish red.

Reaction of bis(tricyclohexylphosphine)nickel *(2)* with acidic compounds HR such as HCl (a), acetic acid (deuterioacetic acid) (b), phenol (c), pyrrole (d), or cyclopentadiene at room temperature leads to yellow, crystalline hydridonickel complexes having the composition $L_2Ni(H)R$ *(3)*; in the case of cyclopentadiene one of the ligands is replaced to give $LNi(H)C_5H_5$ *(4)*. Compound *(3a)* has also recently been prepared from L_2NiCl_2 and $NaBH_4$[2]. Further reaction of *(3b, c)* with trimethylaluminum or phenyllithium at room temperature yields pale yellow hydridomethyl- or hydridophenyl-bis(tricyclohexylphosphine)nickel, *(5a)* or *(5b)*, respectively, *e.g.*



Compounds *(5a)* and *(5b)* are stable at room temperature.

As is shown by the reaction of *(3b)* with triethylaluminum, no corresponding hydrido ethyl compound is stable at room temperature. β-Elimination of hydrogen leads to loss of ethylene, and the known compound ethylenebis(tricyclohexylphosphine)nickel[3] is formed *via* evolution of H_2 (HD) (exactly 1 mole per g-atom of Ni). Unlike *(3)* and *(4)*, compounds *(5)* are sensitive to light; they turn red and lose CH_4 (CH_3D) and C_6H_6, respectively. Treatment of *(3d)* with deuterioacetic acid affords the acetato hydrido complex *(3b)*; under the same conditions *(5a)* also gives *(3b)* along with the calculated amount of CH_3D.

The IR spectra of the compounds *(3)*, *(4)*, and *(5)* exhibit intense absorption bands (νNi–H) in the region between 1800 and 1940 cm^{-1}; in the corresponding deuterated derivatives *(3b)* and *(5a)* these bands are shifted to longer wavelengths (νNi–D).

$L_2Ni(H,D)R$	R =	νNi–H(D) (cm^{-1}); (KBr)
(3a)	Cl	1910
(3b)	$OOCCH_3$	1920 (νNi–H)
		1360 (νNi–D) masked
(3c)	OC_6H_5	1940
(3d)	NC_4H_4	1910
(5a)	CH_3	1800 (νNi–H)
		1300 (νNi–D)
(5b)	C_6H_5	1805
$LNi(H)C_5H_5$	*(4)*	1920

The ^{1}H-NMR spectrum of *(3a)* contains a triplet at 34.6 τ (J_{P-H} = 73.5 Hz) due to the hydrogen bonded to the nickel[2]. In *(5a)* we have established the presence of a hydrogen atom bonded to the nickel by means of its coupling with the methyl group: deuterated *(5a)* shows a triplet due to the methyl group at 10.6 τ ($J_{P-Ni-CH_3}$ = 6.5 Hz); this appears in the spectrum of the corresponding hydrogen compound *(5a)* showing a twofold splitting at 10.7 τ ($J_{P-Ni-CH_3}$ = 6.6 Hz, $J_{H-Ni-CH_3}$ = 1.6 Hz).

Preparation of (3b) and (5a):

Argon is passed through a solution of *(1)* (3.2 g, 2.5 mmoles) in toluene (80 ml) until the color of the solution changes from dark red to yellowish red. After extensive concentration of the resulting solution under vacuum, addition of a solution of CH_3COOH (0.3 ml, 5 mmoles) in ether (25 ml) precipitates crystals of *(3b)* (2 g, 60%).

$Al(CH_3)_3$ (0.28 ml, 3 mmoles) is added to *(3b)* (2 g, 3 mmoles) in toluene (40 ml) at −30 °C. The mixture is allowed to reach room temperature, 30 ml of toluene is removed under vacuum, 10 ml of ether is added, and the solution is again cooled

to −30 °C. Compound *(5a)* (1.2 g, 65%) precipitates on standing.

Received: April 29, 1969 [Z 14 IE]
German version: Angew. Chem. *81*, 534 (1969)

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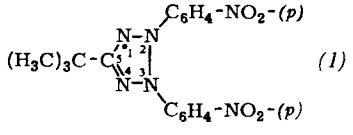
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Crystalline Tetrazolinyl Radical

By *F. A. Neugebauer* [*]

The formation [1], constitution [2], and spin density distribution [3] of the tetrazolinyls, the free-radical intermediates between formazans and tetrazolium salts, have been studied in detail by means of ESR spectroscopic examination of free radical solutions. We have now been able to prepare 5-*tert*-butyl-2,3-bis(4-nitrophenyl)tetrazolinyl, the first tetrazolinyl radical *(1)* to be isolated, by dehydrogenation of 3-*tert*-butyl-1,5-bis(4-nitrophenyl)formazan (m.p. 212–213 °C) with di-*p*-tolylaminyl in benzene at 40 °C; it precipitates from benzene/light petroleum as green-black needles (decomp. 126 – 127 °C).



(1)

The radical *(1)* is monomeric in the solid state and in solutions at temperatures down to 77 °K; UV-spectrum in dioxane: λ_{max} = 590 mm (log ε = 3.59), 432 (4.09), 385 (4.03), and 275 (4.18). The low-temperature spectrum at 80 °K shows only slight spectral changes corresponding to the known temperature dependence of electron spectra. The magnetic moments μ_{eff}/μ_B as measured with a magnetic balance are 1.67 at 298 °K, 1.66 at 195 °K, and 1.65 at 90 °K. The values correspond to a free-radical content of 94%. The ESR spectrum in benzene consists of nine groups: $a_{1,4}^{N}$ = 5.6, $a_{2,3}^{N}$ = 6.1, $a^{H(o)}$ = 1.0, and $a^{H(m)}$ = 0.5 gauss.

In weakly acid media (*e.g.* methanol), compound *(1)* immediately decomposes to the reactant formazan and 5-*tert*-butyl-2-(4-nitrophenyl)tetrazole.

As in the case of diphenylpicrylhydrazyl [4] and verdazylene [5] the stability of *(1)* is due to the nearly equal spin densities at the nitrogen pairs N-1, N-4, and N-2, N-3.

Received: May 7, 1969 [Z 995 IE]
German version: Angew. Chem. *81*, 496 (1969)

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Dinuclear Complexes Containing the Tricarbonylcyclopentadienylchromium Group

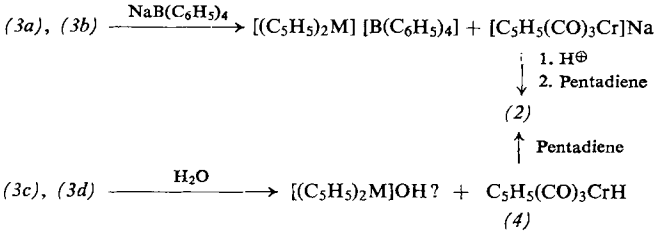
By *A. Miyake, H. Kondo*, and *M. Aoyama* [*]

Chemically, the tricarbonylcyclopentadienylchromium group behaves like a halogen atom; thus, the hydrogenation of polyenes with tricarbonylcyclopentadienylhydridochromium *(4)* [1] resembles the classical reductions carried out with hydrogen iodide [2]. We have now investigated oxidation [3] with the iodine analog bis(tricarbonylcyclopentadienylchromium) *(2)*. A benzene solution of *(2)* is added dropwise at room temperature to a benzene solution of the bis(cyclopentadienyl)metal *(1)*; a smooth redox reaction takes place resulting in the formation of the dinuclear complex *(3)*.

$$\underset{(1)}{2\,(C_5H_5)_2M} + \underset{(2)}{[C_5H_5(CO)_3Cr]_2} \rightarrow 2\,\underset{(3)}{[(C_5H_5)_2M]\,[C_5H_5(CO)_3Cr]}$$

(a), M = Co
(b), M = Cr
(c), M = V
(d), M = Ti

The compositions of both the known complexes *(3a)* and *(3b)* [7] and the complexes *(3c)* and *(3d)* first obtained by the above method were confirmed by elemental analysis. Compound *(2)* can be recovered in good yield from the complexes *(3)* (Scheme 1).



Scheme 1.

As already reported, the complexes *(3a)* and *(3b)* have a salt-like structure and are sparingly soluble in benzene. On the other hand, the complexes *(3c)* and *(3d)* are very soluble in benzene, thus indicating the presence of a covalent metal-metal bond. Further evidence of the existence of a covalent metal-metal bond is afforded by the distinct increase in frequency of the CO stretching vibration in *(3c)* and *(3d)*. The shift [8] to shorter wavelengths of the CO band is explained by the decreased negative charge of the chromium atom

Table 1. CO stretching vibrations of $[C_5H_5(CO)_3Cr]$ complexes.

Compound	ν_{CO} (cm^{-1})		
(3a)	1888		1765
(3b)	1890	1881	1767
(3c)	2020	1928	1840
(3d)	2020	1930	1870
(2)	2015	1942	1912
(7)	1974	1908	1885
(8)	1973	1903	1885

The above mentioned redox reaction applies to many other systems, *e.g.* the reaction of *(2)* with organohydridotin proceeds analogously. If a solution of *(2)* and tribenzylhydridotin *(5)* or triphenylhydridotin *(6)* in benzene is warmed to 80 °C, tricarbonylcyclopentadienyl(tribenzyltin)-chromium *(7)*, m.p. 97–99 °C, and the known tricarbonylcyclopentadienyl(triphenyltin)chromium *(8)* [9], m.p. 220 to 222 °C, are obtained. We could detect both *(4)* and hydrogen in this two-step reaction.

$R_3SnH + (2) \rightarrow C_5H_5(CO)_3CrSnR_3 + (4)$

(5), R = $CH_2C_6H_5$ (7), R = $CH_2C_6H_5$

(6), R = C_6H_5 (8), R = C_6H_5

$2\,(4) \rightarrow (2) + H_2$

The complexes (3), like (2) [1], react as selective hydrogenation catalysts. The complexes (3c) and (3d) have a hydrogenation activity comparable with that of (2), whereas the salt-like compounds (3a) and (3b) exhibit only weak activity. Compound (7) does not catalyze hydrogenation.

Bis(cyclopentadienyl)vanadium-tricarbonylcyclopentadienylchromium (3c)

A solution of (2) (1.07 g) in benzene (140 ml) is treated dropwise with a solution of (1c) (1.03 g) in benzene (15 ml). The mixture is stirred during the addition and the color changes from green to dark-brown, it is concentrated to about 40 ml under vacuum, filtered free of decomposition products, and treated with 200 ml of pentane. The almost black crystals which separate are filtered off and washed with pentane. On cooling, (3c) crystallizes as black-brown needles, m.p. 147 to 149 °C [yield 1.07 g (51%)]. The analogous reaction of (1d) with (2) leads to the formation of (3d) in 56% yield (dark brown crystals that decompose at temperatures above 160 °C). Both complexes are extremely sensitive to air and undergo spontaneous combustion.

Received: May 3, 1969 [Z 998 IE]
German version: Angew. Chem. 81, 498 (1969)

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$(C_5H_5)_2Cr \rightarrow (C_5H_5)_2CrI$ [4]

$(C_5H_5)_2V \rightarrow (C_5H_5)_2VI$ [5]

$(C_3H_5)_3Cr \rightarrow (C_3H_5)_2CrI$ [6]

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tert-Butyl Acetate as Alkylating Agent

By *H. Fernholz* and *H. J. Schmidt* [*]

Dedicated to Professor O. Horn on the occasion of his 65th birthday

tert-Alkyl esters of carboxylic acids are readily accessible by addition of tertiary olefins to a carboxylic acid in the presence of polyphosphoric acid as catalyst [1]. The action of the polyphosphoric acid in such additions is extraordinarily selective and limited exclusively to addition of tertiary olefins. This fact is made use of, for example, in a process for the separation of isobutylene from olefin fractions on a technical scale – the olefin fraction is passed through a polyphosphoric acid-acetic acid mixture [2].

The readily accessible *tert*-butyl acetate that is formed not only very easily decomposes into its components, isobutylene and acetic acid, but also reacts like isobutylene and thus can be trapped and used as "masked" isobutylene. *tert*-Butyl acetate is, in fact, superior to isobutylene as regards manipulation and yields.

Table 1. Examples of the *tert*-butylation of aromatic compounds and conversion of nitriles into *N-tert*-butylcarboxamides (Ritter reaction).

Starting material	mole/mole of TBA	g H_2SO_4/mole TBA	T (°C)	Reaction products	Yield (%)
Benzene	2	100	45	*tert*-Butylbenzene + 1,4-di-*tert*-butylbenzene	76 19
Toluene	2	100	60	1-*tert*-Butyl-4-methylbenzene	96
Phenol	0.7	67	20	*p-tert*-Butylphenol + 2,4,6-tri-*tert*-butylphenol	5 86
Phenol	1.1	20	125	*p-tert*-Butylphenol	96
Hydroquinone	0.5	20	50	2,5-Di-*tert*-butylhydroquinone	87
Anisole	2	20	125	*p-tert*-Butylanisole	86
Acetonitrile	1	100	40	*N-tert*-Butylacetamide	91
Acrylnitrile	1	100	40	*N-tert*-Butylacrylamide	88
Benzonitrile	1	108	40	*N-tert*-Butylbenzamide	94
3-Nitrobenzonitrile	1	108	40	3-Nitro-*N-tert*-Butylbenzamide	95
Malonodinitrile	0.5	100	40	*N,N'*-Di-*tert*-butylmalonodiamide	92

The alkylation of aromatic compounds is best carried out by adding the amount of *tert*-butyl acetate shown in Table 1, with stirring, to a mixture of aromatic compound and conc. sulfuric acid over a period of 2 h and then stirring the reaction mixture for a further 1–3 h before separating and purifying the reaction product. To carry out the Ritter reaction the nitrile is mixed with *tert*-butyl acetate, and concentrated sulfuric acid is added dropwise to the stirred and cooled mixture, the temperature of the reaction mixture not being allowed to exceed the temperature given in Table 1.

The reaction mixture is finally stirred for a further 1–2 h and then poured into ice-water. The precipitated amide is isolated and purified.

Received: May 6, 1969 [Z 994 IE]
German version: Angew. Chem. 81, 496 (1969)

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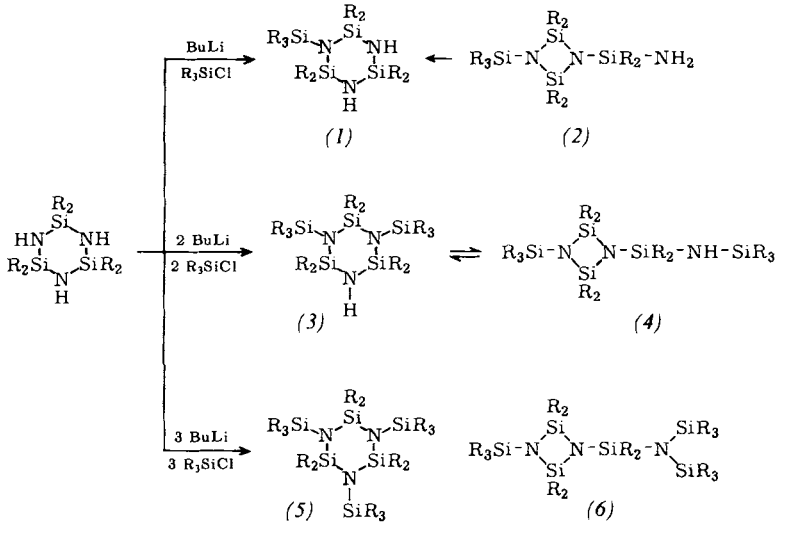
Isomerizations of *N*-Silylated Cyclosilazanes [1]

By *W. Fink* [*]

After metalation, the hydrogen atoms attached to nitrogen in hexamethylcyclosilazane can be replaced by silyl groups [2, 3]. In the case of trimethylsilyl-substituted compounds, intact

cyclosilazane structures are assumed. We have now observed that partial isomerizations take place in these reactions which depend strongly on the reaction conditions.

The monosilylation of hexamethylcyclotrisilazane with butyllithium/trimethylchlorosilane in diglyme at temperatures between −60 and +60 °C affords 2,2,4,4,6,6-hexamethyl-1-trimethylsilylcyclotrisilazane *(1)*. Formation of *(2)*, the isomer of *(1)*, which melts at 36 °C and which can be prepared by ammonolysis of 2,2,4,4-tetramethyl-1-dimethylchlorosilyl-3-trimethylsilylcyclodisilazane, was not observed. Whereas the doubly silylated hexamethylcyclotrisilazane *(3)* is obtained when hexamethylcyclotrisilazane is silylated in diglyme at



(1) *(2)* *(3)* *(4)* *(5)* *(6)*

R = CH_3; Bu = n-C_4H_9

−60 °C, only the cyclodisilazane derivative *(4)*, which is isomeric with *(3)*, can be isolated when the silylation is carried out at +60 °C in the same solvent or at 160 °C in hexane (under pressure). Similarly, the triple silylation of hexamethylcyclotrisilazane in diglyme at −60 °C affords hexamethyl tris(trimethylsilyl)cyclotrisilazane *(5)* in yields of over 62%. A mixture of *(5)* and the isomer *(6)* is obtained when the silylation is carried out at +60 °C (or at 160 °C in benzene). (The physical properties of a few cyclosilazanes are given in Table 1.)

^{1}H-NMR measurements between −60 and 100 °C show that neither hexamethylcyclotrisilazane itself nor the pure compounds *(1)* to *(6)* isomerize. The rearrangements are base-catalyzed and occur during the metalation step. Thus *(2)*, in diglyme or hexane, is already converted to a great extent at 20 °C into *(1)* as a result of a rapid but spectroscopically observable reaction that is catalyzed by small amounts of butyllithium. Likewise, in the presence of equivalent amounts of butyllithium, compounds *(3)* and *(4)* isomerize until equilibrium is established, which, at low temperatures, lies wholly on the side of *(3)*. Thus, 78% of the isomer *(5)* and only 11% of compound *(6)* are obtained by metalation, at −60 °C, and subsequent silylation of *(4)*.

Table 1. Physical properties of a few cyclosilazanes.

Compd.	B.p. (°C/torr)	M.p. (°C)	n_D^{20}	^{1}H-NMR [a], δ (H_7)
(1)	108/12		1.4613	3.96 (6H), 8.68 (9H), 11.30 (12H)
(2)		36		0.34 (6H), 1.20 (9H), 15.24 (12H)
(3)	107/1.1		1.4725	10.20 (18H), 11.71 (12H), 21.00 (6H)
(4)	82/2		1.4422	0.80 (9H), 2.12 (6H), 3.76 (9H), 15.36 (12H)
(5)	126/0.4	54–57		12.20 (27H), 21.50 (18H)
(6)	108/0.3	69–70		1.08 (9H), 12.40 (6H), 13.29 (18H), 17.00 (12H)

[a] Chemical shift (at lower field strengths) at 60 MHz; tetramethylsilane as internal standard.

Received: May 7, 1969 [Z 999 IE]
German version: Angew. Chem. *81*, 499 (1969)

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Synthesis of Metal Complexes Having Fluorine-Containing Phosphine Ligands[1]

By *Th. Kruck*, *M. Höfler*, *H. Jung*, and *H. Blume*[*]

As previously reported[2,3] for the case of strong bases of high or low concentration, the nucleophilic replacement of fluorine atoms by $RO^{\ominus}$ and $HO^{\ominus}$ ions affords a general synthetic route for the preparation of trialkoxy-, difluoroalkoxy-, and difluorohydroxyphosphine complexes, which are either inaccessible or difficultly accessible by conventional methods. We have now extended the use of these solvolyses to systems involving reaction of PF_3 ligands in complexes with amines (as prototype of relatively weak bases). Since tetrakis (trifluorophosphine)nickel(0) *(1)* is readily obtainable we have now directed our attention to all model reactions which are required for a formulation of the reaction; the applicability of the method to the PF_3 complexes of other metals has meanwhile been established.

To avoid polymerization[4], only secondary amines were reacted with *(1)* (molar ratio 12:1) in the preliminary experiments.

$$\underset{(1)}{Ni(PF_3)_4} \xrightarrow[-n[R_2NH_2]F]{+2nR_2NH} \underset{(2)}{Ni(PF_3)_{4-n}(PF_2NR_2)_n} \quad (n=4,3,2)$$

We have found that these reactions proceed rapidly and almost quantitatively with separation of ammonium fluoride according to the above equation – even at temperatures between 0 and 25 °C. Such aminolyses, which have also been investigated for the case of primary amines and sodamide, yield monomeric homogeneous reaction products, *i.e.* n is constant for a particular amine. A few of the difluoroaminophosphine complexes of nickel that have previously been prepared by this method are given in the following Table.

Compounds *(2)* render possible for the first time the synthesis of, *inter alia*, definite complexes of chlorodifluorophosphine, whose attempted preparation by substitution reactions of $PClF_2$ with tetracarbonylnickel leads instead to the formation

Base	Reaction product *(2)*	Properties
$(CH_3)_2NH$	$Ni[PF_2N(CH_3)_2]_4$	colorless crystals, m.p. 106 °C
$(C_2H_5)_2NH$	$Ni(PF_3)_2[PF_2N(C_2H_5)_2]_2$	colorless oil
$(n\text{-}C_3H_7)_2NH$	$Ni(PF_3)_2[PF_2N(n\text{-}C_3H_7)_2]_2$	colorless oil
Piperidine	$Ni(PF_3)(PF_2NC_5H_{10})_3$	colorless crystals, m.p. 41 °C

of a complex mixture[5] owing to dismutation of the free ligands. Here we utilized the ready fission of the P–N bond[6] by subjecting the complex *(2)* to acid cleavage in ether at room temperature, *e.g.*:

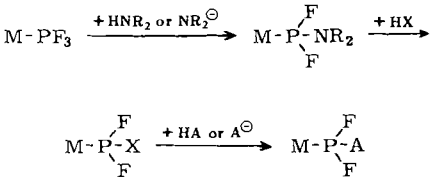
$$Ni[PF_2N(CH_3)_2]_4 + 8\ HCl_{(g)} \rightarrow Ni(PF_2Cl)_4 + 4[(CH_3)_2NH_2]Cl$$
(3)

After filtering off the ammonium chloride and removal of the ether there remains the previously unknown tetrakis(chlorodifluorophosphine)nickel(0) *(3)* as a clear, colorless liquid (yield *ca.* 70%), which can be purified by recondensation under high vacuum or by distillation (b.p. ≈ 64 °C/0.5 torr).

Because of the high reactivity of the P–Cl bond and the low nucleophilicity of the chloride ion, nucleophilic Cl substitutions in the PF_2Cl complexes are possible with weak and very weak bases; they are thus the first members of a series of PF_2Y complexes (Y = OR, CN) of metals in low oxidation states. As prototype of this reaction only methanolysis of *(3)*, which proceeds quantitatively at room temperature in the absence of solvent, need be mentioned.

$$(3) + 4\ CH_3OH \rightarrow Ni(PF_2OCH_3)_4 + 4\ HCl$$
(4)

The difluoromethoxy compound *(4)* can be isolated, after removal of the excess of methanol, as a colorless oil that is soluble in pentane and distillable under vacuum. Starting from the trifluorophosphinemetal complex, the reaction scheme outlined below opens up a route for the preparation of a wide variety of metal complexes having fluorine-containing phosphine ligands.



(R = H, organic group; X = acid radical; HA, $A^{\ominus}$ = weak to medium-strength nucleophile.)

Received: April 29, 1969 [Z 12 IE]
German version: Angew. Chem. *81*, 533 (1969)

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$Xe(OTeF_5)_2$, Xenon Bis(pentafluoroorthotellurate)

By *F. Sladky*[*]

Xenon difluoride reacts with equimolar amounts of pentafluoroorthotelluric acid[1] with loss of HF to give fluoroxenon pentafluoroorthotellurate, $FXeOTeF_5$[2], in quantitative yield. If a five-fold excess of $HOTeF_5$ is used, the second fluorine atom is also replaced by a F_5TeO group.

$$XeF_2 + 2\ HOTeF_5 \rightarrow 2\ HF + Xe(OTeF_5)_2$$
(1)

$Xe(OTeF_5)_2$ is also formed in small amounts when $FXeOTeF_5$ is distilled in a glass apparatus in presence of traces of HF.

$$SiO_2 + 4\ HF \rightarrow SiF_4 + 2\ H_2O$$
$$FXeOTeF_5 + H_2O \rightarrow HOTeF_5 + HF + Xe + {}^1/_2\ O_2$$
$$FXeOTeF_5 + HOTeF_5 \rightarrow HF + Xe(OTeF_5)_2$$

Xenon bis(pentafluoroorthotellurate) *(1)* (m.p. 35–37 °C) is a colorless substance, which is solid at room temperature and which readily crystallizes: IR (solution in CCl_4; range 4000 to 400 cm^{-1}), 780 w, 705 vs, 628 s, 475 m. As expected, the band due to the Xe–F stretching vibration at 520 cm^{-1} in the spectrum of $FXeOTeF_5$ is absent. ^{19}F-NMR (CCl_4 solution; CF_3COOH as external standard): AB_4 type; $\delta_{TeF} = 34.9$ ppm; $J_{TeF} = 1830$ Hz. The stability of *(1)*, which is probably only kinetic, is comparable with that of XeF_2. Compound *(1)* reacts slowly with H_2O in which it is only slightly soluble; in a strongly alkaline medium decomposition takes place with vigorous development of xenon and oxygen and is complete within a few seconds.

$$Xe(OTeF_5)_2 + H_2O \rightarrow 2\ HOTeF_5 + Xe + {}^1/_2O_2$$

(1) is very soluble in CH_3CN and CCl_4; solutions in CCl_4 are also stable over long periods of time. Explosive or very vigorous reactions take place in the presence of ethanol, acetone, and benzene. Compound *(1)* is stable up to temperatures of about 120 °C in prefluorinated Monel vessels.

At higher temperatures, bis(pentafluorotellurium) oxide, TeF_5OTeF_5[3], is obtained along with Xe, O_2, and TeF_6; the still unknown bis(pentafluorotellurium)peroxide TeF_5OOTeF_5 was not formed.

Experimental:

All reactions are carried out gravimetrically and tensimetrically in readily weighable reaction vessels (Kel-F). XeF_2 was prepared by irradiation of Xe/F_2 mixtures with sunlight[4]. 7.40 g of $Xe(OTeF_5)_2$ (97% yield) could be obtained by reaction of 2.12 g of XeF_2 with 14 g of $HOTeF_5$.

XeF_4, purified by treatment with AsF_5 in BrF_5[5], does not react with $HOTeF_5$ under similar reaction conditions.

Received: April 30, 1969 [Z 15 IE]
German version: Angew. Chem. *81*, 536 (1969)

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Determination of the n-Ionization Potential of 2-Trimethylsilylpyridine by Photoelectron Spectroscopy[1]

By *E. Heilbronner* and *V. Hornung*[*], and *H. Bock*, and *H. Alt*[**]

It is still uncertain whether the first ionization potential of pyridine ($IP_{1,\,adiabatic} = 9.27$ eV[2,3]) is to be described as an ionization of the nitrogen lone pair or of the highest occupied π-molecular orbital π_3 (C_{2v} : A_2). No decision can be reached from an analysis of the electronic spectrum, in which one can recognize the fine-structured $\pi^* \leftarrow n$ absorption as a shoulder at the longwave end of the ^1L_b band[4].

It has previously been reported[5] that the strong positive inductive effect of trimethylsilyl substituents raises the energy of the orbitals of a molecule. If the perturbed orbital has π symmetry and if a finite overlap with unoccupied orbitals of the silicon atoms occurs, then the destabilization due to the inductive effect is either over-compensated (π^* level[6]), or largely compensated (π level[7]) by ($Si \leftarrow \pi^*$) back donation, depending on the energy gap between the interacting orbitals. For example, the influence of a $(CH_3)_3$ Si group on the highest occupied molecular orbital of a carbon-π-system is about the same as that of a methyl group[7]. Therefore, one would expect the following characteristic deviations of the orbital energies of 2-trimethylsilylpyridine from those of 2-methylpyridine:

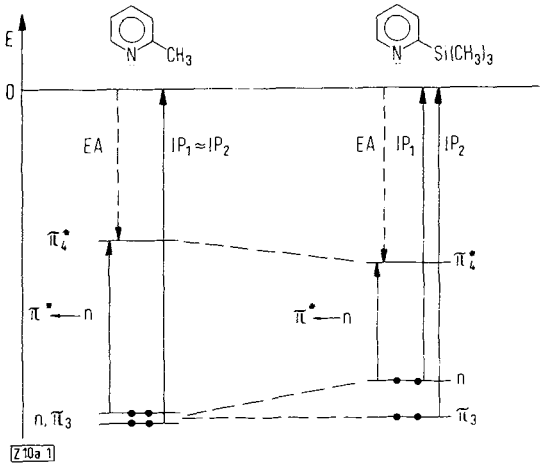


Fig. 1. Qualitative energy-level diagram for the inner molecular orbitals of 2-methyl- and 2-trimethylsilylpyridine.

The following experimental data are in agreement with this prediction:

X	$E^{Red}_{1/2}$ (V)	$\tilde{\nu}_{max}$ (cm^{-1})/ε_{max} (l mol^{-1} cm^{-1})		
		$\pi^* \leftarrow n$	^1L_b	^1L_a
CH_3	−2.17	–	39000/2500	49400/5800
$Si(CH_3)_3$	−2.06	$(35000/500)_{sh}$	39300/3000	47600/8400

sh = shoulder

The fact that the halfwave reduction potential $E^{Red}_{1/2}$ (*i.e.* the electron affinity EA; Fig. 1) of the trimethylsilyl derivative is the more positive one, is an indication of the lowering of the π_4*-orbital (C_{2v} : B_1).

Presumably, this lowering also accounts for the reduced ^1L_a excitation energy. The slightly intensified[8], but unshifted ^1L_b band is preceeded by a pronounced shoulder that shifts towards shorter wavelengths in polar solvents and thus may be ascribed to a $\pi^* \leftarrow n$ transition. Additional information can be obtained by comparing the photoelectron spectra[11] of 2-trimethylsilyl- and 2-methylpyridine (Fig. 2).

The photoelectron spectrum of 2-methylpyridine differs from that of pyridine[3,9] in a predictable way. In the section

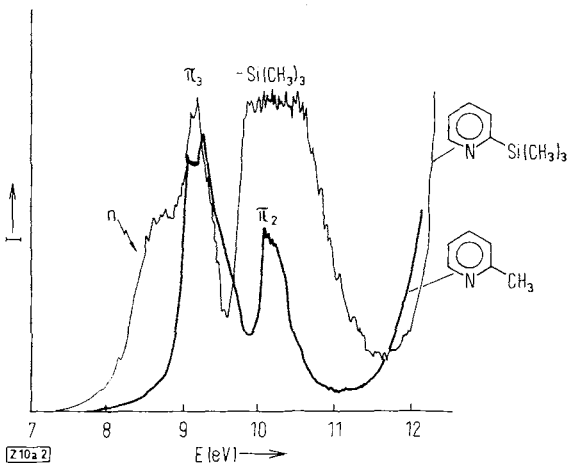


Fig. 2. Photoelectron spectra of 2-trimethylsilyl- and 2-methyl-pyridine. Intensity in arbitrary units.

of the spectrum shown in Fig. 2 one observes bands at 9 and 10 eV which can be assigned to ionization from $\pi_3(A_2)$ and $\pi_2(B_1)$ respectively. These bands occur at lower energies than in unsubstituted pyridine. The bands corresponding to the n-orbital ionization presumably still coincide with the π_3 band.

In contrast, the photoelectron spectrum of 2-trimethyl-silylpyridine shows a well detached fine-structured shoulder in front of the π_3 band. Based on the qualitative energy-level diagram of Fig. 1 and on other experimental data we ascribe this new band to the ionization of the nitrogen lone pair, which now takes place at lower potentials as a consequence of the inductive effect of the trimethylsilyl substituent. Due to the absence of a finite overlap, there is no $Si \leftarrow n$ back donation which would compensate the inductive effect[5]. On the other hand, the previously discussed $Si \leftarrow C_\pi$ back donation, which reduces the donor effect of a trimethylsilyl group to that of a methyl group, is confirmed by the fact that the position of the π_3 band is the same as that observed with the methyl derivative. The broad band occurring between 9.5 and 11 eV is due mainly to the σ-orbital ionization of the trimethyl-silyl residue ($IP_{Si(CH_3)_4} = 9.98$ eV[10]).

Received: April 24, 1969 [Z 10a IE]
German version: Angew. Chem. *81*, 537 (1969)

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[1] Part 1 of Applications of Photoelectron Spectroscopy, also Part 17 of d-Orbital Effects in Silicon-Substituted π-Electron Systems. This work was supported by the Schweizerischer Nationalfonds (Project No. 4651) and by the Deutsche Forschungsgemeinschaft. – Part 16: *H. Bock* and *H. Alt*, Chem. Ber. *102*, 1534 (1969).

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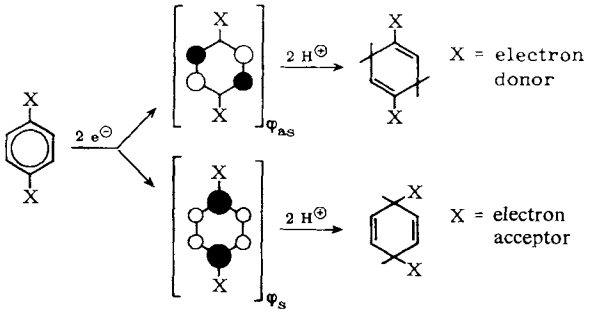
[11] The photoelectron spectra were recorded on a modified spectrometer (Perkin-Elmer Ltd., Beaconsfield, England).

Birch Reductions of Trimethylsilyl Substituted Aromatic Compounds Controlled by (Si ← C_π) Interactions[1]

By *H. Alt, E. R. Franke,* and *H. Bock* [*]

Silyl and alkyl substituents exert a differing electronic influence on the lowest unoccupied ψ_{-1} molecular orbital of π-electron systems: Half-wave reduction potentials[2] and ESR coupling constants[3] verify that alkyl groups act as electron donors, whereas the stronger positive inductive effect of silyl groups is overcompensated by a coupled (Si← C_π) acceptor function of the unoccupied silicon atomic orbitals. Consequently, trimethylsilyl substituents stabilize anions in which the ψ_{-1} molecular orbital is occupied. (Si← C_π) interactions, therefore, should also determine the products of reactions of π systems which proceed *via* anionic transition states or intermediates.

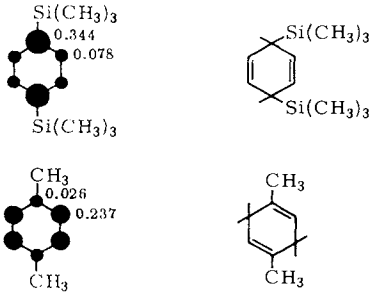
A suitable model reaction is the Birch reduction of aromatic compounds in which dianions or radical anions occur as intermediates and are subjected to kinetically controlled protonation at the center of greatest electron density[4]. In the case of monosubstituted or 1,4-disubstituted benzenes two different reaction products are possible depending on whether the electrons will occupy the antisymmetric ψ_{as} or symmetric ψ_s of the antibonding e_{2u} molecular orbitals[3]. The



electron density distribution in the singly occupied ψ_{-1} molecular orbitals of radical anions can be inferred from the ESR coupling constants a_H, which according to the McConnell relation $a_H = {}_iQ_\mu \rho_\mu^\pi$ [5] are proportional to the π-spin populations and hence, within the HMO approximation, to the squared coefficients $(c_{-1\eta}^{HMO})^2$ at the individual centers μ. From the "experimental MO pictures" thus obtained it should be possible to predict, in the case of alternant aromatic compounds, the centers of greatest electron density and, therefore, the structures of the Birch reduction products. In fact, in the reaction of 1,4-bis(trimethylsilyl)benzene with sodium and ammonium chloride in liquid ammonia[6] one obtains, in agreement with the ESR data[3], exclusively the 1,4-dihydro derivative to be expected on account of the (Si← C_π) acceptor function. On the other hand, as is already known[4], the 1,2-dihydro compound is obtained from *p*-xylene because of the electron donor functions of the alkyl groups.

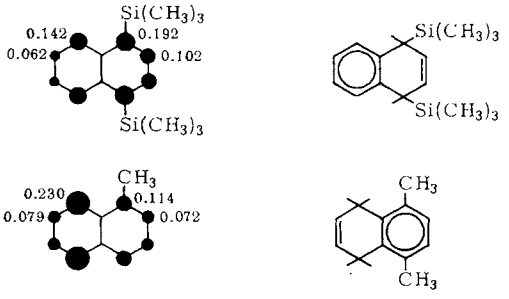
The monosubstituted benzenes (X = CH_3, $Si(CH_3)_3$) are reduced similarly.

π-spin populations [7] reduction product

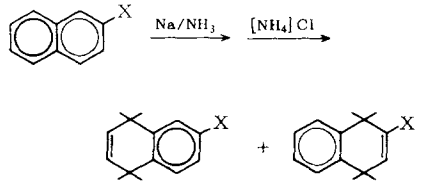


In the Birch reduction of silyl- and of alkyl-naphthalenes the electrons occupy the same molecular orbital ψ_6. However, alkyl donor and silyl acceptor substituents lead, in accordance with ESR data[3,8], to different electron-density distributions so that in the case of the 1,4-dimethyl derivative the unsubstituted ring is reduced whereas only the substituted ring is reduced in the case of the 1,4-bis(trimethylsilyl)-derivative.

π-spin populations [7] reduction product



Once again, analogous results are obtained with 1-substituted naphthalenes. On the other hand, 2-substituted naphthalenes, in which according to HMO coefficients ($c_{61}^2 = 0.181$, $c_{62}^2 = 0.069$) an essentially less directing influence of the substituents is to be expected, yield mixtures of isomers.



X = CH_3:	75%	25%
X = $Si(CH_3)_3$:	20%	80%

The different isomeric ratios, however, are to be ascribed to the opposite electronic effects of alkyl and silyl substituents.

The structures of the reaction products as predicted from ESR spin populations confirm that the anionic intermediates of the Birch reduction are protonated in each case at the centers of greatest electron density. The different types of dihydro derivatives of alkyl and silyl substituted aromatic compounds thus confirm the (Si← C_π) acceptor function of trimethylsilyl groups already proved by physical measurements.

Received: May 8, 1969 [Z 10b IE]
German version: Angew. Chem. *81*, 538 (1969)

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[2] Cf. *H. Bock* and *H. Alt,* Angew. Chem. *79*, 932 (1967); Angew. Chem. internat. Edit. *6*, 941 (1967); *H. Bock, H. Alt,* and *H. Seidl,* Angew. Chem. *80*, 906 (1968); Angew. Chem. internat. Edit. *7*, 885 (1968); J. Amer. chem. Soc. *91*, 355 (1969).

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Organosilicon Chemistry

The Second International Symposium on Organosilicon Chemistry at Bordeaux (July 9–12, 1968) – like the previous Symposium at Prague in 1965 – aroused world-wide interest; it was organized by *J. Valade*. 13 plenary lectures and almost 100 discussion lectures, presented in three concurrent subconferences, confronted the participants, numbering about 400, with such a broad spectrum of the present state of organosilicon chemistry that, apart from a few notable exceptions, the reasoning and scientific depth of individual papers became somewhat lost in the sheer volume of subject material.

Organosilicon technology (direct synthesis as well as manufacture and characterization of polymers) seems to make few bounds forward; developments appear to be overshadowed by the more academically oriented investigation of the "monomeric" compounds. Before very long there will probably be only few chemists working with organosilicon compounds that will remember their benefactors who provided, and still generously provide, the "minerals" that form the very basis of this field.

Plenary Lectures

Except for the contributions by *V. Bažant* (Prague): "Studies on the mechanism of direct synthesis", *K. A. Andrianov* (Moscow): "Polymerization of ring-shaped organosilicon compounds", and *H. Kriegsmann* (Berlin): "Intramolecular and intermolecular interactions in some organosilicon compounds", which were concerned with vibration spectroscopic, mass spectrometric, and ^{1}H-NMR spectroscopic studies on polysiloxane chains, and particularly with the range of electronic effects in a siloxane chain, all the plenary lectures were about the chemistry of monomeric organosilicon compounds.

Attention was focused primarily on papers dealing with formation and cleavage of SiC linkages. *H. Gilman* (Ames, Iowa) reported on the silylation of halogenohydrocarbons after metalation with Li or Mg. Thus propyne, hexahalogenobenzenes, and hexachloropropene react with Li and $(CH_3)_3SiCl$ *in situ* to give $[(CH_3)_3Si]_2C{=}C{=}C[Si(CH_3)_3]_2$; under these conditions perchloroalkanes and ethylene yield $(CH_3)_3SiC{\equiv}CSi(CH_3)_3$; and trichlorobenzene and pentachloropyridine afford tris(trimethylsilyl)trichlorobenzene and 4-trimethylsilyltetrachloropyridine, respectively. Novel reaction routes have also become available *via* copper compounds such as R_3SiCu and R_3GeCu, which can be obtained from the corresponding lithium compounds and C_6H_5Cu or C_6Cl_5Cu. *D. R. Weyenberg* (Midland, Michigan) has found the pyrolysis of alkoxypolymethylsilanes at 225 °C to be a suitable reaction for the production of dimethylsilylene $(CH_3)_2Si$:, which can be detected by mass spectrometry and intercepted, *e.g.*, by diphenylacetylene to form the 1,4-disila-2,5-cyclohexadiene system. Pyrolytic formation of the silylene occurs only when the $(CH_3)_2Si$ group is bonded to an atom bearing a lone pair of electrons; the same applies to the silylenes $(CH_3)CH_3OSi$: and $(CH_3O)_2Si$:. In the absence of a silylene interceptor such as an alcohol or a diene the resulting R_2Si: can also be used for the lengthening of the alkoxypolysilane chain. Investigations on the tributylamine-catalyzed addition of trichlorosilane to phenylacetylene were the subject of a paper delivered by *R. A. Benkeser* (Lafayette, Indiana). An essential step in this reaction is the formation of the ion pair $R_3NH^+SiCl_3^-$. The primary products, α- and *cis*-β-trichlorosilylstyrene, react further with $HSiCl_3$ to give α,β-bis(trichlorosilyl)ethylbenzene. *trans*-β-Trichlorosilylstyrene is also found as a product but its formation is attributed to isomerization of the *cis*-β compound. On the basis of the analogy between CH and CSi bonds, *C. Eaborn* (Brighton) presented a review of the cleavage of SiC bonds and compared this bond with GeC, SnC, and PbC bonds. Triorganosilyl-substituted aryl carboxylic acid derivatives, whose reactivity is determined by the interplay of inductive and resonance effects, represent suitable model substances. Ethynyl-Si compounds behave similarly to their aryl analogs; the high reactivity of the ≡CSi bond has permitted the development of a new synthesis of polyacetylene compounds.

E. Frainnet (Bordeaux) gave an account of the addition of triorganosilanes to carbonyl compounds such as ketones, aldehydes, esters, carboxylic anhydrides, and carboxylic acid halides, and of the reaction of alkoxysilanes with aromatic compounds, esters, and lactones for an extremely wide range of reactants. Anionic rearrangements of organosilicon compounds were discussed by *R. West* (Madison, Wisconsin). They are responsible for the isomerization of silyl hydrazines in the presence of catalytic amounts of alkyllithium, proceed *via* an intramolecular mechanism, and occur frequently in organosilicon chemistry because silicon can expand its valence shell and thus stabilize the intermediates required by the rearrangement. Thermodynamic preference of the 1,1-disilylhydrazines is probably due to the increased stability of the SiNSi group. On the other hand, disilylethylenediamines undergo 1,4 rearrangement; electronic effects such as phenyl-substitution can reverse the direction of rearrangement. A report on the preparation, structure, and reactions of silyl-substituted alkali-metal amides was presented by *U. Wannagat* (Braunschweig). It appears from recent publications that the great versatility and reactivity of the alkali-metal bis(triorganosilyl)amide is exceeded by $LiN(SiCl_3)_2$. Vibration-spectroscopic and other physicochemical measurements on $LiN[Si(CH_3)_3]_2$ indicate the presence of dimeric molecules in the fused compound and in solution, whereas an X-ray structure analysis has established that the crystalline compound exists as the trimer in the form of a six-membered $(LiN)_3$ ring having ∢ SiNSi = 118 ° and *d* SiN = 1.72 Å [1].

The impressive advances made in the chemistry of silicon-metal compounds in recent years became evident in two lectures: *G. A. Razuvaev* (Gorki) dealt mainly with the silyl and germyl derivatives of main-group elements such as Hg [2], and *A. G. MacDiarmid* (Philadelphia, Pennsylvania) concentrated on carbonyl complexes containing SiMn, SiFe, and SiCo bonds. The thermal stability of such bonds is strongly dependent on the nature of the substituents and decreases in the series SiFe–SiMn–SiCo; these bonds show a remarkable stability toward, *e.g.*, PF_3, PF_5, and SO_2. The energy of the SiCo bond (105–124 kcal/mole, as determined by mass spectrometry) is exceptionally high and suggests $SiCo{-}d_\pi d_\pi$ bonds. In $Cl_3SiCo(CO)_4$, the Si atom occupies an axial position of a trigonal bipyramid; the CO groups *cis* to the Si are displaced by 4.8 ° toward the latter. $(CH_3)_3SiMn(CO)_5$ has an octahedral structure; *d* MnSi is 2.50 ± 0.02 Å, a value lower than that expected for a single bond.

M. G. Voronkov (Riga) reported on the biological activity of compounds containing silicon. Thus compounds containing SiC bonds occur in certain bacteria, and silicon compounds are undoubtedly partly responsible for silicosis. The silatranes, polycyclic alkoxysilanes of the general formula $RSi(OCH_2{-}CH_2)_3N$, are unexpectedly poisonous; with a lethal dosage of 0.2 mg/kg they are considerably more toxic than strychnine. Their toxicity is strongly dependent on the nature of the substituent R: the compound with R = *p*-tolyl is more than 10^4 times more poisonous than that with R = methyl.

Preparation and properties of monomeric organosilicon compounds were also dealt with in most of the discussion lectures. In a number of cases the part of the molecule investigated was so far removed from an organosilicon group that the effects observed could hardly be attributed with certainty to the silicon. This report will now consider an arbitrary selection of the topics that were discussed.

Whereas the papers presented by *M. Dvořak* (Prague), *N. P. Lobusevich* (Moscow), and *H. Ya. Zueva* were devoted to the catalyst systems used in direct syntheses and the effects of foreign atoms, that by *A. I. Gorbunov* (Moscow) dealt with kinetic aspects of direct synthesis. *M. Bartholin* (Villeurbanne) has succeeded in incorporating Al and Cr into phenylpolysiloxanes in aqueous media at pH values between 2.5 and 5, and *J. A. C. Watt* (Stevenston) has found the perphenylpoly-*p*-silphenylene/asbestos system to be a stable combination up to 400 °C. *I. M. White* (Farnborough) has introduced P(O)R and isophthaloyl groups into neopentyl-substituted polysiloxanes by co-condensation; however, the properties of the products are no more favorable than those of the usual silicones. The stereochemistry of the polymerization of a trimethyltriphenylcyclotrisiloxane in the presence of various catalysts has been studied by *E. E. Bostick* and *J. B. Bush Jr.* (Schenectady, New York).

SiC Compounds

Silylboranes, which possess considerable potential as polymer building units, were presented by *S. Papetti* (New Haven, Connecticut), silicon-containing four-, five-, and ten-membered rings having C–C, C=C, and C≡C groups by *G. Fritz* (Karlsruhe), and a sila-steroid by *S. Barcza* (Hanover, New Jersey). According to *Sheng-lieh Liu* (Taipeh), four $(CH_3)_2C_6H_5Si$ groups may be bonded to a central carbon atom. *H. Schmidbaur* (Würzburg) has observed stabilization of the P=C bond by $(CH_3)_3Si$ groups in $(CH_3)_3P{=}CHSi(CH_3)_3$; the silyl shift involved in the conversion of $(CH_3)_3SiCH_2P(CH_3)_2{=}CHSi(CH_3)_3$ into $(CH_3)_3P{=}C[Si(CH_3)_3]_2$ is remarkable. According to *M. J. Newlands* (Manchester), 1,3-disilacyclobutanes can undergo either electrophilic or nucleophilic cleavage. On cleavage with bromine, the reactive dislacyclobutane $CH_3(C_6H_5)SiCH_2SiCH_3(Br)CH_2$ can be intercepted and the Br replaced by H on treatment with $LiAlH_4$. The rate of catalytic chlorination of arylsilanes and the σ constants of various organosilyl groups, determined from half-wave potentials and the rate of bromination of phenylsilanes, respectively, were shown by *V. Chvalovský* (Prague) and *F. Mareš* (Prague), respectively, to evidence pronounced (p→d)π interactions in the Si-phenyl bond.

SiO and SiN Compounds

Siloxycarbenes have been obtained by *A. G. Brook* (Toronto) on irradiation of α-silyl ketones. They are nucleophilic in character and may be intercepted with ketones and fumaric esters. *J. Caussé* (Bordeaux) reported that triorganosilanes add to ketenes to form enoxysilanes; both possible stereoisomers are formed with ketenes of the type RR'C=C=O. Careful examination of the reaction of $(RO)_2PONa$ with triorganochlorosilanes led *N. L. Orlov* (Leningrad) to the conclusion that the reaction product is not $(RO)_2P(O)SiR_3$ but a mixture of $(RO)_2POSiR_3$ and $R(RO)P(O)OSiR_3$, the latter arising by isomerization of the former. The major product on irradiation of acetone/triorganosilane mixtures has been found by *A. Ritter* (Mülheim) to be isopropoxysilane; with benzophenone, on the other hand, *O*-triorganosilylbenzopinacol could be isolated as main product. Optically active 2-sila-5-oxazolidones have been obtained by *J. F. Klebe* (Schenectady, New York) on reaction of optically active *N*-substituted amino acids with diaminosilanes at room temperature. The diastereomers differ in their proton magnetic resonance spectrum; equilibrium is established in solution within a few days. *K. Rühlmann* (Berlin) discussed the merits of bis(trimethylsilylimino) compounds for the synthesis of new heterocycles. Olefins add to silyl azides to give *N*-silyltriazolines, which yield silylaziridines on thermolysis. Benzimidazolines bearing a metal substitutent (Li, Na, Fe) attached to the nitrogen atom constituted the subject of the paper by *D. Kummer* (Karlsruhe). These thermally unstable compounds can be converted into the *N,N*-bis(trimethylsilyl) derivatives; in their chemical behavior they resemble alkali-metal disilylamides. *I. Schumann-Ruidisch* (Würzburg) reported on the synthesis of mono- and bis(trimethylsilyl)-*tert*-butylamine; one of the Si atoms can also be replaced by Ge, Sn, or Pb. The long-sought-after pale blue compound, bis(trimethylsilyl)diimine (azotrimethylsilane)[3], which decomposes to tetrakis(trimethylsilyl)hydrazine and N_2 at −35 °C has been prepared by *N. Wiberg* (München). The diimine ignites in the presence of O_2; controlled oxidation affords bis(trimethylsilyl) peroxide. *R. P. Bush* (Barry) has studied the rearrangement of *N*-metalated six- and eight-membered siloxane rings; ring contraction to cyclodisilazanes and six-membered rings, respectively, always proceeds *via* excision of a $OSiR_2$ unit. As shown by *V. L. Sheludjakov* (Moscow), β-eliminations in SiNCX systems (→ SiX + −NC−) determine the courses of many reactions in SiN chemistry: decomposition of *N*-silylurethanes, *N*-silylcarbamoyl chlorides, *N*-silylimino carboxylic acid derivatives. *O. J. Scherer* (Würzburg) has shown scission of SiN bonds by thionyl halides to be a universally applicable reaction for the preparation of sulfinylamine derivatives such as $(CH_3)_3SiN{=}S{=}O$, NC–N=S=O, and RS–N=S=O. Alkali-metal silylamides $[MNR'(SiR_3)]$ react with transition-metal carbonyls M'–C≡O to give $MOSiR_3$ and M'–C=NR'. *G. Schirawski* (Braunschweig) has elucidated the mechanism of this reaction and exploited it for the preparation of new isocyanide complexes.

Other Silicon Compounds

The synthesis of $(C_6F_5)_3SiSi(C_6F_5)_3$ has been accomplished by *E. Hengge* and *G. Starz* (Graz); the intermediate $(C_6F_5)_3SiH$ is characterized by an unusually high νSiH vibration at 2295 cm^{-1}. *E. A. Chernyshev* (Moscow) has studied interception reactions of dichlorosilylene $:SiCl_2$ with naphthylsilanes and obtained a large number of derivatives of 1,2-disilacyclopentane and -hexane. Preparation and vibration spectra of methylated isotetrasilanes and neopentasilane were treated in the lecture by *U. Goetze* (Braunschweig). The compound $[(CH_3)_3Si]_3SiH$, with νSiH = 2051 cm^{-1} and $J(^1H^{29}Si)$ = 155 ± 2 Hz, provides a particularly clear illustration of the extreme electron-releasing effect of the $(CH_3)_3Si$ group. Like other phosphines, $[(CH_3)_3Si]_3P$ can also act as ligand in transition-metal complexes; according to *H. Schumann* (Würzburg), it forms air-stable compounds, admittedly of low thermal stability, with the groups $Ni(CO)_3$, $Fe(CO)_4$, $Cr(CO)_5$, and $Co(CO)_2NO$.

Silicon-Metal Compounds

In addition to the Si-alkali-metal compounds [*E. Amberger* (München)] and tris(trimethylsilyl)thallium, which was reported upon by *A. G. Lee* (Cambridge), Si-transition-metal compounds received considerable attention. Homolysis of $(R_3Si)_2Hg$ produces R_3Si radicals, which add readily to unsaturated systems [*W. P. Neumann* (Giessen)]. Compounds having Si–Ti linkages have also been obtained for the first time: according to *H. Zimmermann* (Graz), reaction of $TiCl_4$ and $(C_6H_5)_3SiK$ affords $[(C_6H_5)_3Si]_4Ti$[4]; the synthesis of silyl cyclopentadienyltitanium derivatives has also been accomplished by *M. F. Lappert* (Brighton). ^{57}Fe-Mössbauer and IR spectra show the compounds $(SiH_3)_nFeH_{2-n}(CO)_4$ (n = 1,2) to have a *cis*-octahedral structure; other SiH_3 compounds such as $H_3SiCo(CO)_4$ and $H_3SiMn(CO)_5$ have also been prepared and studied by *B. J. Aylett* (London). *F. Glockling* (Durham) has utilized the reaction between PtH and HSi groups, which is exothermic to the extent of 20 kcal/mole, for the synthesis of new SiPt compounds. H_2, HCl, CH_3I, and H_2O cleave the SiPt bond under mild conditions.

Physicochemical Measurements

In conclusion, a broad selection of physicochemical studies were reported, ranging from structure determinations on new cage-type disilylmethylenes by nuclear magnetic resonance and mass spectrometry [*W. J. Owen* (Barry)] to quantum-chemical calculations on benzyl, aryl-, and alkenylsilanes [*J. Nagy* (Budapest)]. *H. Bock* (München) considered why silyl ketones are yellow, as opposed to the colorless aryl ketones. On the basis of ionization energies, half-wave reduction potentials, and charge-transfer and electron-excitation energies, he has drawn up an experimental MO scheme which shows that the reduced excitation energy of the long-wavelength $n \rightarrow \pi^*$ transition is to be attributed to promotion of the oxygen n-electron pair by the strong inductive effect of the R_3Si group and a simultaneous lowering of the π^* energy level by back-donation of electrons in the sense $(O=C)_\pi \rightarrow Si$. Dipole-moment measurements and $p_\pi d_\pi$ contributions have been correlated by *S. Ferenczi-Gresz* (Budapest) for organo-oxysilanes and by *V. Vaisarová* (Prague) for phenylhalogenosilanes. Interactions between proton donors of the type −CH, −NH, or −OH and SiO or SiN compounds have been detected by infrared spectroscopy [*M. Jakoubková* (Prague)], and the assignment of the infrared spectra of siloxanes and alkoxysiloxanes was reported on by *A. Marchand* (Bordeaux). A simple universal set of force constants for representation of vibration spectra of phenyl-Si compounds was presented by *F. Höfler* (Münster). The paper read by *H. Bürger* (Braunschweig) was concerned with normal coordinate analysis of all trimethylsilyl compounds of Group IV–VII elements (El) that contain a full complement of $(CH_3)_3Si$ groups. The relevant calculations afford not only the SiEl stretching force constants and the limits of the SiElSi bond angle but also correlations between C_3Si deformation vibrations and the mass of the fourth substituent. With the aid of nuclear magnetic resonance studies, *E. G. Rochow* (Cambridge, Massachusetts) has shown that methylpolysilazane chains are flexible and that their flexiblity is increased by branching; free rotation of the CH_3 group is retained in such chains. *J. Schraml* (Prague) has analyzed the ^{1}H-NMR spectra of a large number of silyl-2,2-dichlorocyclopropanes and reached the conclusion that no π bond can be detected, at least by NMR spectroscopy, between the cyclopropane ring and Si. *H. Bürger* [VB 202 IE]

German version: Angew. Chem. *81*, 500 (1969)

[1] *D. Mootz, A. Zinnius,* and *B. Böttcher,* Angew. Chem. *81*, 398 (1969); Angew. Chem. internat. Edit. *8*, 378 (1969).

[2] *N. S. Vyazankin, G. A. Razuvaev,* and *O. A. Kruglaya,* Organometallic Chem. Rev. *A 3*, 323 (1968).

[3] *N. Wiberg, W.-Ch. Joo,* and *W. Uhlenbrock,* Angew. Chem. *80*, 661 (1968); Angew. Chem. internat. Edit. *7*, 640 (1968).

[4] *E. Hengge* and *H. Zimmermann,* Angew. Chem. *80*, 153 (1968); Angew. Chem. internat. Edit. *7*, 142 (1968).

Polyoxymethylenes

By *H. Cherdron* [*]

Polyoxymethylenes can be prepared in a number of ways:

1) Cationic or anionic polymerization of formaldehyde,

2) Polycondensation of formaldehyde in aqueous solution (*via* the unstable methylene glycol),

3) Cationic polymerization of cyclic trimers and tetramers of formaldehyde.

The homopolymerization and copolymerization of trioxane, which exhibit a variety of particular features, have been thoroughly studied. These ring-opening polymerizations are characterized by various side reactions of the growing polyoxymethylene cations such as chain transfer, transacetalization, and hydride shifts. Not only do the side reactions determine the nature of the end group and the molecular weight, but they are also responsible for the chemical and molecular regularity of the polyoxymethylene.

Owing to their predominantly regular molecular structure polyoxymethylenes crystallize extremely readily, two crystal modifications being encountered: an orthorhombic modification and an hexagonal one. The former rearranges irreversibly to the latter at temperatures above 80 °C. Many of the physical properties arise from this highly crystalline state, as for example the insolubility of polyoxymethylenes in organic solvents at room temperature, the high modulus of elasticity, and the favorable combination of hardness and rigidity.

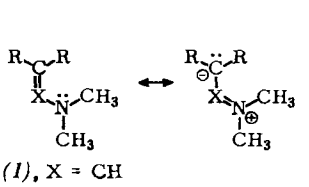
Lecture at Freiburg on April 25, 1969 [VB 203 IE]
German version: Angew. Chem. *81*, 502 (1969)

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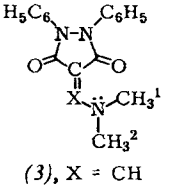
Intramolecular Motions in Enamines and Hydrazones. Separation of Rotational Isomers

By *A. Mannschreck* and *U. Kölle* [*]

Rotation about the =C–N bond of enamines *(1)* occurs more slowly than the corresponding process in saturated amines, whereas *cis-trans* isomerization at the C=C bond in *(1)* is faster than in alkenes containing no hetero atom [1,2]. Some



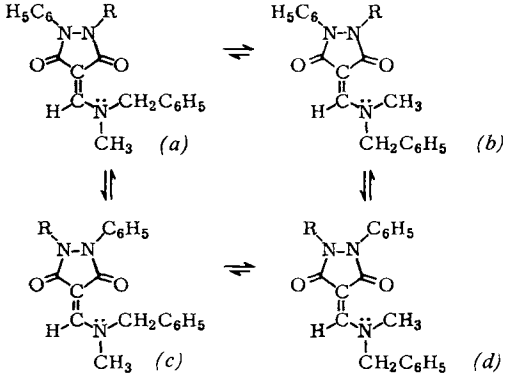
(1), X = CH
(2), X = N



(3), X = CH
(4), X = N

indications of similar phenomena in hydrazones *(2)* have been obtained [1]. However, the free enthalpies of activation $\Delta G^{\neq}$ for rotation about the =N–N bond in *(2)* are lower by about 4 kcal/mole than the values for the corresponding motion at =C–N in *(1)*. This was concluded, for example, from the coalescence of the ^{1}H-NMR methyl signals of *(3)*, $\Delta G_c^{\neq}$ = 21.5 kcal/mole at 160 °C, and of *(4)*, $\Delta G_c^{\neq}$ = 17.6 kcal/mole at 73 °C, in diphenyl ether. These findings are in agreement with the fact, deduced from ^{1}H/^{1}H coupling constants in fulvenes [3], that dipolar resonance structures contribute more to the ground state of enamines than to that of hydrazones.

The high barrier to rotation about the =C–N bond in *(3)* led us to attempt the separation of isomers in suitable cases. For instance, *(5b)*, m.p. 185–186 °C, was obtained in the pure



(5), R = C_6H_5
(6), R = CH_3
(7), R = H

state by crystallization, whereas the samples of *(5a)*, m.p. 185–186 °C, isolated by chromatography still contained 7% of *(5b)*. When *(5a)* or *(5b)* is dissolved in $CDCl_3$ at 28.5 °C an equilibrium is established which shows 40% of *(5a)*. The chemical shifts for the alkyl protons of the two isomers differ markedly. This represents the first identification and separation of enamines which are rotational isomers with respect to the =C–N bond.

(5a) and *(5c)*, as well as *(5b)* and *(5d)*, cannot be distinguished. However, four isomers are possible for *(6)*, the pyrazolidine ring of which is unsymmetrically substituted. Crystallization of the reaction product obtained from *(7)* and CH_3I yielded a 1:1 mixture of *(6b)* and *(6d)* having m.p. 130 °C. When equilibrated, the $CDCl_3$ solution at 13 °C contained 20% each of *(6a)* and *(6c)* as well as 30% of *(6b)* and of *(6d)*. The time dependence of the isomer ratio resulted in $\Delta G^{\ddagger}$ = 21.3 kcal/mole for the =C–N isomerization process *(6b)* → *(6a)*, whereas $\Delta G^{\ddagger}$ = 19.2 kcal/mole was measured by coalescence at 70 °C in $Cl_2CHCHCl_2$ for *(6b)* → *(6d)*, the corresponding motion at the C=C bond. Therefore, in such enamines the transition state of C=C rotation is more favorable than that of =C–N isomerization.

Lecture at München on May 12, 1969 [VB 204]
German version: Angew. Chem. *81*, 540 (1969)

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[1] *A. Mannschreck* and *U. Kölle*, Tetrahedron Letters *1967*, 863.

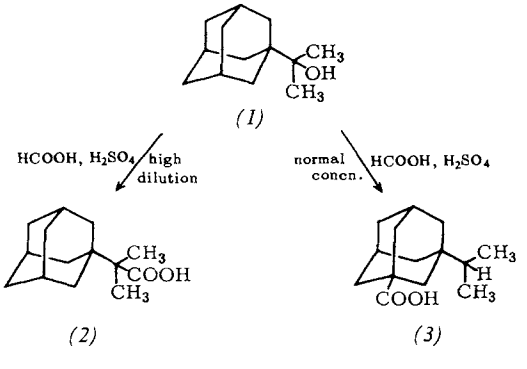
[2] *Y. Shvo, E. C. Taylor*, and *J. Bartulin*, Tetrahedron Letters *1967*, 3259.

[3] *A. Mannschreck* and *U. Kölle*, Chem. Ber. *102*, 243 (1969).

Recent Developments in the Chemistry of Adamantane and Diamondoid Molecules

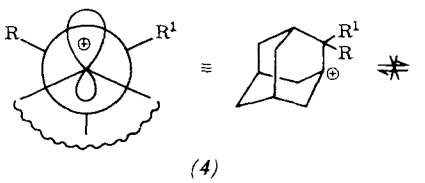
By *P. v. R. Schleyer* [*]

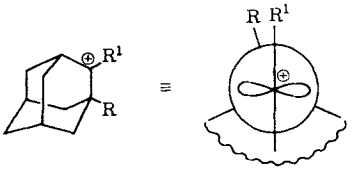
In the adamantane series, intermolecular hydride shifts occur very readily. Under ordinary Koch-Haaf conditions, *(1)* is converted into *(3)* [1]. However, when the reaction is carried out in the same way but with *(1)* in high dilution, the unrearranged product *(2)* is formed. If the rearrangement of *(1)* to the carbonium ion precursor of *(3)* is unimolecular, there should have been no effect of dilution; however, dilution should inhibit bimolecular, intermolecular hydride transfers.



This behavior is quite general. Under ordinary concentrations the Koch-Haaf reaction of 2-adamantanol gives only adamantane-1 carboxylic acid, while under high dilution conditions the unrearranged adamantane-2 carboxylic acid is formed [2]. This result demonstrates that 1,2-hydride shifts do not occur intramolecularly under these conditions.

Although there are many cases of apparent 1,2-shifts in adamantane chemistry, *e.g.*, the interconversion of 1- and 2-adamantanol in sulfuric acid [3], we believe that these shifts do not take place by the simple intramolecular rearrangement *(4)* ⇌ *(5)*. The relationship of the vacant orbitals and the migrating groups is highly unfavorable in *(4)* and *(5)*, and the 1,2-migration transition state is badly distorted.





Further, direct examples of the inability of simple intramolecular 1,2-shifts to occur in adamantane are provided by NMR studies of stable adamantyl cations themselves, in SbF_5 solution [4]. Even though only a seemingly simple sequence of 1,2-shifts should convert the 3-methyladamantyl-1 cation to the more stable 2-methyladamantyl-2 cation [*(5)*, $R^1 = CH_3$; R = H], no rearrangement occurs and both cations are indefinitely stable in SbF_5 [5]. Even more strikingly, the 2,2-dimethyladamantyl-1 cation [*(4)*, $R = R^1 = CH_3$] does not rearrange to its more stable isomer, the 1,2-dimethyl-adamantyl-2 cation [*(5)*, $R = R^1 = CH_3$].

Although hydride shifts can occur intermolecularly, methyl shifts cannot. Despite this, there are many cases of apparent 1,2-methyl shifts in adamantane [3], *e.g.*, the interconversion of 1-methyl and 2-methyladamantane and the rearrangement of 2,2-dimethyladamantane first to 1,2-dimethyladamantane and then to the 1,3-dimethyl isomer with AlX_3 catalysis. Although work in progress is not complete, we believe that these rearrangements probably are not simple 1,2-shifts, but rather follow more complicated paths. Ring expansion-contraction or rearrangement through skeletal isomers of adamantane, such as protoadamantane [5], are the most likely alternatives.

Lecture at Basel on May 8, 1969 [VB 205 IE]
German version: Angew. Chem. *81*, 539 (1969)

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[1] *E. Wiskott* and *D. Raber*, unpublished results; *H. Stetter*, unpublished results.

[2] *L. Lam*, unpublished results; *J. Burkhard, J. Vais*, and *S. Landa*, Z. Chem. *9*, 29 (1969).

[3] *H. W. Geluk* and *J. L. M. A. Schlatman*, Tetrahedron *24*, 5361, 5369 (1968); Recueil Trav. chem. Pays-Bas *88*, 13 (1969); *M. A. McKervey, J. R. Alford, J. F. McGarrity*, and *E. J. F. Rea*, Tetrahedron Letters *1968*, 5165.

[4] *L. Lam, J. L. Fry*, and *V. Buss*, unpublished results in collaboration with *G. Olah* and *G. Mateescu*.

[5] *H. W. Whitlock, Jr.* and *M. W. Siefken*, J. Amer. chem. Soc. *90*, 4929 (1968).

Unusually large Stokes shifts and fluorescence decay times have been found by *G. Briegleb, J. Trencséni,* and *W. Herre* for the charge-transfer fluorescence of donor-acceptor ion pairs of *N*-methylpyridinium salts with the anions Br^-, I^-, N_3^-, SCN^-, and 1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadienide. The Stokes shifts, *i.e.* the difference between the maxima of the absorption and fluorescence bands, amount to 11000–20000 cm^{-1}, and the decay times to 10^{-4} to 10^{-5} s. These findings are explained in the following way: In the ground state the donor D and the acceptor A are held together by strong electrostatic forces; in the excited state the picture is rather one of a relatively loosely bound radical pair $D^{\bullet}\cdot\cdot A^{\bullet}$; the equilibrium distances $D^{-}\cdot\cdot A^{+}$ in the ground state and $D^{\bullet}\cdot\cdot A^{\bullet}$ differ considerably. Since the bonding forces in the excited state are relatively weak, the nuclear coordinates can assume equilibrium values during the lifetime of the excited state. If the symmetry properties of the equilibrium configuration in the excited state are not conducive to electron demotion to the ground state, then an unusually long fluorescence decay time will be observed. / Chem. Physics Letters *3*, 146 (1969) / –Hz. [Rd 24 IE]

The products of charge transfer on collision of H^+, H_2^+, and He^+ with H_2, N_2, O_2, CO_2, H_2O, NH_3, and CH_4 have been investigated by *D. W. Koopman.* The charged products whose kinetic energies are not too high are removed from the collision region by means of electric fields and analyzed in a simplified mass spectrometer. Uncharged products and those having a high kinetic energy are not registered. With all target gases, collision with He^+ gives cleavage products, whereas only charge transfer occurs with H_2^+ and H^+. The results are discussed in terms of the potential energy curves of the participating molecules and molecular ions in their ground states and excited states. In the case of the polyatomic molecules, the investigations provide information about the energy of states from which dissociation can take place. / Physic. Rev. (2) *178*, 161 (1969) / –Hz. [Rd 27 IE]

The ^{19}F-NMR spectra of 3-substituted 2-chloro-1,1,2-trifluorocyclobutanes have been studied by *R. R. Ernst.* The compounds were present as *cis,trans* isomeric pairs; each isomer can exist in two conformations, depending on whether the substituent attached to C-3 is in the axial or the equatorial position. All the signals of the isomers could be assigned by comparison of the chemical shifts of the ^{19}F resonances. The F–F coupling constants were investigated with regard to their dependence on the dihedral angle between the two neighboring C–F bonds: in the regions of 0° and 180° they are negative, and for angles of about 90° they are positive. Analysis of the spectra was simplified by irradiation with a strong noise spectrum in the region of the proton resonances in order to suppress H–F coupling. / Molecular Physics *16*, 241 (1969) / –Hz. [Rd 28 IE]

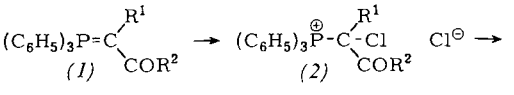
The fluorescence spectrum of estrone, which has been discussed by *A. Weinreb* and *A. Werner,* is distinguished by the presence of two strong emission bands at 310 and 430 nm. The fluorescence of freshly prepared solutions in ethanol is independent of concentration and of the wavelength of the exciting light. The first finding rules out excimer fluorescence as the cause of the band at 430 nm; the second finding makes the presence of impurities appear unlikely. Comparison with related steroids containing only one of the two chromophores present in estrone (aromatic ring and carbonyl group) suggest that the short-wave band should be assigned to the aromatic ring and the long-wave band to the carbonyl group. For this to apply, an energy transfer from the aromatic ring to the carbonyl group must occur in estrone; the remarkably low fluorescence quantum yield of estrone lends further support to this assumption. / Chem. Physics Letters *3*, 231 (1969) / –Hz. [Rd 29 IE]

Variation of the dielectric properties of weakly polar liquids with temperature and pressure has been studied by *F. I. Mopsik.* It was found that the polarization, calculated by the Clausius-Mosotti equation

$$[(\varepsilon - 1)/(\varepsilon + 2)]\ (M/\rho) = P$$

(ε = dielectric constant, M = molecular weight, ρ = density), falls linearly with increasing density, the gradient being independent of the temperature. The dipole moment of the substance investigated can be determined from the temperature dependence of P at constant density. As expected, $\mu = 0$ was found for CCl_4 and CS_2; other values obtained were $\mu = 0.085$ D for *n*-hexane, $\mu = 0.105 \pm 0.004$ D for isopentane, and $\mu = 0.332 \pm 0.006$ D for toluene. The method runs into difficulties with dipole moments as high as the last-mentioned example since the slope of the P-ρ curve then becomes temperature dependent. / J. chem. Physics *50*, 2559 (1969) / –Hz. [Rd 30 IE]

A new method for the synthesis of non-symmetrical α-chloro ketones is given by *E. Zbiral* and *M. Rasberger.* β-Oxoalkylenephosphoranes *(1)*, which are readily accessible from alkylenephosphoranes and acyl chlorides, react with an equimolar amount of $C_6H_5ICl_2$ in benzene at room temperature to form the phosphonium chlorides *(2)* (yield 70 to

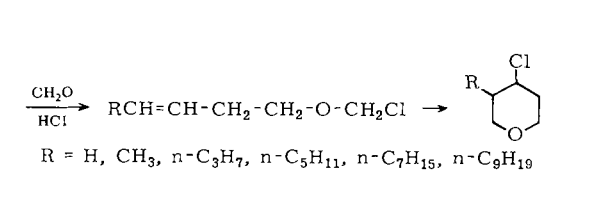


(1) *(2)*

$$R^1\text{-}CHCl\text{-}CO\text{-}R^2 \quad (3)$$

95%). On treatment with dilute Na_2CO_3 solution at 0–25 °C, these compounds decompose into $(C_6H_5)_3PO$ and the α-chloro ketones *(3)* (50–90%). The ease with which the carbon skeleton is removed from the positive phosphorus atom is remarkable. / Tetrahedron *25*, 1871 (1969) / –Ma. [Rd 31 IE]

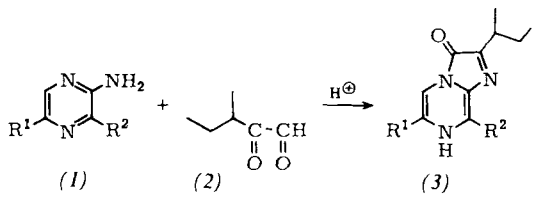
A new tetrahydropyran synthesis has been described by *P. R. Stapp.* α-Olefins condense with paraformaldehyde and hydrogen halide in a non-aqueous medium to give 3-alkyl-4-halogenotetrahydropyrans. The best yields (50–80%) are obtained at –70 to –60 °C and with HCl. Trioxane does not react



R = H, CH_3, n-C_3H_7, n-C_5H_{11}, n-C_7H_{15}, n-C_9H_{19}

under such conditions. Reaction probably proceeds, with participation of carbonium ions, *via* homoallyl alcohols, which cyclize with formaldehyde and acid. / J. org. Chemistry *34*, 479 (1969) / –Ma. [Rd 32 IE]

A new route for the synthesis of Cypridina luciferin and its analogs is described by *S. Inoue, S. Sugiura, H. Kakoi,* and *T. Goto*. α-Keto aldehydes can condense with 2-aminopyrazines in dilute HCl under mild conditions to give dihydroimidazopyrazinone derivatives. A solution of etioluciferin dihydrobromide *(1)* and racemic 1-formyl-2-methyl-1-butanone react in boiling aqueous methanol in the presence of HBr to give racemic luciferin dihydrobromide *(3)*, m.p.

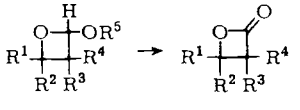


(1) *(2)* *(3)*

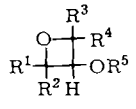
R^1 = 3-Indolyl; $R^2 = (CH_2)_3\text{-}NH\text{-}C(=NH)\text{-}NH_2$

252–253 °C in 70% yield (yield of pure product *ca.* 30%). The bioluminescence activity corresponds to that of the natural luciferin. The same synthesis can be applied to 2-aminopyridines: 2-aminopyridine and phenylglyoxal afford 2-phenylimidazo[1,2-*a*]pyridin-3-ol. / Tetrahedron Letters *1969*, 1609 / –Ma. [Rd 33 IE]

A new β-lactone synthesis is described by *S. H. Schroeter*. Reaction of photoexcited carbonyl compounds R^1R^2CO with vinyl or enol ethers $R^3R^4C{=}CH{-}O{-}R^5$ affords a mixture of 2- and 3-alkoxyoxetanes *(1)* and *(2)*, the product ratio depending primarily on the nature of the substituents R^3–R^5. In the presence of an excess of carbonyl compound, the amount of *(1)* decreases as the duration of irradiation increases since it reacts with the photoexcited carbonyl compound to give the β-lactone *(3)*. For example, 2-methoxy-,



(1) *(3)*

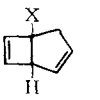


(3a), R^1-R^4 = CH_3

(2)

2-ethoxy-, 2-*n*-propoxy-, or 2-*n*-butoxy-3,3,4,4-tetramethyloxetane reacts with acetone giving tetramethyl-β-propiolactone *(3a)*, m.p. 131 °C. Compound *(3a)* (yield 37%) is obtained in one step, *e.g.*, by irradiation of methyl or *n*-propyl β,β-dimethylvinyl ether (0.2 mole) and acetone (1 mole) in acetonitrile with a 450 W Hg lamp; 29% of a 1:1 mixture of *(1)* and *(2)* is also formed. The β-lactone formation is of a general nature and probably proceeds *via* dehydrogenation at C-2 and subsequent decomposition of the resulting dialkoxy radical into an alkyl radical and the β-lactone. / Tetrahedron Letters *1969*, 1591 / –Ma. [Rd 34 IE]

Detection of the cyclobutadienocyclopentadienide ion *(2a)*, an antiaromatic molecule, has been accomplished by *R. Breslow, W. Washburn,* and *R. G. Bergman*. These authors first prepared the chlorodiene *(1b)* by reaction of *(1a)* with BCl_3 at –75 °C; when allowed to stand with $KOC(CH_3)_3$ in THF, *(1b)* loses HCl. The resulting *(2b)* dimerizes immediately. If *(1b)* is treated with $KOC(CH_3)_3$ in the presence of C_4H_9OD, the dimer is then formed in 40% yield; 65% of the product contained 2.0 atoms of D per molecule of dimer. The 60% of



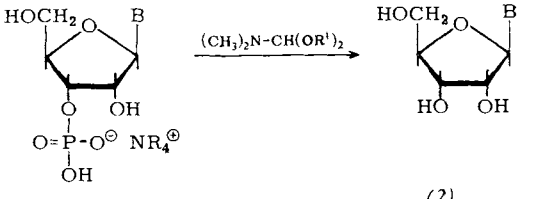
(1a), X = OCH_3
(1b), X = Cl



(2a), X = O
(2b), X = H
(2c), X = D

unchanged *(1b)* contained no deuterium; no H/D exchange occurs with the dimer. Addition of $[D_6]$-DMSO gives a product containing 100% of molecules having 2.0 atoms of D per molecule of dimer. The NMR spectrum of the dimer is in accord with the assumption that it is formed from *(2c)*. These facts appear to confirm the HMO prediction that *(2b)* and *(2c)* are readily converted into the anion *(2a)*. / J. Amer. chem. Soc. *91*, 196 (1969) / –Kr. [Rd 35 IE]

A new method for the dephosphorylation of ribonucleoside 2'- or 3'-phosphates is recommended by *J. Žemlička* and *S. Chládek*. The nucleotide is first converted into the tetra-*n*-butylammonium salt *(1)*, which is then dried and heated with dimethylformamide dimethyl or dineopentyl acetal in DMF. The nucleotide *(2)* can be obtained in very high yield from the mixture after it has been dried under vacuum, *e.g.*,



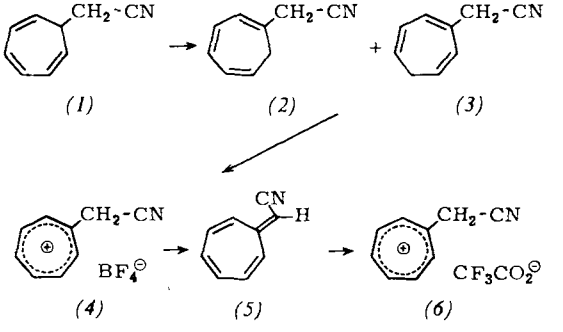
(+ 2'-Isomer)

(1) *(2)*

R = $n\text{-}C_4H_9$
R' = CH_3, $(CH_3)_3C\text{-}CH_2$

by paper chromatography. If the acetals mentioned are replaced, for example, by triethylamine and methanol the yields are reduced considerably. / Tetrahedron Letters *1969*, 115 / –Kr. [Rd 36 IE]

The synthesis of 8-cyanoheptafulvalene *(5)* has been accomplished by *M. Oda* and *Y. Kitahara* from 7-cyanomethylcycloheptatriene *(1)*, which was isomerized to *(2)* and *(3)* by



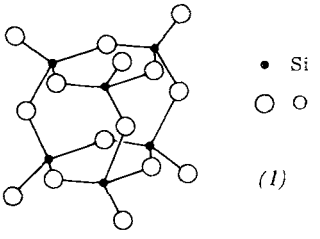
(1) *(2)* *(3)*

(4) *(5)* *(6)*

heating it to 140–150 °C. Treatment of this mixture with triphenylmethyl fluoroborate yielded the tropylium fluoroborate *(4)*, which exists as moderately stable, colorless, hygroscopic crystals of m.p. 108–109 °C (decomp.). Compound *(5)* could be obtained as a red liquid by reaction of *(4)* with triethylamine in CH_2Cl_2. According to the NMR spectrum, the protonated form *(6)* is present in trifluoroacetic acid. Compound *(5)* reacts with dimethyl acetylenedicarboxylate to give dimethyl 1-cyanoazulene-2,3-dicarboxylate, m.p. 175 to 176 °C. / Chem. Commun. *1969*, 352 / –Kr. [Rd 37 IE]

A new method for the production of titanium compounds having low iron content from ilmenite is given by *P. T. Joseph* and *P. M. Mathew*. In laboratory experiments, these authors oxidized the iron(II) of the ilmenite to iron(III) with air at temperatures above 1000 °C. The product is mixed with carbon and a catalyst (*e.g.* iodine) and heated to 700 °C in the absence of air. On heating to 500 °C with NH_4F, the cooled, powdered mass affords iron-free TiF_4. On chlorination in the presence of a little NaCl and iodine, $TiCl_4$ distills over at 200–250 °C. It contains less than 0.1 % of iron. The halogenation residue consists of iron carbide. / Chem. Commun. *1969*, 374 / –Kr. [Rd 38 IE]

A novel silicon-oxygen anion has been found by *Yu. L. Smolin* in $[Ni(NH_2{-}CH_2{-}CH_2{-}NH_2)_3]_3$, Si_6O_{15}, 26 H_2O, one of the few silicates that crystallizes from aqueous solution at room temperature. The most important components of the



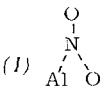
(1)

hexagonal crystals (space group $P6_3$, $a = 17.37 \pm 0.01$, $c = 15.18 \pm 0.01$ Å, $Z = 6$) are the $Ni(en)_3^{2+}$ cation and the novel anion $Si_6O_{15}^{6-}$ *(1)*. Bond angles and bond lengths are in the usual range. Cation and anion are joined by hydrogen bonds. / Chem. Commun. *1969*, 395 / –Kr. [Rd 39 IE]

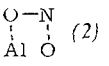
The oxidation of sulfur hexafluoride by oxygen has been studied by *B. Siegel* and *P. Breisacher*. These authors started the reaction of the highly inert SF_6 by explosion of electrically heated platinum or copper wire. Reaction of $\approx 9.7 \times 10^{-3}$ mole of SF_6, in which only 1.13 % of the starting material were consumed (conditions: 220–230 torr of SF_6, approx. equal partial pressure of O_2, 60 torr of Ar, 0.1 mg of Pt vaporized), yielded SOF_4, SOF_2, SO_2F_2, and SO_2 in the ratio 53:33:12:1.4. Under the same conditions, SF_4 reacts extremely rapidly with O_2 to give SOF_2 (major product), SOF_4, SO_2F_2, SO_2, and SF_6. The oxidation of SF_5Cl is also fast compared to that of SF_6; the main product is SOF_2. / J. inorg. nuclear Chem. *31*, 675 (1969) / –Kr. [Rd 40 IE]

The molecular geometry of tricarbonylcyclobutadieneiron, $Fe(CO)_3(C_4H_4)$, has been determined by *H. Oberhammer* and *H. A. Brune* by electron diffraction in the vapor phase. In agreement with the results of NMR measurements in liquid crystal solutions a square structure was found for the cyclobutadiene ring. The most important geometric parameters are: $C_{ring}{-}C_{ring}$ = 1.440 Å; $Fe{-}C_{ring}$ = 2.053 Å; $Fe{-}C_{carb}$ = 1.780 Å; $C_{carb}{-}O$ = 1.148 Å; $C_{carb}{-}Fe{-}C_{carb}$ = 98.1 °. The hydrogen atoms of the cyclobutadiene ring are bent about 8.6 ° towards the iron. The position of the carbonyl groups relative to the cyclobutadiene ring could not be ascertained; there is evidence of free rotation. / Z. Naturforsch. *24a*, 607 (1969) / –Hz. [Rd 43 IE]

The ESR spectrum of NO adsorbed on a Linde molecular sieve, Type 4A, has been investigated by *B. M. Hoffman* and *N. J. Nelson*. Two types of spectra are obtained, depending on the pre-heating temperature of the molecular sieve: after activation at *ca.* 300 °C, two signals appear in the spectrum; after activation at *ca.* 500 °C three signals occur; at intermediate heating-out temperatures both spectra are superposed. At 300 °C the NO is in an axially symmetric environment; in the case of a strongly heated sieve one can, by comparison of the ESR spectra of molecules that can be regarded as substituted NO radicals, exclude single bonding between



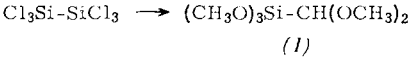
(1)



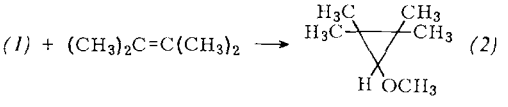
(2)

NO and surface. The adsorption models *(1)* and *(2)* are in accord with findings on strongly heated sieves. / J. chem. Physics *50*, 2598 (1969 / –Hz. [Rd 44 IE]

The formation of methoxycarbene $H(CH_3O)C$: on thermolysis (125 °C) of (dimethoxymethyl)trimethoxysilane *(1)* has been observed by *W. H. Atwell, D. R. Weyenberg*, and *J. G. Uhlmann*. In the reaction of hexachlorodisilane with methyl orthoformate, compound *(1)* was obtained in 20% yield along with bis(trimethoxysilyl)methoxymethane and tetramethoxysilane. The thermolysis of *(1)* in the presence of 2,3-dimethyl-2-butene yields almost quantitatively 3-methoxy-1,1,2,2-tetramethylcyclopropane *(2)* while the decomposition



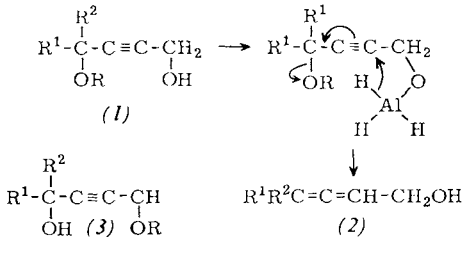
(1)



(2)

of *(1)* in cyclohexene affords 7-methoxynorcarane in 48% yield. In *trans*-2-butene and *cis*-2-butene, 1-methoxy-*trans*-2,3-dimethylcyclopropane and *exo*/*endo*-1-methoxy-*cis*-2,3-dimethylcyclopropane were formed in 66 and 75% yields respectively. The reactions indicate the formation of methoxycarbene as intermediate. Methoxycarbene produced in this way reacts further with methanol, vinylsilanes, *etc.* / J. Amer. chem. Soc. *91*, 2025 (1969) / –Ma. [Rd 47 IE]

A new route for the synthesis of allene alcohols *(2)* is, according to *J. S. Cowie, P. D. Landor*, and *S. R. Landor*, afforded by elimination of tetrahydropyranyloxy residue from monotetrahydropyranyloxy derivatives *(1)* of 2-butyne-1,4-diols by reduction with $LiAlH_4$. Compounds *(1)* are readily accessible from 2-propyn-1-ols and dihydropyran and subsequent reaction with C_2H_5MgBr and CH_2O gas. For example: 4-(tetrahydropyran-2-yloxy)-2-heptyn-1-ol *(1a)* → 2,3-heptadien-1-ol *(2a)* 95% yield; *(1b)* → *(2b)*, 75% yield. This method is also suitable for the synthesis of terminal allene



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

(a), R = tetrahydropyran-2-yl, $R^1 = C_3H_7$, R^2 = H
(b), R = tetrahydropyran-2-yl, $R^1 = C_2H_5$, $R^2 = CH_3$

alcohols; in this case one starts from substituted 2-butyne-1,4-diols having a protected primary OH group *(3)*. / Chem. Commun. *1969*, 541 / –Ma. [Rd 48 IE]

Anorganische Chemie (Inorganic Chemistry). By *F. A. Cotton* and *G. Wilkinson*. Transl. from the American by *H. P. Fritz*. Verlag Chemie GmbH., Weinheim/Bergstr./ Interscience Publishers, New York-London 1968. 2nd Edit., xiv, 1066 pp., 292 illustrations, 145 tables. Plastic-cover DM 69.–.

The enthusiastic reception given to the German translation of *Cotton* and *Wilkinson*'s book "Advanced Inorganic Chemistry" is now confirmed by the fact that a second edition has become necessary after barely a year and a half. Since it is a new edition of a translation there have been no large alterations, but the opportunity has been taken to correct some misleading typographical errors in the first edition and also to make some additions to the references.

Naturally some things have been overlooked; for instance, the so-called γ-tin, whose existence has been refuted. Also the guidelines of the Nomenclature Commission have sometimes not been observed: for example, in the Periodic Table the element 103 is given the symbol Lw whereas the symbol Lr was recommended by IUPAC three years ago; further, the name "zircon" should be reserved for the mineral and the element should be called "zirconium". In the structural chemistry section the reader may be led to false conclusions where on page 42 it is stated that cesium chloride, zinc sulfide, and rutile structure types are representatives of "typical important ionic lattices", whereas these structure types include numerous compounds of both mainly metallic and mainly covalent valence type.

Since this book is certainly not intended for first year students, it would have been worthwhile to express this in the title. Although the text has been translated literally and German idiom suffers occasionally in consequence, literal translation of the title has been avoided: "Advanced Inorganic Chemistry" could have been rendered by, *e.g.*, "Vertiefte Anorganische Chemie".

These few remarks should, however, not be taken as serious criticism of the arrangement, content, or presentation. The new edition can be expected to enjoy the same favor as was given to the first edition of this excellent book.

V. Gutmann [NB 806 IE]

Analyse von Mineral- und Syntheseölen mit radiometrischen Methoden (Analysis of Mineral Oils and Synthetic Oils by Radiometric Methods). By *G. Brunner*, *E. Dahn*, and *M. Geisler*. Akademie-Verlag, Berlin, 1968, xii + 225 pp., 40 figures, 38 tables, DM 21.–.

This book surveys the radiometric methods applicable in the analysis of mineral and lubricating oils. The radiometric determination of hydrogen is particularly useful, partly because the hydrogen content of hydrocarbons is correlated with many important industrial characteristics, and partly because the conventional determinations of hydrogen are too involved for routine petrochemical plant control. Nearly half of the book therefore deals with the determination of hydrogen. By contrast, only about 50 pages are devoted to the determination of sulfur, which is perhaps even more important (catalysis in the petroleum industry, quality of fuels, lubricating oil additives), the reason being that only low-energy irradiation can be used here. However, the procedure can be extended to other elements such as chlorine.

The authors also discuss neutron activation analysis, which is sometimes very sensitive, and is used mainly to determine traces of metals such as V, Ni, Cu, Mn, Mo, Cr, Zn, and Au in mineral oil, and to determine oxygen and additives in lubricating oils. X-ray fluorescence analysis has also been used for years to determine metals and additives in oils. The fourth part of the book deals with the use of radionuclides as sources of exciting radiation instead of X-ray tubes, and gives a description of the method modified accordingly.

Each chapter starts with the physical basis of the technique discussed. This is followed by the description of the procedure and the evaluation of the method. Then comes a discussion of commercial equipment and related problems. Radiometric methods are compared with one another and with conventional methods in connection with experimental publications and selected analyses. This part greatly benefits from the use of instructive tables. Each chapter ends with a bibliography. While no detailed analytical procedures are given, this book will be of great help in the choice of fast, nondestructive, contactless methods for the analysis of mineral and synthetic oils.

B. Knoll [NB 813 IE]

Radiochemisches Lexikon der Elemente und ihrer Isotope. Wichtige Eigenschaften und Anwendungen. (Radiochemical Dictionary of the Elements and their Isotopes. Important Properties and Uses). By *M. Haïssinsky* and *J. P. Adloff*. Translated from the English by *Peter Mayer*. Ferd. Dümmlers Verlag, Bonn-Hannover-München 1968. 1st Edit., 229 pp., stitched DM 19.–.

Radiochemical textbooks usually contain a considerable quantity of theory on radioactive decay, nuclear reactions, *etc.* A detailed description of the nuclear properties of the elements is understandably avoided as a collection of largely repetitive facts.

The practical industrial scientist, to whom a knowledge of the radiochemical properties of an element is a prime necessity for the solution of special problems, has until now had only the nuclide cards for reference. To be able to extract all the necessary information from these, however, detailed radiochemical knowledge is essential. This gap has now been filled by the present dictionary with a somewhat dry but, for the practical worker, very useful account of the nuclear data for all the elements up to atomic number 104. The book is a sort of supplement to radiochemical textbooks, and should be particularly useful to practical workers and engineers.

F. Baumgärtner [NB 803 IE]

Grundbegriffe der Kybernetik (Fundamental Concepts of Cybernetics). By *H.-J. Flechtner*. Wiss. Verlagsgesellschaft mbH, Stuttgart 1969. 4th Edit., xi + 423 pp., 152 figs., stitched; DM 40.–.

This is already the fourth edition of this book, which was first published in 1966. The good reception given to it can be seen from the fact that the third edition sold out in a few months. The new edition differs only by "minor changes", and it still has 423 pages.

This is an introduction to Cybernetics, but not in the same sense of the word as used in the titles of textbooks. Instead, it is intended for those "who are interested in Cybernetics, but lack the mathematical and technical prerequisites for studying it as a branch of science". The indispensible mathematics is at secondary-school level.

In the first chapter entitled "What is Cybernetics?", in which the historical aspects are dealt with, the author gives the answer: "Cybernetics is the general, formal science of structure, relationships, and the behavior of dynamic systems". The fundamental concepts of general Cybernetics are then discussed under the following headings: Communication (behavior of systems, effect of information, control, *etc.*); Information (signs, codes, signals, combinations, redundance, *etc.*); Transmission of Information (sources, channels, decoders, receivers, stores, *etc.*); Processing of Information (connections, cybernetic models and machines, *etc.*); and Behavior of Systems (learning and thinking in the cybernetic sense, regulation, *etc.*). Interesting illustrations are taken from special Cybernetics (*e.g.* theory and construction

of computers, learning machines, and biological and sociological models) and from applied Cybernetics (application of cybernetic concepts, methods, and knowledge to *e.g.* Physics, Chemistry, Biology, Physiology, Medicine, and Sociology). The reader is greatly aided by the inclusion of many references and a subject index.

Theory-of-science considerations complete the description of Cybernetics as a fundamental and as an "auxiliary science, which resembles mathematics in the role it plays in natural sciences".

H. Weber [NB 800 IE]

Transition Metal Intermediates in Organic Synthesis. By *C. W. Bird.* Logos Press – Academic Press, London-New York, 1967, 1st Edit., vii + 280 pp., many illustrations and tables, $ 13.00.

The author, who is a lecturer in Chemistry at Queen Elizabeth College, University of London, has written this book mainly for Organic Chemists, informing them of the many preparations made possible by transition metal intermediates. A variety of topics, such as the oligomerization of acetylenes and olefins, hydroformylation, and hydrogenation, is treated in such a way that the result is a comprehensive literature survey combined with connective passages. The fact that both Russian literature and the patent literature are also covered deserves praise. This book is valuable to all chemists using transition metal compounds in organic syntheses. On the other hand, the superabundance of the material may frighten many uninitiated Organic Chemists from reading and utilizing this book.

The main advantages of organic syntheses with the aid of transition metal compounds are not specified clearly, and they are often submerged in a multitude of apparently anarchic reactions. Despite the price and the fact the literature is covered only up to 1966, this book can be recommended to those who are specialists in this field. Organic Chemists wanting to learn about this new branch of preparative organic chemistry, however, may find the book too expensive for what they can derive from it.

P. Heimbach [NB 815 IE]

Problems for Introductory University Chemistry (With Complete Solutions). By *J. N. Butler, B. A. Dunell,* and *L. G. Harrison.* Addison-Wesley Publ. Comp., London 1967. 1st Edit., vii, 213 pp., 22 s.

The present book contains problems in stoichiometry and important fields of physical chemistry, as well as exercises from analytical and inorganic chemistry. It is intended mainly for beginners, and contains, *inter alia,* problems on fundamental laws of thermodynamics and electrochemistry, *e.g.* on the applications of the *Clausius-Clapeyron, van't Hoff,* and *Nernst* equations. The problems set can be solved on the basis of an elementary knowledge of algebra. Solutions to all the problems are given at the end of the book, which is therefore particularly suitable for private study. A total of 241 problems are given in 13 chapters. A guide to the solution of the problems set in each section is provided in the Appendix. This book can be recommended without reservation as excellently suited for the introduction of students to the quantitative relations of chemistry. The teacher will also find it a useful source of problems for practice and for tutorials. The book is therefore warmly recommended to both students and teachers.

A. Haas [NB 796 IE]

Extrusion Reactions. By *B. P. Stark* and *A. J. Duke.* Pergamon Press, Oxford 1967, 1st Edit., x, 190 pp., numerous figures, 63 s.

In view of the rapidly growing volume of facts in organic chemistry, any attempt to systematize organic reactions seems very sensible and worthwhile. "Extrusion Reactions" is therefore very welcome from this point of view.

Extrusion reactions are processes in which part of the ring of an organic compound is removed as a small, usually inorganic, fragment (CO, CO_2, SO_2, oxygen, sulfur, nitrogen, *etc.*), with formation of a cyclic end product, the ring system of which is smaller or less condensed than that of the starting compound.

A classification of extrusion reactions is followed by the discussion of the experimental results in sections arranged as far as possible according to the fragment removed. Numerous literature data are included; however, evaluation of the aldol-like addition of diazocarbonyl compounds to di- and triketones would have been welcomed in Chapter 10, which deals with the problem of the formation of 1,2,3-oxadiazolines (from diazo compounds and ketones) and the removal of N_2 therefrom.

Otherwise this stimulating book can be wholeheartedly recommended to those involved in research in this direction.

M. Regitz [NB 798 IE]

Marine Chemistry. Vol. 1: Analytical Methods. By *D. F. Martin,* Marcel Dekker Inc., New York 1968, 1st Edit., viii + 280 pp. with many illustrations and tables, $ 5.75.

This book deserves attention, because it gives very clear and logical schemes for analysis. The author has thought of everything, including many tips for avoiding difficulties. However, it is not only a very good "cookbook", but also contains many chapters on general subjects, such as the analysis of polluted water. In addition, the instructions are preceded by a general discussion of analytical possibilities and of interference encountered in analysis. This book requires no specialized knowledge, and seems particularly suitable for training nonchemists in the analysis of water. The main stress is on the analysis of the most important substances featuring in the routine analysis of water, carried out mainly by the latest variants of the conventional methods. Many points can be applied to the analysis of freshwater as well. There is also a brief discussion of the more complicated methods such as atomic absorption spectroscopy and the measurement of bioproduction with ^{14}C.

W. Kölle [NB 801 IE]

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 4 50 75, Telex 46 1855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 8
AUGUST 1969
PAGES 535–622

Mechanisms and Stereochemistry of Heterolytic Fragmentation

By C. A. Grob[*]

Heterolytic fragmentation can proceed by several mechanisms. A study of the solvolysis of γ-aminoalcohol derivatives N–C–C–C–X, where X equals halogen or –OSO_2R, shows that fragmentation may occur by a one-step mechanism or by several multi-step mechanisms depending on structural, electronic, and steric factors. The one-step synchronous mechanism has rigorous stereoelectronic requirements. It is associated with an increased reaction rate as evidenced by the "frangomeric" effect. Ketoxime derivatives RR'C=N–X may undergo Beckmann fragmentation by the synchronous mechanism or by prior rearrangement depending on their α-substituents. Fragmentation is frequently accompanied by conventional substitution, elimination, and rearrangement reactions. Under such circumstances knowledge of all possible mechanisms of a given substrate is essential to bring about a desired transformation.

1. Introduction

Heterolytic fragmentation is a widely occurring type of reaction in organic chemistry[1]. Molecules containing certain combinations of carbon and hetero atoms, such as O, N, S, P, and halogens, undergo a regulated cleavage (fragmentation) into three fragments[2]. In the general formulation of equation (1)

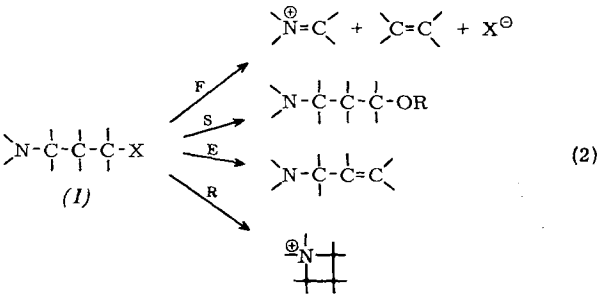
$$a\text{–}b\text{–}c\text{–}d\text{–}X \rightarrow a\text{–}b + c{=}d + :X \qquad (1)$$

a–b denotes an electrofugal group[3], which leaves as the fragment a–b without the bonding electron pair. The middle group –c–d affords the unsaturated fragment c=d, while the nucleofugal group[3] –X leaves in the form of a fragment :X with the bonding electron pair. A number of these groups, combinations of which lead to the principal classes of fragmentable compounds[1], are listed in Table 1.

Table 1. Groups leading to heterolytic fragmentation.

Electrofugal groups a–b	Middle groups –c–d	Nucleofugal groups –X
HO–CR_2	–CR_2–CR_2	–Cl
RO–CR_2	–CR=CR	–Br
HOOC	–CR_2–NR	–I
R_2N–CR_2	–CR_2–O	–SO_3R
R_3C	–CO–O	–OCOR
RCO	–N=N	–$OH_2^{\oplus}$
$R_2\overset{\ominus}{C}$–CR_2	–CO	–$NR_3^{\oplus}$
H_2N–NH		–$SR_2^{\oplus}$
HN=N		–$N_2^{\oplus}$

Of the many fragmentation reactions known, only a few have to date been subjected to mechanistic and stereochemical studies. Probably the most fundamental investigation of this type has been carried out with



(2)

F = fragmentation, S = substitution, E = elimination, R = ring closure

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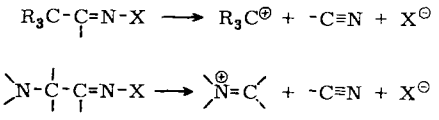
[1] *C. A. Grob* and *P. W. Schiess*, Angew. Chem. *79*, 1 (1967); Angew. Chem. internat. Edit. *6*, 1 (1967).

[2] *C. A. Grob* and *W. Baumann*, Helv. chim. Acta *38*, 594 (1955); *C. A. Grob*, Experientia *13*, 126 (1957); Theoretical Organic Chemistry, Report on the Kekulé Symposium. Butterworth, London 1958, p. 114.

[3] *J. Mathieu*, *A. Allais*, and *J. Valls*, Angew. Chem. *72*, 71 (1960).

γ-aminohalides and γ-aminosulfonates (1) (X = halogen or $-OSO_2R$), fragmentation of which leads to an imonium salt and an olefin [eq. (2), route F]. These compounds are obtainable in acyclic, monocyclic, and bicyclic variants, though often only by rather involved syntheses. Compounds of the type (1) react directly in aqueous and alcoholic solutions. Since the courses and rates of their reactions can be readily determined, they are particularly suitable for the study of heterolytic fragmentation.

Similarly certain ketoxime derivatives and their α-amino derivatives, fragment in polar solvents into nitriles and carbonium or imonium ions (see Section 10)



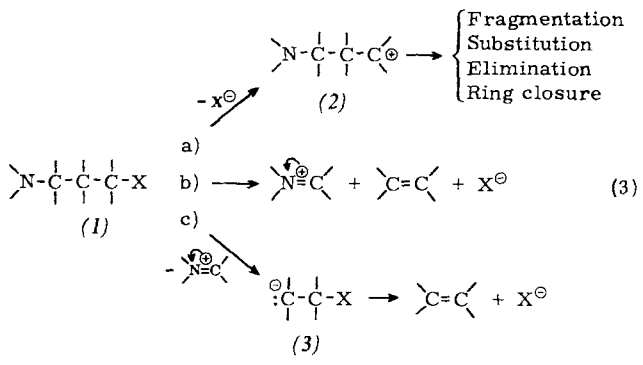
2. Review of the Reaction Paths of the System N–C–C–C–X

Amines *(1)* with nucleofugal substituents in the γ position can react in several ways. In addition to fragmentation into an imonium salt and an olefin [path F in eq. (2)], at least three other reaction paths are possible. In nucleophilic solvents, such as water or alcohols, they can undergo substitution (S) and elimination (E) as well as ring closure (R) to form an azetidinium salt. Examples will be given to show that the course of the reaction depends on the structure, configuration, and conformation of the substrate. The mechanism (and hence the products formed) thus depends on steric as well as electronic factors.

3. The Three Basic Mechanisms

Though the structural and electronic requirements and the number of bonds broken are the same in all fragmentations in accordance with eq. (1), the sequence with which bond rupture occurs may be different. The process may thus take place in one or two steps, *i.e.* the fragments a–b and –X may be released from the central group –c–d either simultaneously or successively. For amines *(1)* with nucleofugal substituents in the γ position, three basic mechanisms are therefore possible [eq. (3)]. These are the one-step process (b) and two-step processes (a) and (c), all of which follow the first order kinetic law.

The two-step process (a) begins with the loss of the nucleofugal group –X to form a γ-amino carbonium ion *(2)*. This then breaks down in a faster step into an imonium ion and an olefin, thus completing the fragmentation. The cationic intermediate *(2)* may, however, react further by substitution, elimination, and ring closure.



(3)

In the one-step or synchronous process (b), the electrofugal imonium ion and the nucleofugal group –X leave simultaneously from C_β and C_α, respectively. In the third case (c), the imonium ion leaves first. The remaining carbanion (3) is stabilized by conversion into an olefin and $X^\ominus$ or by protonation.

These three basic mechanisms have certain structural and stereo-electronic requirements, and may be compared to the three known mechanisms of 1,2-elimination to form olefins [4]. In the elimination, however, a hydrogen or halogen atom is split off as an electrofugal species by an external base or reducing agent, whereas in fragmentation a polyatomic group leaves spontaneously [eq. (1)].

The two-step fragmentation mechanism (a) and the synchronous mechanism (b) have been detected in many cases. The rare two-step mechanism (c) was only recently confirmed by experiment.

4. The Two-Step Carbonium Ion Mechanism

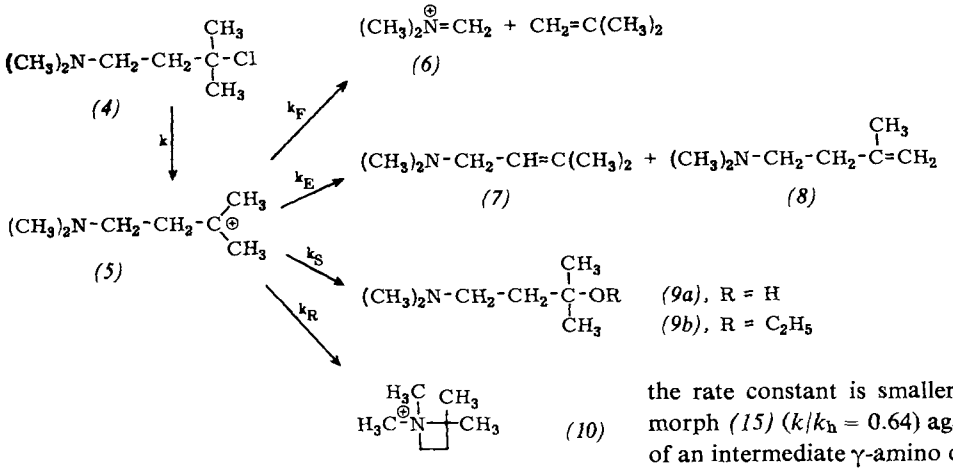
The rate-determining step in this mechanism is the ionization to form a carbonium ion [path (a) in eq. (3)]. It is thus identical with that of unimolecular substitution (S_N1) and elimination (E1) [4]. As in these cases, the tendency to ionize is greatest when a tertiary, and hence particularly stable, carbonium ion is formed. This applies *e.g.*, to 3-chloro-*N*,*N*,3-trimethylbutylamine *(4)* [5].

The reaction of this compound in 80 vol-% ethanol [6] leads to 38% of fragmentation products, *i.e.* isobutene together with dimethylamine and formaldehyde, the latter arising from hydrolysis of the imonium ion *(6)*. In addition 37% of the aminoolefins *(7)* and *(8)* are formed by elimination, 23% of the alcohol *(9a)* and of the ethyl ether *(9b)* by substitution, and 2% of the azetidinium ion *(10)* by ring closure. The product ratio is almost unchanged when the bromide or

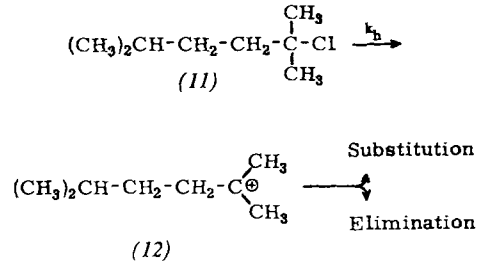
[4] *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. Cornell University Press, Cornell 1953, p. 419ff; J. chem. Soc. (London) *1962*, 265.

[5] *C. A. Grob* and *F. Ostermayer*, Helv. chim. Acta *45*, 1119 (1962); *C. A. Grob*, *F. Ostermayer*, and *W. Raudenbusch*, *ibid. 45*, 1672 (1962).

[6] Except where otherwise specified, the reactions described in this article were carried out in 0.01–0.001 M solution in 80 vol.% ethanol.



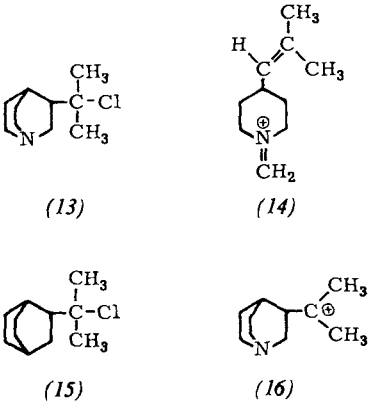
iodide corresponding to *(4)* is used (for example, the bromide gave 40% of fragmentation products, the iodide 42%). The reaction rate, on the other hand, increases in the order customary for ionization reactions, *i.e.* Cl < Br < I. These observations indicate that the rate-determining step k leads to the formation of the γ-aminocarbonium ion *(5)*, which reacts further in fast secondary steps k_F, k_E, k_S, and k_R.



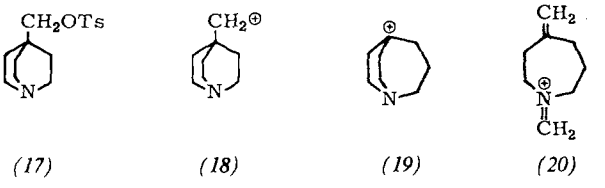
Further support of this mechanism is provided by a comparison of the rate constants for the γ-chloroamine *(4)* with those for the sterically equivalent *i.e.* homomorphous chloroalkane *(11)*. Tertiary chloroalkanes of this type are known [4] to react *via* carbonium ions *(12)* under solvolytic conditions. The comparison of the rate constants k of *(4)* and k_h of *(11)* provides information about the possible participation of the nitrogen atom in the ionization step. If it does not participate, k should be equal to or smaller than k_h ($k/k_h \leq 1$). If, however, the ionization of the γ-chloramine is favored by the nitrogen atom, the chloroamine should react more rapidly than the homomorphous chloroalkane ($k/k_h > 1$).

The ratio of the rate constants of the compounds *(4)* and *(11)* is 0.52 at 25 °C. Thus the only effect of the nitrogen atom is its electron-withdrawing inductive effect which causes the γ-chloroamine *(4)* to react more slowly than its homomorph, *i.e.* the ionization to give the carbonium ion *(5)* is more difficult.

Another example of the two-step carbonium ion mechanism is provided by 3-(chlorodimethylmethyl)-quinuclidine *(13)*, which reacts to give 62% of the fragmentation product *(14)* together with 30% of substitution products and 6% of elimination products [7]. The formation of several products and the fact that the rate constant is smaller than that of the homomorph *(15)* ($k/k_h = 0.64$) again point to the formation of an intermediate γ-amino carbonium ion, *i.e. (16)* in the rate-determining step.



A fragmentable γ-amino carbonium ion can also be produced by rearrangement of an amine with a nucleofugal substituent in the δ position. Thus the ionization of the *p*-toluenesulfonyl ester *(17)* leads to the primary carbonium ion *(18)*, which undergoes a Wagner-Meerwein rearrangement into the bicyclic γ-amino carbonium ion *(19)*, the precursor of the fragmentation product *(20)* [8].



5. The Synchronous Mechanism

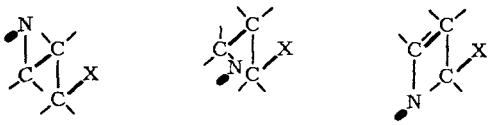
Since five atomic centers of one molecule are involved in the transition state it was expected that this mechanism would have rigorous structural and stereoelectronic requirements. Thus the synchronous mechanism should operate only if both the C_α–X bond and the orbital of the lone pair of electrons on the nitrogen (N-electron pair) are *anti* and parallel anti-periplanar [9] to the C_β–C_γ bond.

These conditions are satisfied by the staggered conformation *(21)*, and by all rotamers derived from it by rotation of the amino group about the C_β–C_γ

[7] *H. G. Enderle*, Dissertation, Universität Basel 1967.

[8] *C. A. Grob*, *R. M. Hoegerle*, and *M. Ohta*, Helv. chim. Acta *45*, 1823 (1962).

[9] *W. Klyne* and *V. Prelog*, Experientia *16*, 521 (1960).



(21) (22) (23)

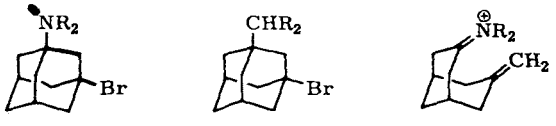


(24)

bond. Two rotamers of this type are the skew *(22)* and the eclipsed conformation *(23)*. Only such conformations permit maximum overlap of the p orbitals of the sp^2-hybridized atoms formed in the unsaturated fragments in the transition state *(24)*. Rotations about the $C_\alpha-C_\beta$ and $C_\gamma-N$ bonds, on the other hand, lead to energetically less favorable transition states with the result that the synchronous process is suppressed. However, the stereoelectronically favorable conformations are not always the sterically most favorable ones as *e.g.* the eclipsed form *(23)*.

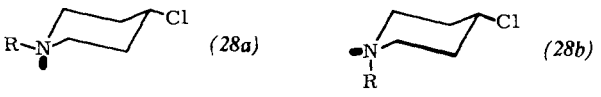
The synchronous mechanism can be detected mainly on the basis of kinetic criteria. The positive charge formed on the cation in the ionization process is transferred to the relatively stable imonium ion. Therefore N–C–C–C–X systems that undergo synchronous fragmentation react more rapidly than homomorphous compounds without nitrogen, in which the positive charge remains localized on the C_α atom. A k/k_h ratio greater than 1 thus indicates the participation of the amino group and points to a synchronous process.

Another kinetic criterion for the participation of this group is provided by comparison of the rate constants for γ-nucleofugally substituted amines, in which the substituents R on the N atom are varied. Since the amino group acquires the positive charge in the transition state *(24)* of the synchronous fragmentation, the reaction rate must depend on the number and nature of these substituents.

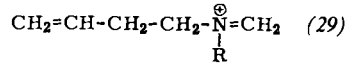


(25) (26) (27)

3-Bromoadamantylamines *(25)* (R = H or CH_3) react faster than the homomorphous 1-alkyl-3-bromoadamantanes *(26)* (R = H or CH_3), and undergo quantitative fragmentation with formation of the imonium salts *(27)* [10]. As the number of methyl groups on the nitrogen atom is increased, the absolute and relative rates with respect to the homomorphs *(26)* increase. Thus k/k_h is 30 for the primary amine, 222 for the secondary amine, and 520 for the tertiary amine. The increase in the reactivity with the number of *N*-methyl substituents corresponds to the increasing electromeric effect of the amino group, as also observed in the electrophilic substitution of aniline derivatives. The atoms taking part in the synchronous fragmentation have the staggered conformation *(21)* and so satisfy the antiparallelism principle mentioned above. (The antiparallel electron pairs are indicated by bold type.)

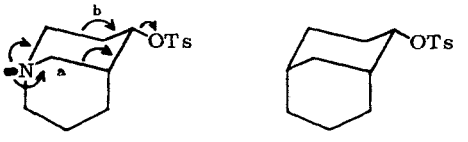


(28a) (28b)



(29)

4-Chloropiperidine and its *N*-alkyl derivatives *(28)* react about 100 times as rapidly as chlorocyclohexane, with quantitative fragmentation to give the imonium ions *(29)* [11]. When the N-electron pair assumes the equatorial position *(28b)*, these compounds *(28)* have the skew conformation *(22)*. However, in the conformational equilibrium *(28a)* ⇌ *(28b)* the population of the less favorable form *(28a)* (N-electron pair in the axial position) will increase with the size of the substituent R. This is the only explanation for the fact that 4-chloropiperidine *(28)* (R = H) reacts somewhat faster than the *N-tert*-butyl derivative *(28)* [R = $C(CH_3)_3$].

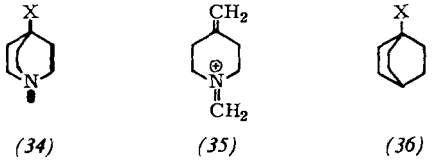


(30) (31)



(32) (33)

The more rigid *exo*-4-*p*-toluenesulfonyloxy-1-azabicyclo[3.3.1]nonane *(30)*, which reacts 16 times as fast as the homomorphous *exo*-2-*p*-toluenesulfonyloxybicyclo[3.3.1]nonane *(31)*, has the same conformation as *(28b)*. It is interesting to note that the reaction of *(30)* leads exclusively to the relatively strained imonium ion *(32)* of the *cis*-1-aza-4-cyclooctene (path a), and none of the imonium ion *(33)* of the 3-vinylpiperidine (path b) is formed [12]. The preferred formation of the thermodynamically less stable product *(32)* is difficult to explain, since paths a and b are stereoelectronically equivalent.



(34) (35) (36)

[10] *C. A. Grob* and *W. Schwarz*, Helv. chim. Acta *47*, 1870 (1964).

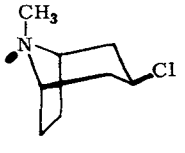
[11] *R. D'Arcy*, *C. A. Grob*, *T. Kaffenberger*, and *V. Krasnobajew*, Helv. chim. Acta *49*, 185 (1966).

[12] *T. Kaffenberger*, Dissertation, Universität Basel 1966.

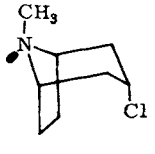
The eclipsed conformation *(23)* is present in the 4-halogeno- and 4-*p*-toluenesulfonyloxyquinuclidines *(34)* (X = halogen or OTs). These compounds undergo quantitative fragmentation at different rates, with formation of the 1,4-dimethylenepiperidinium ion *(35)*. The reaction rates are extremely high in comparison with those of the homomorphous 1-substituted bicyclo[2.2.2]octanes *(36)*. Thus 4-bromoquinuclidine *(34)* (X = Br) reacts about 50000 times as fast as 1-bromobicyclo[2.2.2]octane *(36)* (X = Br), even though bridgehead halides are normally very inert It is worthy of note that the ratio of the rate constants of the *p*-toluenesulfonate and of the bromide k_{OTs}/k_{Br} is approximately 10^3 in both systems It must therefore be concluded that the rupture of the C–X bond is advanced to the same degree in the transition state in both cases [13], despite the fact that the homomorphs *(36)* give a localized carbonium ion whereas the 4-substituted quinuclidines lead to a cation with a delocalized charge.

6. Stereochemistry and Mechanism

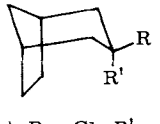
The examples in Section 5 show that systems that satisfy the antiparallelism principle undergo synchronous fragmentation. This does not, however, prove that the aforementioned stereochemical conditions are essential. Such proof can be obtained by a comparison of the reactivity of two stereoisomers only one of which satisfies the stereoelectronic conditions. The form that does should fragment by the synchronous mechanism, while its stereoisomer should react by the two-step carbonium ion mechanism. In the latter case, therefore, fragmentation should be accompanied by conventional reactions, *i.e.* by substitution, elimination, and ring closure, in accordance with path (a) in eq. (3).



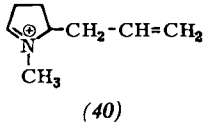
(37)



(38)

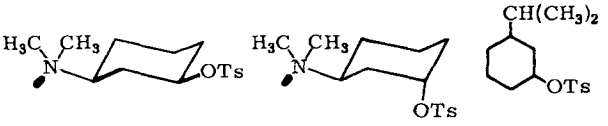


(39a), R = Cl, R' = H'
(39b), R = H, R' = Cl



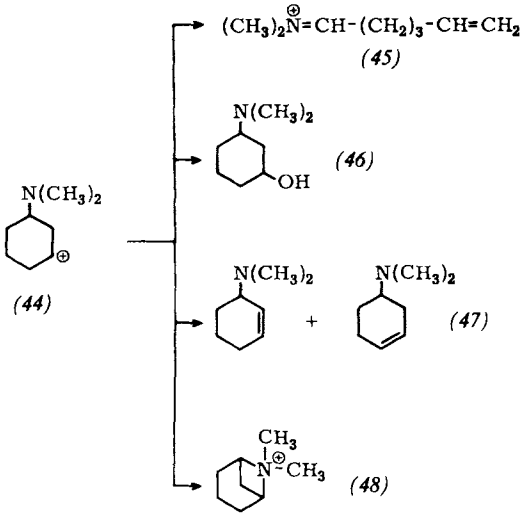
(40)

This hypothesis can be checked with the aid of the stereoisomeric 3-chlorotropanes *(37)* and *(38)*. The 3β-chloride *(37)* contains the skew conformation *(22)*, and should thus fragment by the synchronous mechanism, not however the 3α-chloride *(38)*, since its C–Cl bond is not antiparallel to the C_β–C_γ bond. It is in fact found that the 3β-chloride reacts 13500 times as fast as the homomorphous *exo*-3-chlorobicyclo[3.2.1]-octane *(39a)*, and gives only the fragmentation product *(40)*. The 3α-chloride, on the other hand, does not react appreciably faster than the homomorph *(39b)*, and gives only substitution and elimination products [14].



(41) *(42)* *(43a), cis* *(43b), trans*

A similar situation is found for the stereoisomeric 3-dimethylaminocyclohexyl *p*-toluene sulfonates *(41)* and *(42)* [15]. The *cis* form *(41)*, which satisfies the stereoelectronic requirements, reacts 39 times as fast as the homomorphous *cis*-3-isopropylcyclohexyl *p*-toluenesulfonate *(43a)*, with quantitative fragmentation to form the imonium ion *(45)*. The *trans* form *(42)*, on the other hand, reacts more slowly than the homomorphous *trans*-3-isopropylcyclohexyl *p*-toluenesulfonate *(43b)* (k/k_h = 0.64) and yields the expected products of the γ-amino carbonium ion *(44)*, *i.e.* the fragmentation product *(45)*, the *cis* and *trans* forms of the amino alcohol *(46)*, the aminoolefins *(47)*, and the bicyclic ion *(48)*.



(44) *(45)* *(46)* *(47)* *(48)*

The influence of configuration on the reaction course is very pronounced in the case of the stereoisomeric 10-chloro-*N*-methyldecahydroisoquinolines *(49)* and *(50)* [16]. Whereas the *trans* isomer is fixed in the rigid double chair conformation *(49)*, the *cis* isomer is an equilibrium mixture of the conformers *(50a)* and *(50b)*. The position of the chlorine atom favors synchronous fragmentation only in the form *(50a)*, but not in the conformation *(50b)* or in the *trans* isomer *(49)*.

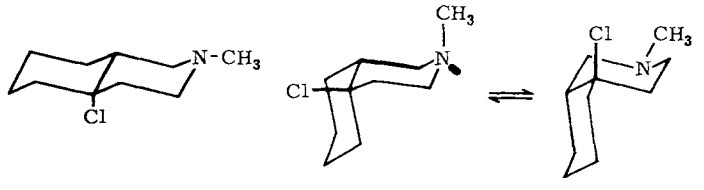
As expected *cis*-10-chloro-*N*-methyldecahydroisoquinoline *(50)* reacts about 128 times as fast as the

[13] *C. H. DePuy* and *C. A. Bishop*, J. Amer. chem. Soc. *82*, 2535 (1960); *H. M. R. Hoffmann*, J. chem. Soc. (London) *1965*, 6753.

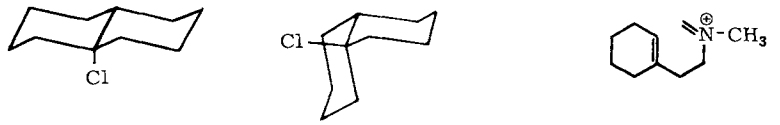
[14] *A. T. Bottini, C. A. Grob, E. Schumacher*, and *J. Zergenyi*, Helv. chim. Acta *49*, 2516 (1966).

[15] *U. Burckhardt, C. A. Grob*, and *H. R. Kiefer*, Helv. chim. Acta *50*, 231 (1967).

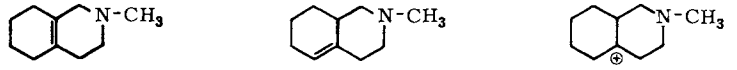
[16] *C. A. Grob, R. A. Wohl*, and *M. Geisel*, unpublished results.



(49) (50a) (50b)



(51) (52) (53)

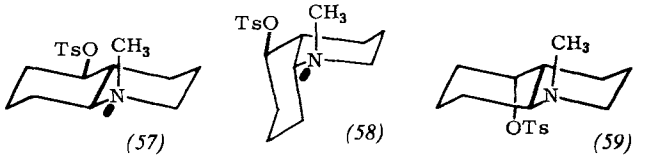


(54) (55) (56)

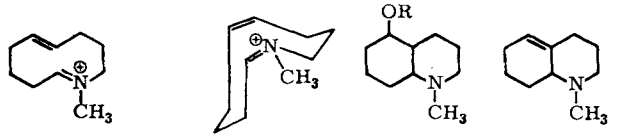
homomorphous *cis*-9-chlorodecalin *(52)*, with exclusive fragmentation to give the imonium ion *(53)*. The reaction of the *trans* isomer *(49)*, however, is slower by a factor of 4.5 than that of the homomorph *(51)*, and leads to the imonium salt *(53)* besides the olefins *(54)* and *(55)*. [The reasonable assumption is made that the absence of a methyl group on C-3 of the homomorphs *(51)* and *(52)* has little or no effect on their reaction rates.] Thus the *cis* isomer *(50)* must undergo synchronous fragmentation, while the *trans* isomer *(49)* fragments in two steps *via* the carbonium ion *(56)*. The *trans* homomorph *(51)* significantly gives the corresponding olefins, *i.e.* 1,2,3,4,5,6,7,8- and 1,2,3,4,4a,5,6,7-octahydronaphthalenes [CH_2 instead of NCH_3 in *(54)* and *(55)*]. The example *(50)* shows further that γ-halogeno amines react by the synchronous mechanism even when they give rise to stable tertiary carbonium ions.

The high stereospecificity of the synchronous fragmentation is even more clearly demonstrated in the case of the three stereoisomeric *N*-methyldecahydroquinol-5-yl *p*-toluenesulfonates *(57)*, *(58)*, and *(59)* [17]. Of these only the 5α-*trans* *(57)* and the 5α-*cis* isomers *(58)* with equatorial *p*-toluenesulfonyloxy groups exhibit the theoretically necessary antiparallelism of the electron pairs involved, while the 5β-*trans* isomer *(59)* does not. The two compounds *(57)* and *(58)* are in fact found to undergo exclusive fragmentation to give the unsaturated ten-membered imonium ions *(60)* and *(61)* (or their hydrolysis products). Whereas the *trans* olefin *(60)* is formed in the first case, the *cis* olefin *(61)* is obtained in the second. That these are synchronous processes is apparent from the fact that the reaction rates are higher for the compounds *(57)* and *(58)* than for the homomorphous 1-decalyl *p*-toluenesulfonates *(64)* and *(65)*.

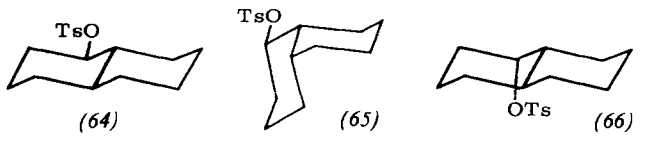
The 5β-*trans* *p*-toluenesulfonate *(59)*, on the other hand, reacts more slowly by a factor of about 8 than the homomorphous 1-decalyl *p*-toluenesulfonate *(66)*, *i.e.* $k/k_h = 0.12$. Since only the substitution and elimination products *(62)* and *(63)* are formed, this reaction must proceed by the two-step carbonium ion mechanism.



(57) (58) (59)



(60) (61) (62) (63)



(64) (65) (66)

The steric orientation of the N-electron pair has not been considered so far. Instead it has been tacitly assumed that because of the fast inversion of the nitrogen atom, this electron pair can adopt the antiparallel orientation required for the synchronous mechanism. The compounds *(57)* and *(58)*, as well as the *N*-methylamines mentioned earlier that undergo synchronous fragmentation, were formulated accordingly, though it must be assumed that the *N*-methyl group will more often occupy the equatorial position. The following study on the 7α- and 7β-*trans*-1-methyldecahydroquinolyl *p*-toluenesulfonates *(67)* and *(68)* is of particular interest with respect to the influence of the orientation of the N-electron pair [17].

In these compounds the N-electron pair cannot occupy the orbital antiparallel to the $C_\beta-C_\gamma$ bond, since

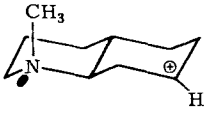
[17] *C. A. Grob, H. R. Kiefer, H. J. Lutz,* and *H. J. Wilkens,* Helv. chim. Acta *50*, 416 (1967).



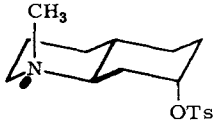
(67)



(70)



(69)



(68)



(71)

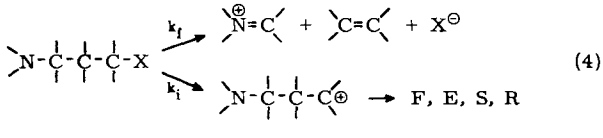
this space is taken up by the σ-electron pair of the bond between N and C-2. The N-electron pair must oscillate in a plane perpendicular to the ring. Thus in the equatorial 7α-*p*-toluenesulfonate *(67)* fragmentation by the synchronous mechanism should not be possible even though the C_α–OTs and the C_β–C_γ bonds are antiparallel. The two-step fragmentation *via* the γ-amino carbonium ion *(69)* should also be impossible for the same reason.

In fact neither the 7α nor the 7β *p*-toluenesulfonate *(67)* or *(68)* undergoes fragmentation. Both compounds exhibit only substitution and elimination *via* the carbonium ion *(69)* by the S_N1 and E1 mechanisms. (In both cases, mixtures of the 7α- or 7β-alcohol and ethyl ether, as well as 1,2,3,4,4a,5,8,8a- and 1,2,3,4,4a-, 5,6,8a-octahydro-1-methylquinoline are obtained.) The non-participation of the amino group also follows from a comparison of the rate constants with those of the homomorphous 2-decalyl *p*-toluenesulfonates *(70)* and *(71)*; the k/k_h values are 0.37 and 0.43. The ionization rates are thus appreciably reduced by the inductive effect of the nitrogen atom. These results show that the orientation of the electron pair on the donor atom is decisive for fragmentation.

7. The Frangomeric Effect

A synchronous fragmentation can occur only if the rate constant k_f of this process is comparable with or greater than the rate constant k_i of ionization to the γ-amino carbonium ion, *i.e.* if $k_f \geq k_i$ in eq. (4). As shown by previous examples, the synchronous process k_f always predominates when the stereoelectronic requirements are satisfied.

For convenience the increase in reactivity due to synchronous fragmentation has been called the frango-



(4)

meric effect *f*. It is defined as the ratio of the rate constants k_f and k_i.

$$f = k_f/k_i$$

With few exceptions [11], however, k_f and k_i cannot be determined for a single compound, since only one of the two processes is generally observable. To determine k_i for cases in which the synchronous mechanism predominates, it is necessary to use the ionization rate of a homomorphous compound. In cases where it can be measured directly, however, the constant k_i is always smaller than the constant k_h of the homomorphous compound by a factor *i*, as a consequence of the inductive effect of the nitrogen atom. The inductive factor *i*

$$i = k_h/k_i$$

has values between 2 and 8 for cyclic γ-halogeno amines and γ-amino sulfonates. It depends on the environment and direction of the dipoles in these compounds as well as on the solvent. (The inductive factor *i* increases with the degree of transmission of the effect inside the molecule, *i.e.* through a region of low dielectric constants.) Frangomeric effects *f* (see Table 2) can be calculated approximately from the known rate constants for homomorphous compounds with the aid of an estimated inductive factor.

$$f = k_f \times i/k_h$$

Table 2. Approximate values of the frangomeric effect *f*.

Compound	k/k_h	*f*
(25), R = CH_3	520	10^3
(28), R = H	113	280
(28), R = $C(CH_3)_3$	34	85
(30)	16	80
(34), X = Br	5.4×10^4	10^5
(37)	1.35×10^4	10^4
(41)	39	10^2
(50)	128	6×10^2
(57)	46	2×10^2
(58)	1.5	10

The *f* values vary considerably. As an aid to understanding these figures it must be noted that they are based on a comparison of the rates of two different reactions, and that steric effects on each may be different. For example, in the case of 4-bromoquinuclidine *(34)* (X = Br) k_f is high because of the decrease in steric strain in the transition state of fragmentation, whereas the rate of formation k_i of a carbonium ion on the bridgehead of a bicyclic system is low. The value of *f* is consequently very large. (If several equivalent fragmentation paths are available, *e.g.* three for *(34)* and two for *(37)*, a statistical correction must be made to the *f* values.) For 5α-*cis*-*N*-methyldecahydroquinolyl *p*-toluenesulfonate *(58)*, on the other hand, fragmentation leads to the strained ten-membered *cis*-*cis*-imonium ion *(61)*, with the result that the value of k_f is decreased. The ionization of the *p*-toluenesulfonyl group, however, is sterically accelerated by the *cis* C4–C1 bond (*cis*-2-alkyl effect) [18], and k_i is accordingly increased. The result is a relatively low *f* value. Finally in the determination of the *f* values in Table 2 no allowance was made for the fact that in flexible systems, the conformation leading to synchronous fragmentation is often present only to a small extent. This results in a decrease in k_f, as in the

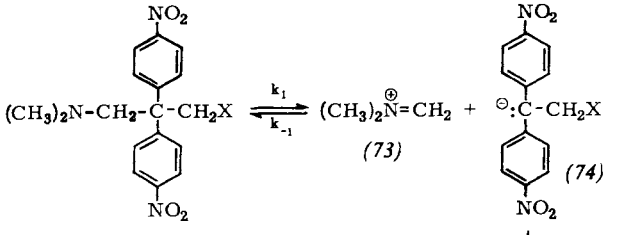
[18] *C. A. Grob* and *S. W. Tam*, Helv. chim. Acta *48*, 1317 (1965).

case of 4-chloropiperidines *(28)*. An accurate treatment of the frangomeric effect thus entails corrections for steric and inductive effects, the reliability of which is questionable.

A frangomeric effect is thus always observed when a system fragments by the synchronous mechanism. A comparison of the activation energies and activation entropies with those of homomorphous compounds suggests that the increased reactivity is largely due to a more positive activation entropy[19]. This tendency becomes more pronounced as the number of degrees of freedom lost in the transition state of the fragmentation decreases, as *e.g.* in the rigid molecules of 4-bromoquinuclidine *(34)* (X = Br) and 1-dimethylamino-3-bromoadamantane *(25)* (R = CH_3). In the more flexible *cis*-3-dimethylaminocyclohexyl *p*-toluenesulfonate *(41)*, for example, the activation entropy is only slightly more positive than in the homomorph, since both the rotation of the amino group and the movements of the cyclohexane ring are suppressed in the transition state.

8. The Two-Step Carbanion Mechanism

In the cases considered so far, the fragmentation process was either initiated by the release of the nucleofugal moiety $-X$ or it involved the simultaneous release of $-X$ and the electrofugal group [paths (a) and (b) in eq (3).] In the third basic mechanism, the electrofugal imonium ion separates from a carbanion in a reversible reaction [path (c) in eq. (3)]; subsequently $-X$ leaves in a fast secondary reaction. This mechanism can occur only if the carbanion is stabilized by electron-attracting substituents and if the nucleofugal activity, *i.e.* the tendency of $-X$ to leave, is low.



(72), X = OH
(72a), X = C_6H_5COO
(72b), X = p-$CH_3C_6H_4COO$
(72c), X = p-$CH_3OC_6H_4COO$
(72d), X = p-$NO_2C_6H_4COO$

These requirements are satisfied by the esters *(72a–d)* of 3-dimethylamino-2,2-bis(*p*-nitrophenyl)propanol *(72)*[20]. As free bases, these esters decompose into 1,1-bis(*p*-nitrophenyl)ethylene *(75)* [*via* the carbanion *(74)*] and the imonium ion *(73)* or its hydrolysis products dimethylamine and formaldehyde.

The two-step carbanion mechanism is supported primarily by the fact that the first order rate constants of the esters *(72a–d)* differ by only a small factor. Thus, the ionization of X alone cannot be the deciding factor. The observed rates are in fact probably determined by the ratio k_2/k_{-1}, as is the case with other reactions involving the reversible formation of a short-lived intermediate. Further evidence of the existence of the carbanion intermediate *(74)* is provided by the fact that esters of structure *(72a–d)* without *p*-nitro substituents undergo ester hydrolysis instead of fragmentation under the same conditions. Systematic studies on this fragmentation mechanism are, however, still in their early stages.

9. Combined Mechanisms

As was shown in Section 4, the open-chain, freely rotating 3-chloro-*N*,*N*,3-trimethylbutylamine *(4)* reacts by the two-step carbonium ion mechanism, though it can adopt a conformation suitable for the synchronous fragmentation, such as *(21)*, *(22)*, or *(23)*. An explanation for this unexpected behavior is that owing to thermal motion, the molecule does not remain in these conformations often or long enough and that the synchronous process is disturbed by rotations about the C_α–C_β and C_γ–N bonds. The formation of the transition state is thus associated with the loss of degrees of freedom. It is therefore unfavorable on entropy grounds.

We are now faced with the question whether acyclic systems with free rotation are in fact capable of undergoing synchronous fragmentation. To this end the reactivities of primary, secondary, and tertiary γ-

Table 3. Influence of methyl substitution on the reactivity of γ-chloro amines in 80 vol-% ethanol at 56 °C (Me = CH_3)

Compound	$k \times 10^5$	k/k_h	Products (%) [a]
$Me_2N-CH_2-CH_2-CH_2-Cl$ *(76)*	10.8	$4.3 \cdot 10^3$	100 R
$Me_2N-CH_2-C(Me)_2-CH_2Cl$ *(77)*	98	$3.4 \cdot 10^6$	100 R
$Me_2N-CH_2-CH_2-CHCl(Me)$ *(78)*	1.87	520	100 R
$Me_2N-CH_2-C(Me)_2-CH(Me)-Cl$ *(79)*	28.2	4100	72 R, 19 F
$Me_2N-CH_2-C(Me)_2-C(Me)_2-Cl$ *(80)*	14500	125	70 F, 30 E
$Me_2N-C(Me)_2-CH_2-C(Me)_2-Cl$ *(81)*	41200	24	80 F, 20 E
$Me_2N-CH_2-CH_2-C(Me)_2-Cl$ *(4)*	35.5	0.52	38 F, 37 E, 23 S, 2 R

[a] R = ring closure, F = fragmentation, E = elimination, S = substitution.

[19] A relatively positive activation entropy is often observed in reactions in which several bonds are broken in the transition state; cf. *B. G. Gowenlock*, Quart. Rev. (Chem. Soc., London) *14*, 133 (1960).

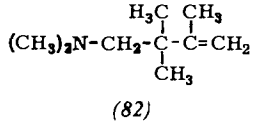
[20] *C. A. Grob, F. M. Unger, E. D. Weiler*, and *A. Weiss*, unpublished results.

chloroamines with varying numbers of methyl groups in the α, β, and γ positions have been compared (Table 3).

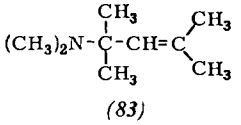
The primary chloroamines *(76)* and *(77)* exhibit exclusive ring closure. The high k/k_h values show that intramolecular nucleophilic substitution is accelerated by neighboring group participation, *i.e.* anchimerically[21]. The fact that the rate for the β-dimethylated compound *(77)* is about 10 times higher than *(76)* illustrates the geminal dialkyl effect, which increases the frequency of the quasi-cyclic conformations that lead to ring closure.

In the secondary chlorine compound *(78)*, ring closure is still the only reaction, but the rate of the intramolecular substitution (and hence also k/k_h) is lower because of the greater steric hindrance at the α carbon atom. The introduction of two geminal methyl groups into the β-position, as in compound *(79)*, again increases the reaction rate and the k/k_h value considerably. However, since fragmentation now occurs as well as ring closure, the problem arises whether an anchimerically accelerated ring closure reaction is combined with a synchronous fragmentation.

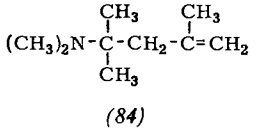
The tertiary chlorine compound *(4)* is the prototype of a γ-chloro amine that reacts by the two-step carbonium ion mechanism. The mechanism surprisingly changes on introduction of additional geminal methyl groups into the β and γ positions. Thus the α,α,β,β-tetramethylated compound *(80)* and the α,α,γ,γ-tetramethylated isomer *(81)* react 125 and 24 times as fast as their respective homomorphous chloroalkanes. The ionization is therefore assisted by the nitrogen atom in both cases. Since the only products formed aside from fragmentation products are the aminoolefins *(82)* or *(83)* and *(84)*, the accelerated fragmentation must be accompanied by accelerated elimination.



(82)



(83)



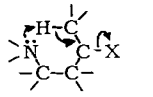
(84)

Both reactions are independent of the addition of external bases. The aforementioned aminoolefins must therefore be formed by a hitherto unknown elimination mechanism in combination with accelerated fragmentation[22].

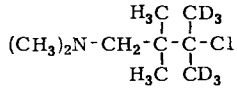
This result cannot be explained by the accelerated formation of an azetidinium salt *(85)* that subsequently suffers fragmentation and elimination, since these salts are stable or else they are not formed under the conditions of the reaction[23]. (This was demonstrated in the case of the symmetrical 2,2,4,4-tetramethylazetidine by labeling with ^{14}C[24].) The combination of a synchronous fragmentation and an anchimerically accelerated elimination in accordance with *(86)*[25] is also unlikely, since the reaction of the deuterated γ-chloroamine *(87)* shows no primary isotope effect such as would be expected for the removal of a proton in the transition state in accordance with *(86)*[26].



(85)



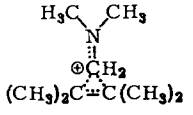
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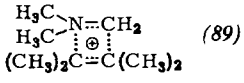
(87)

The formation of a symmetrical π complex *(88)*, which could conceivably be a precursor of the fragmentation and elimination products, was excluded by experiments with the γ-chloroamine *(80)* labeled with ^{14}C[27]. Although the alternative unsymmetrical π complex *(89)* has not been ruled out, its formation is unlikely since tetramethylethylene cannot be condensed with the imonium salt from dimethylamine and formaldehyde to give the aminoolefin *(82)*.

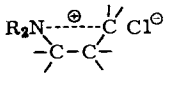
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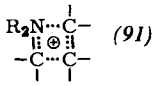
(89)



(90)



(91)



We suggested several years ago[23] that the ionization of the tertiary chlorine atom in γ-chloro amines such as *(80)* could be assisted by the nitrogen atom without leading to covalent ring closure. According to this view, an internally solvated carbonium ion pair *(90)* is formed as an intermediate. This can fragment *via* the transition state *(91)*, lose a proton to give an aminoolefin such as *(82)*, or form the azetidinium salt *(85)* by covalent ring closure.

In the internally solvated cation *(90)*, which corresponds to the transition state of a nucleophilic substitution, the amino group assumes the stabilizing role normally played by the solvent. For the formation of the cation *(90)*, the nitrogen must be able to approach the α carbon atom from the rear, and the quasi-cyclic conformation must be easily attainable. This effect is achieved by geminal methylation in the β and γ positions. However, ring closure does not occur readily in the chlorides *(80)* and *(81)*, owing to the strain in the four-membered ring and the steric hindrance at the tertiary α carbon atom. In the secondary chloride *(79)*, on the other hand, steric hindrance is sufficiently less that ring closure can compete with the fragmentation. It is interesting to note that 3-(chlorodimethylmethyl)quinuclidine *(13)*, in which internal solvation is impossible for steric reasons, reacts by the two-step carbonium ion mechanism.

The reactive behavior of the diastereoisomeric forms *(92)* and *(93)* of 3-dimethylamino-1,2-diphenylpropyl methanesulfonate can also be reconciled with this hypothesis[28]. The *erythro* form *(92)* reacts 77 times as fast as the homomor-

[21] *S. Winstein et al.*, J. Amer. chem. Soc. *75*, 147 (1953).

[22] Of the elimination mechanisms known at present, two (E2 and E1cB) are base-induced. The third (E1) proceeds *via* a carbonium ion, and should be slower by the inductive factor *i* than the reaction of the homomorph, *i.e.* $k/k_h < 1$.

[23] *C. A. Grob* and *F. A. Jenny*, Tetrahedron Letters *1960*, 25.

[24] *C. A. Grob* and *A. Friederang*, unpublished results.

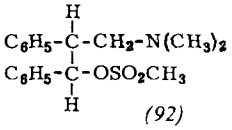
[25] *A. M. Braun, C. E. Ebner, C. A. Grob*, and *F. A. Jenny*, Tetrahedron Letters *1965*, 4733.

[26] *C. A. Grob, A. M. Braun*, and *H. C. Guggisberg*, unpublished results.

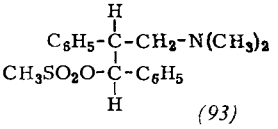
[27] *W. Raudenbusch*, Dissertation, Universität Basel 1963.

[28] *C. A. Grob* and *J. Zergenyi*, unpublished results.

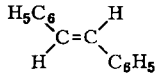
phous compound *(92)* [$(CH_3)_2CH$ instead of $(CH_3)_2N$] in ethanol, with exclusive fragmentation and ring closure to give *trans*-stilbene *(94)* and the *trans*-azetidinium ion *(95)*,

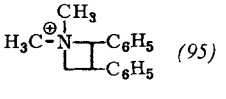


(92)



(93)

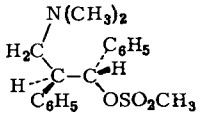
(94) 



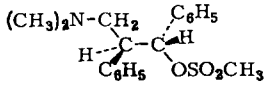
(95)

$(CH_3)_2N-CH_2-CH(C_6H_5)-CH(C_6H_5)-OC_2H_5$ *(96)*

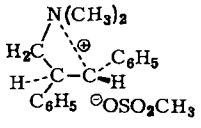
respectively. The *threo* isomer *(93)*, on the other hand, reacts more slowly than its homomorph ($k/k_h = 0.75$), indicating a two-step carbonium ion mechanism. (The question whether phenonium ions occur as intermediates in the latter case is not relevant in this connection.) This is in agreement with the formation of *threo* and *erythro* ethers *(96)* and *cis* and *trans* azetidinium ions *(95)* together with *trans*-stilbene *(94)* by fragmentation.



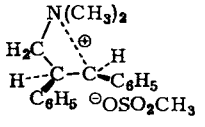
(97)



(98)



(99)



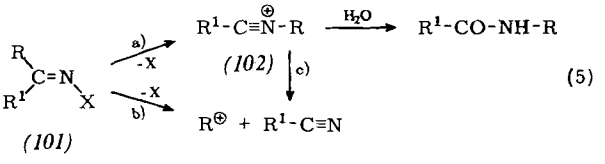
(100)

The fact that the *erythro* isomer *(92)* reacts faster than its homomorph proves the participation of the nitrogen atom. However, it is not clear whether ring closure and fragmentation are competing reactions of two rotamers *(97)* and *(98)* or both reactions proceed *via* the same internally solvated carbonium ion pair *(99)*. In the latter structure the bulky phenyl groups are *trans* to each other. In the cation of the *erythro* form *(100)*, the phenyl groups are *cis* to each other. The resulting steric hindrance appears to rule out any participation of the nitrogen atom.

The amines with nucleofugal substituents in the γ position have available to them a variety of reaction paths and mechanisms that is practically unequaled in other classes of organic compounds. The three expected basic mechanisms are observed, depending on their structure, configuration, and conformation, as well as on the electron influence of the substituents. More higly substituted acyclic members of this class exhibit an unexpected participation of the nitrogen atom, which is ascribed to internal solvation. If this interpretation proves to be correct, current views on the course of many substitution and elimination reactions may have to be reexamined [29].

[29] It has recently been postulated that the transition states of many substitutions and eliminations are similar; cf. *A. J. Parker, M. Ruane, G. Biale*, and *S. Winstein*, Tetrahedron Letters *1968*, 2113.

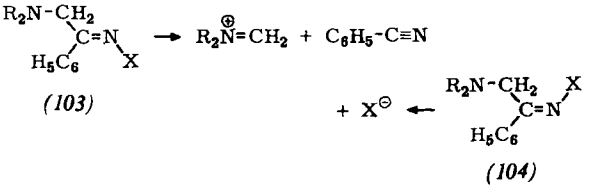
When the hydroxyl group of a ketoxime *(101)* (X = OH) is converted into a more active nucleofugal group by protonation or esterification, a Beckmann rearrangement generally occurs. The group R in the *trans* position with respect to X migrates to form a nitrilium ion *(102)*, which gives an amide with water [path (a) in eq. (5)]. If, however, R is potentially electrofugal, it can be split off with simultaneous formation of a nitrile [path (b) in eq. (5)]. This reaction is thus one of the group of nitrile-forming fragmentations [1].



(101) *(102)* (5)

The fragmentation could again proceed synchronously, *i.e.* in one step (path b) or in more than one step, as in the previously described N–C–C–C–X system. An additional possibility in this case is an initial rearrangement to form the nitrilium ion *(102)*, which then fragments (path a,c). The fragmentation would then proceed indirectly *via* a Beckmann rearrangement. As will now be shown, both the synchronous mechanism (path b) and the rearrangement-fragmentation mechanism (path a,c) are observed, depending on the electrofugal group R.

The synchronous mechanism is observed with α-amino ketoxime derivatives, both with *anti* forms such as *(103)* and with corresponding *syn* forms *(104)* [30].

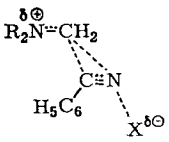


(103) *(104)*

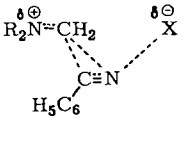
This follows from the observation that the reaction rate is strongly dependent on the substituents on the amino group and on the nature of the nucleofugal group –X. For example, *anti*-α-pyrrolidinoacetophenone oxime benzoate [*(103)*, R–R = $-(CH_2)_4-$, X = C_6H_5COO] reacts about 3000 times as fast as the *anti*-α-methylanilino derivative [*(103)*, R_2N = $C_6H_5(CH_3)N$]. Moreover, *p*-toluenesulfonates (X = *p*-$CH_3C_6H_4SO_3$) react about 10^6 times as fast as benzoates [31]. It must therefore be concluded that the electrofugal fragment $R_2\overset{\oplus}{N}=CH_2$ and the nucleofugal fragment –X are released simultaneously from the middle group in the rate-determining step, in accordance with the formulations of the transitions states for the *anti* form *(105)* and the *syn* form *(106)*.

[30] *H. P. Fischer, C. A. Grob*, and *E. Renk*, Helv. chim. Acta *45*, 2539 (1962).

[31] *H. P. Fischer* and *C. A. Grob*, Helv. chim. Acta *46*, 936 (1963).

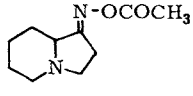


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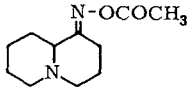


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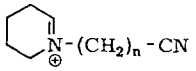
In the *anti* form the process corresponds to a *trans* elimination, while in the *syn* form it represents the unusual case of a *cis* elimination. The superiority of *trans* fragmentation is shown by the fact that its rate is about 10^3 times as high as that of the *cis* form. α-Amino ketoxime derivatives such as *(103)* and *(104)* also react very much faster than homomorphous ketoxime derivatives which contain no amino group and which in the absence of an active electrofugal group undergo a Beckmann rearrangement [path a in eq. (5)]. The large frangomeric acceleration in turn demonstrates the participation of the amino group in a synchronous fragmentation process. There is, however, no direct relation between the basicity of the amino group and the reaction rate. This also holds for the acidity of the acid HX corresponding to X.



(107)



(108)

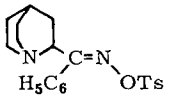


(109a), n = 2

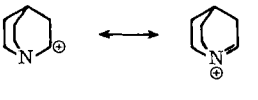
(109b), n = 3

The synchronous Beckmann fragmentation also occurs very readily with monocyclic and bicyclic α-amino ketoxime derivatives[32,33]. For example, 1-oxooctahydroindolizine oxime acetate *(107)* and 1-oxoquinolizidine oxime acetate *(108)* in 80% ethanol give quantitative yields of the imonium nitriles *(109a)* and *(109b)*, which rapidly undergo secondary reactions. The compounds *(107)* and *(108)* react about 10^4 and 10^8 times as fast as their respective homomorphous oxime acetates, *i.e. cis*-hexahydro-1-indanone oxime acetate [*(107)*, CH instead of the bridgehead N] and *trans*-1-decalone oxime acetate [*(108)*, CH instead of the bridgehead N]. The magnitude of these frangomeric effects is surprising in view of the fact that the conformation favorable for synchronous fragmentation, *i.e.* with antiparallel arrangement of the N-electron pair and the C–C bond to be broken, is not the most stable conformation. On the other hand, the two substituents on the C=N double bond are rigidly held in the most favorable coplanar arrangement. Synchronous fragmentation thus predominates even when the stereoelectronically optimal conformation is present to a lesser extent.

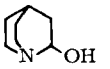
Because of the wide applicability of the Beckmann fragmentation this reaction lends itself to the detection and degradation of natural and synthetic α-aminoketoximes. No exceptions have been found to date, though the rate of the fragmentation may be greatly decreased by steric factors. This is illustrated by the



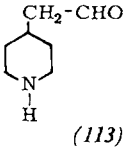
(110)



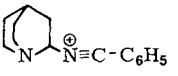
(111a) (111b)



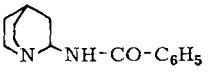
(112)



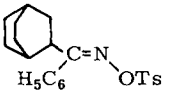
(113)



(114)



(115)



(116)



(117)

reaction of *anti*-2-quinuclidyl phenyl ketoxime *p*-toluenesulfonate *(110)* in aqueous media[34].

The fragmentation of this compound leads to benzonitrile and the 1,2-didehydroquinuclidinium ion *(111)*. Since the structure of this bicyclic cation hinders the formation of a double bond at the bridgehead (Bredt's rule), it can be regarded only with reservations as a resonance-stabilized imonium ion in accordance with *(111a)*↔*(111b)*. The electrofugal activity of the quinuclidyl group must therefore be greatly reduced.

It is in fact found that the compound *(110)* in 80% ethanol reacts only about twice as fast as the homomorphous bicyclo[2.2.2]oct-2-yl phenyl ketoxime *p*-toluenesulfonate *(116)*, which undergoes exclusive Beckmann rearrangement. The ionization of *(110)* is thus only slightly accelerated by the nitrogen atom. The reaction nevertheless yields the fragmentation product benzonitrile and 4-piperidylacetaldehyde *(113)*, (the tautomeric form of 2-quinuclidinol *(112)*) as a secondary reaction product of the cation *(111)*. The principal product, however, is *N*-(2-quinuclidyl)-benzamide *(115)*. On the basis of earlier findings, it may be concluded that this amide results from recombination of part of the benzonitrile with the cation *(111)* to give the nitrilium ion *(114)* after the manner of a Ritter reaction[32]. This in turn affords the amide *(115)* in aqueous solution, thus simulating the result of a Beckmann rearrangement.

The fact that the cation *(111)* is formed as an intermediate shows that it must be more stable than the bicyclo[2.2.2]oct-2-ylium ion *(117)*, and that some delocalization of the positive charge to the bridgehead nitrogen atom must occur in accordance with the limiting form *(111b)*. It follows from these experiments that Bredt's rule is not strictly valid for high-energy intermediates and transition states.

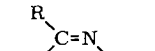
If the electrofugal activity of the group R of an oxime derivative falls below its migratory aptitude, the Beck-

[32] *C. A. Grob, H. P. Fischer, H. Link,* and *E. Renk,* Helv. chim. Acta *46*, 1190 (1963).

[33] *C. A. Grob* and *A. Sieber,* Helv. chim. Acta *50*, 2520 (1967).

[34] *C. A. Grob* and *A. Sieber,* Helv. chim. Acta *50*, 2531 (1967).

mann rearrangement [path a in eq. (5)] takes precedence, as in the case of bicyclo[2.2.2]oct-2-yl phenyl ketoxime *p*-toluenesulfonate *(116)*. However, as the following examples show, indirect fragmentation can occur by loss of a carbonium ion $R^{\oplus}$ from the initially formed nitrilium ion *(102)* (path ac, in eq. (5) [35]).



(118)

(119)

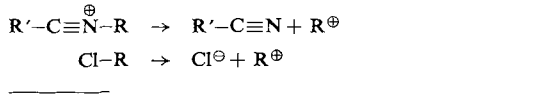
Table 4. Relative reaction rates and degree of fragmentation of ketoxime *p*-toluenesulfonates *(118)* at 23 °C and relative ionization rates of alkyl and aralkyl chlorides *(119)*.

R	*(118)* k_{rel}	*(118)* Fragmentation (%)	*(119)* k_{rel}
CH_3	1	0	
C_2H_5	60	0	
$CH(CH_3)_2$	810	0	<0.001
$C(CH_3)_3$	870	10	1
$CH(C_6H_5)_2$	40	54	186
$C(CH_3)(C_2H_5)(C_6H_5)$	820	80	572

Table 4 lists a number of alkyl and aralkyl methyl ketoxime *p*-toluenesulfonates *(118)* in which the variable group R is always *anti* with respect to the nucleofugal group –OTs. The relative reaction rates (based on R = CH_3) and the degree of fragmentation into acetonitrile and the carbonium ion $R^{\oplus}$ are also given. The reaction rate increases in the order $CH_3 < C_2H_5 < CH(CH_3)_2 < C(CH_3)_3$ with the last compound giving about 10% fragmentation. The first three compounds afford only substituted acetamides $CH_3-CO-NHR$ by Beckmann rearrangement. The reaction rate decreases appreciably with the next ketoxime *p*-toluenesulfonate, which is a benzhydryl derivative, and then increases again for the α-ethyl-α-methylbenzyl derivative.

Thus no relation is apparent between the reaction rate and the degree of fragmentation. Fragmentation cannot therefore occur in the rate-determining step, but in a subsequent step. The k_{rel} values in Table 4 are a measure of the migratory aptitude of the groups in question, which in turn depends on inductive and steric effects [35]. They therefore correspond to the rate of formation of nitrilium ions *(102)*, the necessary intermediates of the Beckmann rearrangement [35]. These in turn are known to break down into nitriles and carbonium ions when the latter are sufficiently stable, as in the case of the *tert*-butyl, benzhydryl, and α-ethyl-α-methylbenzyl cations.

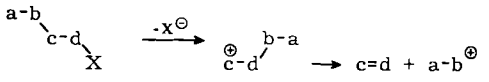
The heterolysis of nitrilium ions proceeds in the same manner as that of secondary and tertiary alkyl halides:



[35] *C. A. Grob, H. P. Fischer, W. Raudenbusch,* and *J. Zergenyi,* Helv. chim. Acta *47,* 1003 (1964).

It is therefore understandable that the fragmentation yields in Table 4 increase in the same order as the ionization rates of the alkyl and aralkyl chlorides *(119)* (see last column in Table 4).

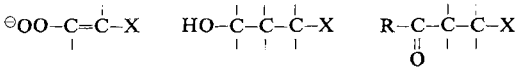
The compounds *(118)* thus react by a multistep rearrangement-fragmentation mechanism, as represented by the following general formulation:



The two conditions for the occurrence of this mechanism are that the migratory aptitude of the group a–b is greater than its electrofugal activity, and that the unsaturated fragment c=d has nucleofugal character, since it leaves the electrofugal group a–b after the rearrangement, taking with it the pair of bonding electrons. This second condition is satisfied not only by nitriles, but also by cyanate ions. No other systems that fragment by this mechanism are known at present.

11. Outlook

There now remains the question whether the findings for amines with nucleofugal substituents in the γ position and for oxime derivatives can be applied to other systems that can undergo heterolytic fragmentation. The experimental data available, though still scanty, already indicates that the same rules are valid, *e.g.* for the solvolytic decarboxylation of α,β-unsaturated β-halogeno acids *(120)* [36]. The dependence of reactivity on steric factors is easier to recognize in unsaturated systems because of the fairly rigid structures. On the other hand, there are many systems whose investigation is complicated by the fact that the fragmentable particle is formed only as a result of a prior reaction. Examples of this are the base-induced fragmentation of alcohols *(121)* with nucleofugal substituents in the γ-position [37] and of carbonyl compounds *(122)* with nucleofugal substituents in the β-position [38].



(120) *(121)* *(122)*

Received: October 2, 1968 [A 709 IE]
Revised: January 27, 1969
German version: Angew. Chem. *81,* 543 (1969)
Translated by Express Translation Service, London.

[36] *C. A. Grob, J. Csapilla,* and *G. Cseh,* Helv. chim. Acta *47,* 1590 (1964).

[37] Cf. *e.g. H. B. Henbest* and *B. B. Millward,* J. chem. Soc. (London) *1960,* 3575.

[38] *A. Eschenmoser* and *A. Frey,* Helv. chim. Acta *35,* 1660 (1952); *F. Nerdel, H. Goetz,* and *M. Wolff,* Liebigs Ann. Chem. *632,* 65 (1960).

Antioxidants

By L. R. Mahoney[*]

The free radical initiated liquid phase oxidation of hydrocarbons is inhibited by phenols and aromatic amines. In the present article the recent results of kinetic and thermodynamic studies of the inhibition are discussed.

1. Introduction

The liquid phase oxidation of organic compounds by molecular oxygen at temperatures less than 100 °C may be represented by the equation

$$RH + O_2 \rightarrow RO_2H$$

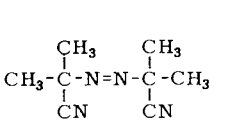
where RH is a hydrocarbon or aldehyde and RO_2H is the corresponding hydroperoxide or peracid. In cases in which the oxidizable material is a vinyl monomer then a copolymer of oxygen and the vinyl monomer is obtained [1]. The reaction has the characteristics of a free radical chain reaction; its rate is strongly catalyzed by light and accelerated by compounds which decompose to form free radicals.

Since the process of oxidation is frequently accompanied by the accumulation of insoluble materials and the concurrent loss of desirable physical properties of the original material, the inhibition of the oxidation process is a subject of considerable technological importance. Thus an enormous number of different additives have been empirically tested and utilized by industry for the purpose of increasing the useful lifetimes of air-sensitive products.

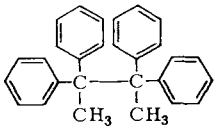
Scientific interest in the inhibition of oxidation has been centered primarily upon the elucidation of the free radical mechanisms by which low concentrations of phenols and aromatic amines are capable of inhibiting the rate of oxidation of hydrocarbons. During the past few years systematic studies have revealed the complexities of the reactions occurring in oxidizing hydrocarbons containing these antioxidants. As a result the accepted mechanisms of antioxidant behavior, particularly those involving phenols, have undergone several dramatic revisions and earlier reviews [2,3] of the subject have become somewhat dated.

2. Kinetics and Mechanism of the Non-Inhibited Oxidation

The measurement of the oxygen absorption as a function of time by an oxygen saturated liquid solution of the hydrocarbon, neat, or in an inert solvent, is the most convenient and widely used technique for the kinetic studies of the oxidation of hydrocarbons. For laboratory studies a compound which decomposes at a known rate and known efficiency to form free radicals is added to the hydrocarbon system. The concentrations of these compounds are such that the rate of formation of free radicals from their decomposition is many orders of magnitude higher than the rate of radical formation produced by the decomposition of the hydroperoxide formed during the measurement. Among the compounds most frequently employed as initiators are azodiisobutyronitrile *(1)*, and 2,2,3,3-tetraphenylbutane *(2)*.



(1)



(2)

The observed initial rates of oxygen absorption are found to be (i) independent of oxygen when the partial pressure of oxygen above the solution exceeds *ca.* 100 torr, (ii) one half order with respect to the concentration of the initiator, and (iii) first order with respect to the concentration of the hydrocarbon. The generally accepted chain mechanism which satisfactorily accounts for these results is the following:

$R - R \rightarrow 2\,R^{\bullet}$	(1)	Initiation
$R^{\bullet} + O_2 \rightarrow RO_2^{\bullet}$	(2)	Propagation
$RO_2^{\bullet} + RH \rightarrow RO_2H + R^{\bullet}$	(3)	Propagation
$2\,RO_2^{\bullet} \rightarrow$ Inert Product	(4)	Termination

where R–R is the initiator and $R^{\bullet}$ and $RO_2^{\bullet}$ represent the carbon radical and the chain-carrying peroxyl radical respectively. At sufficiently high oxygen pressures the rate of reaction (2) is quite high and the possible bimolecular termination reaction of carbon radicals is not significant. Under these conditions reaction (3) is the rate controlling step.

$$dO_2/dt = k_3[RO_2^{\bullet}]\,[RH] \qquad (5)$$

At steady state, the rate of formation of radicals from the initiator is equal to their rate of disappearance from the system *via* reaction (4).

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[1] *F. R. Mayo*, Accounts chem. Res. *2*, 193 (1968) and literature cited therein.

[2] *K. U. Ingold*, Chem. Reviews *61*, 563 (1961).

[3] *G. Scott*: Atmospheric Oxidation and Antioxidants. Elsevier, New York 1965.

$$2k_1[R{-}R] = 2k_4[RO_2^{\bullet}]^2 \quad (6)$$

Solving for $[RO_2^{\bullet}]$ and substituting in equation (5)

$$\frac{dO_2}{dt} = \frac{k_3}{(2k_4)^{1/2}} \left\{ 2k_1[R{-}R] \right\}^{1/2} [RH] \quad (7)$$

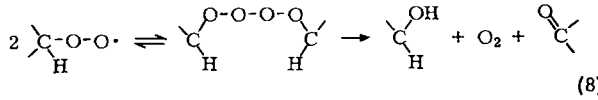
in agreement with experiment.

Provided that the value of $2k_1$ is known, the value of the ratio of rate constants, $k_3/(2k_4)^{1/2}$ may be determined by such oxidation studies. The use of a combination of photochemical initiation and non-steady state techniques allows a determination of the absolute values k_3 and k_4 [4,5,6]. *Howard* and *Ingold* [7] have recently determined the absolute values of these constants for a large number of hydrocarbons. In Table 1 are presented values of k_3, corrected for the number of reactive hydrogens, for some of the hydrocarbons which they examined. Examination of the table reveals the dramatic increase in the value of k_3 upon the introduction of a π-electron system into a position adjacent to the reactive hydrogen.

Table 1. Absolute value of k_3 per reactive hydrogen for hydrocarbons [7].

Hydrocarbon	T (°C)	k_3/reactive hydrogen ($l \cdot mol^{-1} \cdot s^{-1}$)
Cyclohexane	65	0.0061
Cyclohexene	30	1.5
Octalin	30	1.6
9,10-Dihydroanthracene	30	44.0
Cyclopentene	30	7.0
Indan	30	1.2
Toluene	30	0.08
Cumene	30	0.18

From their results *Howard* and *Ingold* have also been able to define a range of values for k_4 as a function of the structure of the hydrocarbon moiety of the peroxyl radical. Primary peroxyl radicals have values of k_4 in the range of 10^8 lmole^{-1} sec^{-1}, secondary peroxyl radicals 10^6–10^7 lmole^{-1} sec^{-1}, and tertiary peroxyl radicals in the range of 10^3–10^5 lmole^{-1} sec^{-1} at 30 °C. This ordering of values of k_4 fully supports the mechanism of the peroxyl radical termination reaction first proposed by *Russell* [8] in his classic study of the oxidation of ethylbenzene. This mechanism (8) involves the formation of a tetraoxide, which in the case of primary and secondary peroxyl radicals decomposes to form O_2 [9,10] with



(8)

the simultaneous formation of a carbonyl compound and alcohol. In the case of tertiary peroxyl radicals the disproportionation reaction cannot occur and termination is highly inefficient and complex in nature [10,11].

3. Inhibition Period Studies

In Figure 2 is presented a typical plot of the oxygen absorption *versus* time curves obtained from the introduction of a phenolic antioxidant into a system consisting of the reactive hydrocarbon and an initiator. After a period of strong inhibition the rate of oxygen absorption of the sample increases rapidly and finally reaches a rate equal to that observed in the absence of the antioxidant.

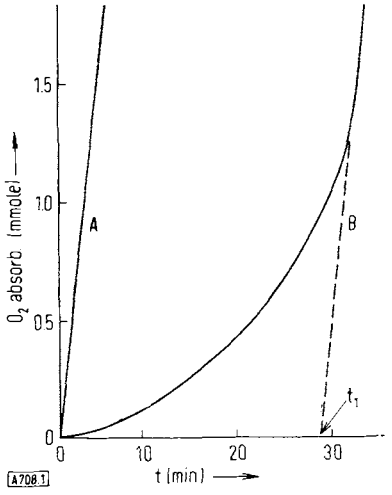


Fig. 1. The oxygen absorption of a chlorobenzene solution of 148 mmoles 9,10-dihydroanthracene at 60 °C containing 31 mmoles 2,2,3,3-tetraphenylbutane and, Curve A: no inhibitor; Curve B: 1 mmole hydroquinone.

In many cases the length of this inhibition period, t, is proportional to the original concentration of the antioxidant. If the initiator is azodiisobutyronitrile *(1)* or tetraphenylbutane *(2)* it is possible to calculate the ratio of the number of radicals produced from the initiator during the inhibition period to the initial concentration of the inhibitor.

$$\frac{1}{[\text{Inhibitor}]_0} \int_0^t 2k_1[R{-}R]dt = n \quad (9)$$

The quantity n, known as the stoichiometric factor [12], is frequently found to have small integral values. Such a result strongly suggests that the inhibitor molecule terminates chains by reacting with peroxyl radicals in stoichiometrically simple processes. For example, hydroquinones manifest values of n equal to two and thus the overall termination reaction corresponds to reaction (10) [13].

[4] *L. Bateman* and *G. Gee*, Trans. Faraday Soc. *47*, 155 (1951).

[5] *H. R. Cooper* and *H. W. Melville*, J. chem. Soc. (London) *1951*, 1994.

[6] *C. H. Bamford* and *M. J. S. Dewar*, Proc. Roy. Soc. (London), Ser. A *198*, 252 (1949).

[7] *J. A. Howard* and *K. U. Ingold*, Canad. J. Chem. *45*, 793 (1967).

[8] *G. A. Russell*, J. Amer. chem. Soc. *79*, 3871 (1957).

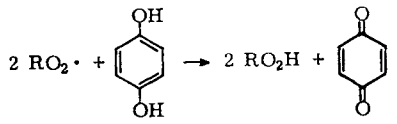
[9] *P. D. Bartlett* and *T. G. Traylor*, J. Amer. chem. Soc. *85*, 2407 (1963).

[10] *J. A. Howard* and *K. U. Ingold*, J. Amer. chem. Soc. *90*, 1056 (1968).

[11] *P. D. Bartlett* and *G. Guaraldi*, J. Amer. chem. Soc. *89*, 4799 (1967).

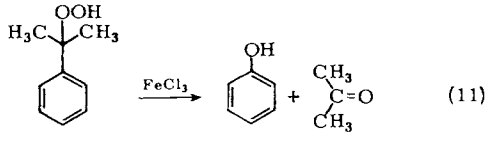
[12] *C. E. Boozer*, *G. S. Hammond*, *C. E. Hamilton*, and *J. N. Sen*, J. Amer. chem. Soc. *77*, 3233 (1955).

[13] *A. F. Bickel* and *E. C. Kooyman*, J. chem. Soc. (London) *1954*, 3211.



(10)

These results imply that in those cases in which large and non-integral values of the stoichiometric factor are observed, a more complex and perhaps non-free radical reaction may be superimposed upon the free radical termination process. For example, large values of n are observed for the highly specific antioxidant $FeCl_3$ in the liquid phase oxidation of arylalkylhydrocarbons[14]. It was demonstrated that the initial action of $FeCl_3$ in such systems is the highly efficient catalysis of the rearrangement of the small amounts of hydroperoxide to produce acetone and the antioxidant, phenol [Eq. (11)].



(11)

The phenol produced in the reaction then functions as the antioxidant and the end of the inhibition period corresponds to that point in which the catalytic effect of $FeCl_3$ is destroyed by complexing with donor molecules (*i.e.* water, acetone, *etc.*) produced during the inhibition period.

4. Kinetics and Mechanism of Inhibition by Phenols

The uninhibited rate of oxidation of a hydrocarbon at a constant rate of formation of free radicals is dependent upon the rate of two reactions (see Section 2). The first is reaction (3), hydrogen abstraction by the chain-carrying peroxyl radical from the hydrocarbon; the second is reaction (4), the bimolecular termination reaction of two peroxyl radicals. The rate of oxidation of a hydrocarbon inhibited by a phenolic antioxidant requires consideration of a larger number of reactions (see Scheme 1).

$R-R \xrightarrow{k_1} 2\,R^{\bullet}$		(1)
$R^{\bullet} + O_2 \xrightarrow{k_2} RO_2^{\bullet}$		(2)
$RO_2^{\bullet} + RH \xrightarrow{k_3} RO_2H + R^{\bullet}$		(3)
$2\,RO_2^{\bullet} \xrightarrow{k_4}$ inert product		(4)
$RO_2^{\bullet} + AH \underset{k_{-12}}{\overset{k_{12}}{\rightleftharpoons}} RO_2H + A^{\bullet}$		(12, −12)
$RO^{\bullet}{}_2 + A^{\bullet} \xrightarrow{k_{13}} AO_2R$		(13)
$2\,A^{\bullet} \xrightarrow{k_{14}} A-A$		(14)
$A^{\bullet} + RH \xrightarrow{k_{15}} AH + R^{\bullet}$		(15)

Scheme 1.

[14] *G. S. Hammond, L. R. Mahoney,* and *U. S. Nandi,* J. Amer. chem. Soc. *88*, 737 (1963).

Where AH and A$^{\bullet}$ represent the phenol and the free radical derived from the phenol respectively. By means of this scheme it is possible to subdivide all phenolic antioxidants into two classes with respect to their kinetic and mechanistic behavior.

The first class consists of sterically hindered phenols, *i.e.* 2,6-di-*tert*-butylphenol and hydroquinones. In hydrocarbon systems containing these compounds the rates of the radical termination, reaction (13) and (14), greatly exceed the rates of reactions (−12) and (15). As a result the peroxyl radical is the sole chain carrying free radical, and the rate of oxygen absorption is given by Eq. (16).

$$-dO_2/dt = 2k_1[R-R] + k_3[RO_2^{\bullet}]\,[RH] \qquad (16)$$

The slow step in termination is reaction (12) and under equilibrium conditions the concentration of free radicals is given by Eq. (17).

$$2\,k_1[R-R] = 2k_{12}[RO_2^{\bullet}]\,[AH] \qquad (17)$$

The rate of oxidation is a function of the values of k_3 and k_{12}.

Non-hindered phenols constitute the second class of antioxidants and their kinetic behavior is consistent with the view that the rates of reaction (−12) and (15) are competitive with the rates of the termination reactions (13) and (14). Under these conditions there are two chain-carrying free radicals, the peroxyl radical and the phenoxyl radical.

$$-dO_2/dt = 2k_1[R-R] + k_3[RO_2^{\bullet}]\,[RH] + k_{15}[A^{\bullet}]\,[RH] \qquad (18)$$

Since reaction (12) is not the slow step in the termination at steady state the rate of oxidation for these systems must be a function of a large number of kinetic parameters.

$$2\,k_1[R-R] = 2\,k_4[RO_2^{\bullet}]^2 + 2k_{13}[RO_2^{\bullet}]\,[A^{\bullet}] + 2\,k_{14}[A^{\bullet}]^2 \qquad (19)$$

4.1. Hindered Phenols and Hydroquinones

A number of studies of the initial rates of oxygen absorption of solutions of hydrocarbons containing hindered phenols and hydroquinones have been reported[15–17]. The rates of oxidation are first order in initiator concentration and independent of oxygen pressure. These results strongly suggest that the rate controlling steps in termination and propagation are first order in peroxyl radicals. The replacement of hydrogen by deuterium on the phenolic −H−O group of the antioxidant increases the rate of the inhibited oxidation by a factor of *ca.* 10[16] for sterically hindered phenols. Thus the O−H bond of the antioxidant is broken in the slow step of the termination process. Since the rate of oxygen absorption is inversely pro-

[15] *A. F. Bickel* and *E. C. Kooyman,* J. chem. Soc. (London) *1956*, 2215.

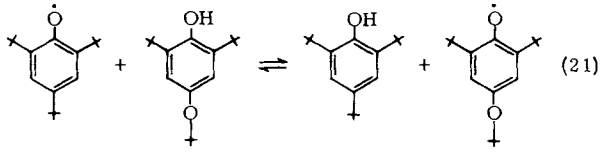
[16] *J. A. Howard* and *K. U. Ingold,* Canad. J. Chem. *40*, 1851 (1962).

[17] *L. R. Mahoney,* J. Amer. chem. Soc. *88*, 3035 (1966).

portional to the antioxidant concentration and at sufficiently high concentrations of the antioxidant the rate is reduced to a value equal to $2k_1[RR]$ [15,17], reaction (15) is negligible for these compounds. Reaction (−12) may also be excluded from the kinetic analysis of these compounds since the addition of high concentrations of hydroperoxide has no effect upon the inhibited rates of oxygen absorption [16–18]. These results are summarized by the rate expression (20), derived from equations (16) and (17).

$$-dO_2/dt = 2k_1[R-R] + \frac{k_3}{2k_{12}}\left\{2k_1[R-R]\right\}\frac{[RH]}{[AH]} \qquad (20)$$

Since the efficiency of these compounds as antioxidants is determined by the value of k_{12}, the effects of the substitution of the *p*-position of the sterically hindered phenols and the structure of the hydroquinones upon the antioxidant efficiency have been the subject of a number of recent studies. The effect of the substituent at the *p*-position upon the rate of reaction (12) has been examined by *Howard* and *Ingold* [19,20]. These workers found that a correlation existed between log $2k_{12}/k_3$ and the σ^+ values of the *p*-substituent. The ρ values equaled −1.36 and −1.12 with tetralin and with styrene as the hydrocarbons at 65 °C. These relatively large ρ values have been interpreted by *Howard* and *Ingold* as being due to a strong polar character in the activated complex of the atom transfer reaction. An alternative explanation involves the effect of the *p*-substituent upon the thermodynamic stability of the product phenoxyl radical. *Cook et al.* [21] examined the equilibrium between 2,4,6-tri-*tert*-butylphenoxyl radical and 2,6-di-*tert*-butyl-4-*tert*-butoxyphenol [Eq. (21)].



(21)

† = $C(CH_3)_3$

At 25 °C in benzene the value of the equilibrium constant is 51.7 ± 4.1. Since the ratio of values of k_{12}/k_3 for these two phenols is approximately 4, the relative rates of the hydrogen abstraction reaction may be merely a manifestation of the product radical stability.

A correlation between the values of log k_{12}/k_3 and the energy of the highest occupied molecular orbitals of the hydroquinones as calculated by the Hückel technique has recently been demonstrated [22]. The theoretical basis for the correlation comes from *Fueno et al.* [23] who argue that for a given series of compounds the rate of reaction (12) should depend upon the dissociation energy of the −OH bond of the hydroquinone. A separation of the dissociation energy into σ and π energy terms may be made and the π energy is related to the energy of the highest occupied molecular orbital of the hydroquinone.

4.2. Non-Hindered Phenols

The kinetic behavior of non-hindered phenols is complex. A systematic study of a number of non-hindered phenols utilizing 9,10-dihydroanthracene as the hydrocarbon and tetraphenylbutane as the initiator has recently been reported [22].

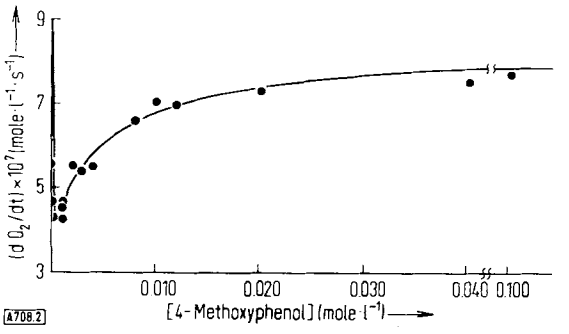


Fig. 2. The rate of oxygen absorption of a chlorobenzene solution of 99 mmoles 9,10-dihydroanthracene at 60 °C containing 31 mmoles 2,2,3,3-tetraphenylbutane as a function of the concentration of 4-methoxyphenol.

In Figure 2 are presented typical results observed in the 9,10-dihydroanthracene-tetraphenylbutane system containing 4-methoxyphenol in chlorobenzene at 60 °C. Since 4-methoxyphenol manifests many of the peculiar kinetic dependencies observed with other non-hindered phenols, it will serve in this discussion as a general example for all of the antioxidants of this class. At sufficiently long kinetic chain lengths the rate of oxygen absorption is accurately one-half order with respect to the initiator concentrations over the entire range of 4-methoxyphenol concentrations and at high concentrations of 4-methoxyphenol the rate is independent of the concentration of 4-methoxyphenol but is first order in hydrocarbon. Thus, in contrast to the hindered phenols, the slow steps in the termination reactions are second order in radical concentration and, moreover, the oxidation rate is not completely suppressed by increasing the concentration of the antioxidant. The addition of the hydroperoxide of 9,10-dihydroanthracene accelerates the rate at low concentrations of 4-methoxyphenol, has little effect in the regions of the minimum, and finally decreases the oxygen absorption rate at higher concentration of 4-methoxyphenol.

All of these results may be accounted for if the non-hindered radical engages in chain restarting reactions with hydroperoxide [18,24–26], reaction (−12), and with

[18] *J. R. Thomas*, J. Amer. chem. Soc. *85*, 2166 (1963).

[19] *J. A. Howard* and *K. U. Ingold*, Canad. J. Chem. *41*, 1744, 2800 (1963).

[20] *J. A. Howard* and *K. U. Ingold*, Canad. J. Chem. *43*, 2724 (1965).

[21] *D. C. Cook*, *C. B. Deptie*, and *E. S. English*, J. Amer. chem. Soc. *81*, 1356 (1959).

[22] *L. R. Mahoney*, J. Amer. chem. Soc. *89*, 1895 (1967).

[23] *T. Fueno*, *T. Ree*, and *H. Eyring*, J. physic. Chem. *63*, 1940 (1959).

[24] *J. R. Thomas*, J. Amer. chem. Soc. *86*, 4807 (1964).

[25] *J. A. Howard* and *K. U. Ingold*, Canad. J. Chem. *42*, 2324 (1964).

[26] *L. R. Mahoney* and *F. C. Ferris*, J. Amer. chem. Soc. *85*, 2345 (1963).

hydrocarbon [26, 27], reaction (15). If under the conditions of the experiment the kinetic chain is long and the non-hindered phenoxyl radical efficiently restarts chains by reaction (−12) and/or (15) we may write

$$k_{12}[RO_2^{\cdot}]\,[AH] = k_{-12}[A^{\cdot}]\,[RO_2H] + k_{15}[A^{\cdot}]\,[RH] \qquad (22)$$

Combining this equation with equations (18) and (19), the general rate expression

$$\frac{1}{\{2k_1[R\text{–}R]\}^{1/2}[RH]}\left\{\frac{dO_2}{dt} + 2\,k_1[R\text{–}R]\right\} = \frac{1+\alpha}{\{(2k_4/k_3^2) + (2k_{13}/k_3k_{15})\alpha + (2k_{14}/k_{15})\alpha^2\}^{1/2}} \qquad (23)$$

where $\alpha = \dfrac{[AH]}{\{(k_3/k_{12})[RH] + (k_{-12}k_3/k_{15}k_{12})[RO_2H]\}}$

may be derived.

This general rate equation is of the same form as would be obtained in the analysis of the co-polymerization of two vinyl monomers in which one monomer is very reactive and yields a radical which is much less reactive toward polymerization than the radical derived from the second monomer. A well known example of this phenomenon in vinyl-polymerization is the styrene-vinyl acetate system in which the addition of a trace amount of styrene strongly inhibits the rate of polymerization of vinyl acetate [28]. The occurrence of the strong minimum in the rate of oxygen absorption of the 4-methoxyphenol-9,10-dihydroanthracene system also has a strong analogy in the theory of copolymerization. *Palit* [29] predicted the occurrence of a minimum in the rates of polymerization of methyl methacrylate and 4-methoxystyrene. However, a minimum could not be clearly deduced from the experimental rate data available. The minimum in the rate of oxygen absorption is readily calculated from the general rate equation. At constant concentrations of R–R, RH, and RO_2H, the concentration of non-hindered phenol at which the minimum occurs is given by Eq. (24). In the case of 4-methoxyphenol

$$[AH] = \frac{k_3}{k_{12}}[RH] + \frac{k_3k_{-12}}{k_{12}k_{15}}[RO_2H]\left\{\frac{(k_{13}/k_3k_{15}) - (2k_4/k_3^2)}{(k_{13}/k_3k_{15}) - (2k_{14}/k_{15}^2)}\right\} \qquad (24)$$

the terms in the bracket are approximately unity, therefore the position of the minimum is proportional to the concentration of the hydroperoxide.

of the concentration of 4-methoxyphenol. The ratio of $(dO_2/dt)_{OD}$ to $(dO_2/dt)_{OH}$ decreases continuously from 2.9 at low concentrations of 4-methoxyphenol to unity at high concentrations. At very low concentrations of 4-methoxyphenol the slow step in the inhibition is reaction (12) and the isotope effect on the rate of oxygen absorption will be approximately proportional to $[(k_{12})_{OD}(k_{12})_{OH}]^{1/2}$. The square of the relative rates is 8.4, in agreement with the isotope effect for the transfer reaction directly measured with the hindered phenol. As the concentration of 4-methoxyphenol is increased, the isotope effect decreases until the reactions (14) and (15) determine the oxygen absorption rates. Under these conditions there will be no isotope effect since the slow step in the rate of oxygen absorption, propagation or termination, does not involve the hydrogen atom transfer, reaction (12).

The general rate equation has been utilized with considerable success for the quantitative analysis of the rate data obtained in our laboratory with the tetraphenylbutane-9,10-dihydroanthracene system [22] and for the analysis of experimental data of earlier workers who employed the azodiisobutyronitrile-tetralin system [25, 26]. The values of the parameters of $2k_4/k_3^2$ and $2k_{14}/k_{15}^2$ are very readily obtained from studies of the uninhibited and the fully inhibited rates of oxidation. The other parameters are conveniently determined by curve fitting using computer techniques. The solid curve in Figure 2 was obtained by means of such curve fitting techniques. This procedure may appear tenuous. However, there is an essentially independent technique (cf. Section 5.3) which yields values of one of the parameters, k_{12}/k_3, in excellent agreement with those derived from the general equation. The values of the adjustable parameters obtained from this analysis have yielded previously unattainable information regarding the relative rates of formation, of hydrogen abstraction, and the termination reaction of phenoxyl radicals. In Table 2 values of parameters for a number of non-hindered phenols are presented.

Table 2. Kinetic parameters calculated from Equation (23) for typical non-hindered phenols [22].

Compound	k_{12}/k_3	k_{-12}/k_{15}	$\{k_{13}/2(k_4)^{1/2}(k_{14})^{1/2}\}$ ($l \cdot mol^{-1} \cdot s^{-1}$)	$k_{15}/(2k_{14})^{1/2} \times 10^3$ ($l^{1/2} \cdot mol^{-1/2} \cdot s^{-1/2}$)
Phenol	9.7	110	2.2	13.2
m-Cresol	1.4	49.1	1.5	1.4
p-Phenylphenol	78.0	59.5	3.5	9.1
4-Methoxyphenol	284	17.5	49.0	19.8
Pyren-3-ol	4400	31.0	1020	29.1

By means of the general rate equation (23) it is possible to analyze the variable isotopic effects observed with non-hindered phenolic antioxidants. *Howard* and *Ingold* [25] have shown that the magnitude of the isotope effect upon the rates of oxygen absorption of 4-methoxyphenol and the *O*-deuterated compound in the tetralin-azodiisobutyronitrile system is a function

The structure of the aromatic ring system from which the phenol is derived has a remarkably large effect on the values of two of the parameters. Values of k_{12}/k_3 derived from the studies of the tetraphenylbutane-9,10-dihydroanthracene system increase from 9.7 for phenol to 4400 for pyren-3-ol.

For hydroxy compounds derived from alternate hydrocarbons a plot of the value of $\log(k_{12}/k_3)$ *versus* the energy of the highest occupied molecular orbital yields a straight line. However, the straight line is displaced from that obtained for hydroquinones (cf. Section 4.1.). Since systematic variation of the values for the coulomb and bond integrals fails to yield

[27] *A. F. Bickel* and *E. C. Kooyman*, J. chem. Soc. (London) *1956*, 2215.

[28] *C. Walling*, J. chem. Soc. (London) *1949*, 1930.

[29] *S. R. Palit*, Trans. Faraday Soc. *51*, 1129 (1955).

a single straight line for both classes of compounds a difference in the σ energy terms for the hydroxy and dihydroxy compounds must exist.

Values of the ratio $k_{13}/(k_4)^{1/2}(k_{14})^{1/2}$ manifest a similar sensitivity to the structure of the phenoxyl radical. Since k_4 is a constant for a given hydrocarbon this quantity represents the ratio of the rate constant for the peroxyl radical-phenoxyl radical termination, to the square root of the rate constant for the bimolecular termination reaction of the phenoxyl radical. An analysis of the available data indicates that the increase in the value of this ratio by a factor of 500 in the series phenol to 3-hydroxypyrene arises primarily from a decrease in the value of k_{14} as the phenoxyl radical becomes more resonance stabilized.

The effect of the structure of the phenoxyl radical on the value of the ratio k_{-12}/k_{15} is quite small; the value for this ratio is in the range of 20–100 for a wide variety of phenols in the tetraphenylbutane-9,10-dihydroanthracene system at 60 °C. This result is consistent with the view that the stability of the phenoxyl radical affects both reactions to approximately the same extent. It should be noted, however, that this ratio for a given phenoxyl radical will vary with the hydrocarbon system since the value k_{15} is very sensitive while k_{-12} should be insensitive to the structure of the hydrocarbon.

A detailed interpretation of the relative values of $k_{15}/(2k_{14})^{1/2}$ is difficult since the values k_{14} and presumably k_{15} also decrease with increasing stability of the phenoxyl radical. However, the value of the reactivity ratio, k_{15}/k_{15}', for a phenoxyl radical, A$^\cdot$ [Eq. (25) and (26)], in hydrogen abstraction from two hydrocarbons, R_1H and R_2H, may be calculated by comparison of the parameters $k_{15}/(2k_{14})^{1/2}$ and $k_{15}'/(2k_{14})^{1/2}$ and k_{-12}/k_{15} and k_{-12}/k_{15}' obtained from the general equation with R_1H and R_2H as the hydrocarbons and AH as the non-hindered phenol.

$$A^\cdot + R^1H \xrightarrow{k_{15}} AH + R^{1\cdot} \qquad (25)$$

$$A^\cdot + R^2H \xrightarrow{k_{15}'} AH + R^{2\cdot} \qquad (26)$$

Such an analysis has been carried out for phenol and 4-methoxyphenol with 9,10-dihydroanthracene and tetralin as the hydrocarbons [22]. Reactivity ratios for hydrogen abstraction were calculated to be approximately 70 for the unsubstituted phenoxyl radical and somewhat larger than 200 for the 4-methoxyphenoxyl radicals. For the corresponding peroxyl radicals, $(k_3)/(k_3')$ was found to be in the range of 17 to 25 at 60 °C. This ratio compares very favorably with the value of 27 at 30 °C calculated from the absolute values of k_3 for the two hydrocarbons.

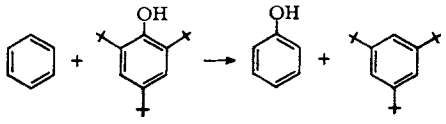
5. Thermodynamic Properties of Hindered and Non-Hindered Phenolic Antioxidants

The thermodynamic properties of the two classes of phenolic antioxidants and the phenoxyl radicals derived from them are fully in accord with and provide a sound basis for the interpretation of the kinetic studies presented in the preceding sections.

5.1. Strain Energy in 2,4,6-Tri-*tert*-butylphenol

Arnett et al. [30] have recently demonstrated that the strain energy in 1,2-di-*tert*-butylbenzene systems amounts to 22 kcal/mole. This strain can be partially relieved upon the loss of a hydrogen atom [31] to form the corresponding 2,6-di-*tert*-butylphenoxyl radical.

A quantitative estimate of the strain energy in 2,4,6-tri-*tert*-butylphenol compared to simple phenols may be made by means of the following analysis. Consider the hypothetical reaction (27)



(27)

in the gas phase at 298 °K. Utilizing the recently determined heats of formation of 1,3,5-tri-*tert*-butylbenzene [32] and 2,4,6-tri-*tert*-butylphenol [33], the heats of sublimation of these compounds [34], and the known heats of formation in the gas phase of benzene and phenol, the heat of the reaction is calculated as -8.0 ± 2.0 kcal/mole. The magnitude of this strain energy is unique to 2,6-di-*tert*-butylphenol systems since the heat of the reaction of benzene with 2-methylphenol or 2,6-dimethylphenol to yield phenol and the corresponding hydrocarbon is equal to 0 ± 0.5 kcal/mole.

5.2. Bond Energies of Hindered and Non-Hindered Phenols

The relief of the strain in a sterically hindered phenol upon the formation of the hindered phenoxyl radical results in an abnormally low value for the OH bond energy for these compounds.

The heat of the reaction of 2,4,6-tri-*tert*-butylphenoxyl radical with hydrazobenzene to form 2,4,6-tri-*tert*-butylphenol and *trans*-azobenzene has recently been measured calorimetrically [35]. From the results of that measurement and estimates of the heat necessary to transfer the phenol and the phenoxyl radical from solution to the gas phase the value of the –OH bond energy is calculated as 79.9 ± 0.5 kcal/mole. This value is approximately 10 kcal/mole lower than that previously suggested for the OH bond energy of simple phenol [36]. This large difference in the –OH bond energies of hindered and non-hindered phenols of course directly affects the values of the equilibrium constant, k_{12}/k_{-12}, for the two classes of antioxidants.

[30] *E. M. Arnett, J. C. Sanda, J. M. Bollinger*, and *M. Barber*, J. Amer. chem. Soc. *89*, 5389 (1967).

[31] The rotation of the OH group in 2,4,6-tri-*tert*-butylphenol is severely hindered, cf. *M. Davis* and *L. Meakins*, J. chem. Physics *26*, 1584 (1956).

[32] *U. Krueske, C. Hoogzand*, and *W. Hubel*, Chem. Ber. *94*, 2817 (1961).

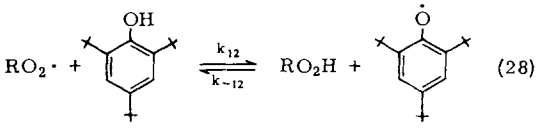
[33] Determined by Dr. *G. Sinke*, Dow Chemical Company, Midland/Michigan.

[34] *M. Davies* and *B. Kybett*, Trans. Faraday Soc. *61*, 1608 (1965).

[35] *L. R. Mahoney* and *M. A. DaRooge*, unpublished results.

[36] *S. W. Benson*, J. Amer. chem. Soc. *87*, 972 (1965).

Our laboratory has recently determined the value of the equilibrium constant as a function of temperature for the reaction where $RO_2^{\cdot}$ is the tetralyl peroxyl



(28)

radical[37]. The absolute values of k_{-12} were directly measured utilizing stop-flow techniques[38] for the study of the reaction of 2,4,6-tri-*tert*-butylphenoxyl radical with tetralin hydroperoxide. The inhibition of the oxidation of tetralin by 2,4,6-tri-*tert*-butylphenol provided values of $2k_{12}/k_3$, from which absolute values of k_{12} were calculated utilizing the previously determined absolute values of k_3 for tetralin[39]. The value of k_{12}/k_{-12} calculated from these results is given by the expression (29).

$$\frac{k_{12}}{k_{-12}} = 1.98\, e^{[5400 \pm 1000]/RT} \qquad (29)$$

The extremely large value of this equilibrium constant, 3×10^4 at 60 °C, accounts for the lack of effect of hydroperoxide on the efficiency of the hindered phenol as an antioxidant.

In contrast to hindered phenols, the value of k_{12}/k_{-12} for non-hindered phenols is quite small. From the value of the absolute rate constant for the dimerization of the unsubstituted phenoxyl radical[40,41] and the values of the parameters determined from the kinetic study of phenol as an antioxidant[22], the value of k_{12}/k_{-12} for phenol at 60 °C is calculated as 0.05.

6. Synergistic Behavior of Mixtures of Phenolic Antioxidants

For some time it has been recognized that certain mixtures of two phenolic compounds, AH and BH, are much more effective in inhibiting autooxidation than either AH or BH alone[42]. A mechanism has recently been proposed which quantitatively accounts for the synergistic behavior of such mixtures where AH is a non-hindered phenol and BH is a hindered phenol[43].

[37] *L. R. Mahoney* and *M. A. DaRooge*, unpublished results.

[38] *M. A. DaRooge* and *L. R. Mahoney*, J. org. Chemistry *32*, 1 (1967).

[39] *A. J. Howard* and *K. U. Ingold*, Canad. J. Chem. *44*, 1119 (1966).

[40] *G. Dobson* and *L. I. Grossweiner*, Trans. Faraday Soc., *61*, 708 (1960).

[41] *E. J. Land*, *G. Porter*, and *E. Stracken*, Trans. Faraday Soc. *64*, 2016 (1963).

[42] *K. U. Ingold*, J. Inst. Petroleum *117*, 375 (1961).

[43] *L. R. Mahoney* and *M. A. DaRooge*, J. Amer. chem. Soc. *89*, 5619 (1967).

The main feature of the mechanism involves a decrease in the steady state concentration of A$^{\cdot}$ and regeneration of AH by the transfer equilibrium (30).

$$A^{\cdot} + BH \underset{k_{-30}}{\overset{k_{30}}{\rightleftharpoons}} AH + B^{\cdot} \qquad (30, -30)$$

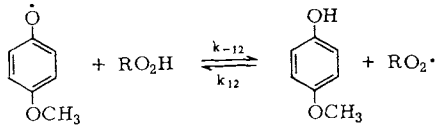
The equilibrium will lie far to the right since the O–H bond energy of BH is much lower than that of AH. (cf. Section 5.2). As a result of the decrease in the steady state concentration of A$^{\cdot}$ the chain restarting reactions of this species with hydroperoxide and hydrocarbon are decreased. Termination of chains in the mixture then occurs through B$^{\cdot}$ *via* the reactions,

$$B^{\cdot} + RO_2^{\bullet} \xrightarrow{k_{13}'} BO_2R \qquad (13')$$

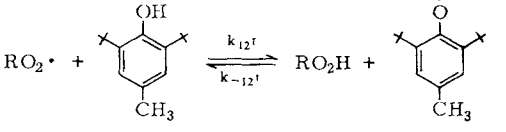
$$B^{\bullet} + A^{\cdot} \xrightarrow{k_{31}} AB^{\bullet} \qquad (31)$$

We shall now consider in some detail the quantitative aspect of the mechanism utilizing as an example 4-methoxyphenol and 2,6-di-*tert*-butyl-4-methylphenol in the 9,10-dihydroanthracene-tetraphenylbutane system.

The ratios of rate constants for the reaction of the 4-methoxyphenoxyl radical with 2,6-di-*tert*-butyl-4-methylphenol and with hydroperoxide, k_{30}/k_{-12}, and with the hydrocarbon, k_{30}/k_{15}, have been obtained



(32)



(33)

from the following analysis. The value of the equilibrium constant, k_{30}/k_{-30}, for the 4-methoxyphenoxyl radical-di-*tert*-butyl-4-methylphenol system is equal to the products (34) of the equilibrium constants for the reactions (32) and (33).

$$\frac{k_{30}}{k_{-30}} = \frac{k_{-12} \cdot k_{12}'}{k_{12} \cdot k_{-12}'} \qquad (34)$$

Rearranging, we obtain (35).

$$\frac{k_{30}}{k_{-12}} = \frac{k_{12}' \cdot k_{30}}{k_{12} \cdot k_{12}'} = \frac{k_{12}' \cdot k_{-30} \cdot k_3}{k_3 \cdot k_{-12} \cdot k_{12}} \qquad (35)$$

The values of k_{12}'/k_3 and k_3/k_{12} are obtained from the oxidation studies of the hydrocarbon inhibited by the hindered and by the non-hindered phenol. The absolute values of k_{-30} and k_{-12}' are obtained from kinetic studies of the reaction of the 2,4,6-tri-*tert*-butylphenoxyl radical with 4-methoxyphenol and with

hydroperoxide[44]. The value of k_{30}/k_{-12} for 4-methoxyphenol at 60 °C calculated from equation (35) is found to be equal to 650. A value of 10^4 is then calculated for the ratio k_{30}/k_{15} from the product of k_{30}/k_{-12} and the value of the parameter k_{-12}/k_{15} obtained from the study of the 4-methoxyphenol-9,10-dihydroanthracene system.

The results of oxidation studies of hydrocarbons containing mixtures of 4-methoxyphenol and hindered phenols are in quantitative agreement with the view that the chain restarting reactions of the 4-methoxyphenoxyl radical are effectively suppressed in the presence of the hindered phenol. For example, the rate of oxygen absorption of tetraphenylbutane (2)-9,10-dihydroanthracene system in the presence of a mixture of 4-methoxyphenol and 2,6-di-*tert*-butyl-4-methylphenol when the ratio of RH to 2,6-di-*tert*-butyl-4-methoxyphenol is less than 10^4 is accurately given by expression (36). Moreover the values of $k_3/2k_{12}$ and $k_3/2k_{12'}$ obtained from these results are in excellent agreement with those obtained from the oxidation study of the individual compounds.

The dramatic effect of the addition of small amounts of hindered phenols on the inhibition period manifested by 4-methoxyphenol (cf. Figure 3) is also fully in accord with the regeneration of 4-methoxyphenol *via* the rapid transfer reaction (30).

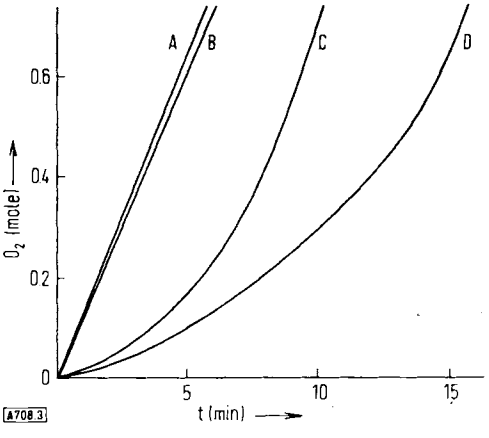
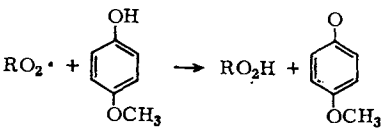
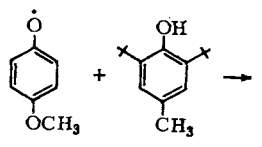


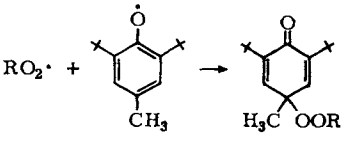
Fig. 3. The oxygen absorption of a chlorobenzene solution of 148 mmoles 9,10-dihydroanthracene at 60 °C containing 124 mmoles 2,2,3,3-tetraphenylbutane and, Curve A: no inhibitor; Curve B: 0.1 mmole 2,6-di-*tert*-butyl-4-methylphenol; Curve C: 0.1 mmole 4-methoxyphenol; and Curve D: 0.1 mmole 2,6-di-*tert*-butyl-4-methylphenol and 0.1 mmole 4-methoxyphenol.

The results of kinetic and product studies under conditions where the rate of reaction (−30) is appreciable, *i.e.*, high concentrations of 4-methoxyphenol, suggest that termination reactions, such as (40) also occur.

This mechanism gives a good account of the synergistic effects observed in practice. Since the necessary step

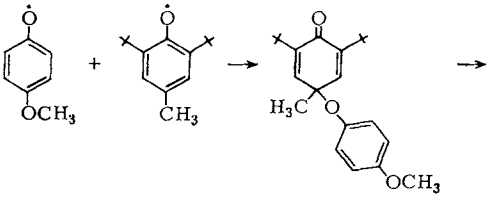

(slow) (37)

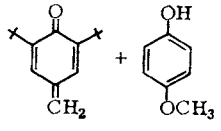

(fast) (38)


(fast) (39)

for synergism to be observed is the favorable competition of the hindered phenol with hydroperoxide and hydrocarbon for the non-hindered phenoxyl radical,

$$\frac{-dO_2}{dt} = 2k_1[R{-}R] + \frac{k_3\,\{2k_1[R{-}R]\}\,[RH]}{2k_{12}[\text{4-methoxyphenol}] + 2k_{12'}[\text{2,6-di-}tert\text{-butyl-4-methylphenol}]} \quad (36)$$


(40)



i.e. the value of k_{30}/k_{-12}, the magnitude of the synergistic effects observed will depend upon the value of this ratio. The values of k_{30}/k_{-12} for 4-*tert*-butylphenol, 4-methoxyphenol, and 2,4,6-trimethylphenol are 100, 600, and much greater than 600 respectively. The values which have been reported for the amount of synergism manifested by these phenols in admixture with 2,6-di-*tert*-butyl-4-methylphenol in a mineral oil at 160 °C are 5, 45, and 160 min[42]. Compounds which failed to manifest a synergistic effect with 2,6-di-*tert*-butyl-4-methylphenol are those which do not restart chains *via* reactions (−12) and (15), namely α-naphthol and 2,4,6-tri-*tert*-butylphenol.

6.2. Mixtures of Non-Hindered Phenols

A number of these systems have recently been studied in our laboratory[45]; at sufficiently high concentrations of a non-hindered phenol the rate of oxidation of

[44] The ratio of hydrogen atom transfer for 2,6-di-*tert*-butyl-4-methylphenol and for 2,4,6-tri-*tert*-butylphenol are very similar, see [42].

[45] *L. R. Mahoney* and *M. A. DaRooge*, unpublished results.

$$\frac{-dO_2}{dt} = 2k_1[R{-}R] + \frac{k_{15}}{(2k_{14})^{1/2}} \left\{ 2k_1[R{-}R] \right\}^{1/2} [RH] \qquad (41)$$

a hydrocarbon is given by expression (41). Under these conditions the propagating free radical is the non-hindered phenoxyl radical and the termination reaction is the dimerization of the chain-carrying phenoxyl radical. If one employs a mixture of two non-hindered phenols, both at a sufficiently high concentration such that equation (41) is obeyed, a system for the study of the independent and the cross reactions of the two non-hindered phenoxyl radicals is available. The results of the oxygen absorption of the tetraphenylbutane (*2*)-9,10-dihydroanthracene system containing 4-methoxyphenol in admixture with phenol and in admixture with 3,5-di-*tert*-butylphenol are shown in Figure 4.

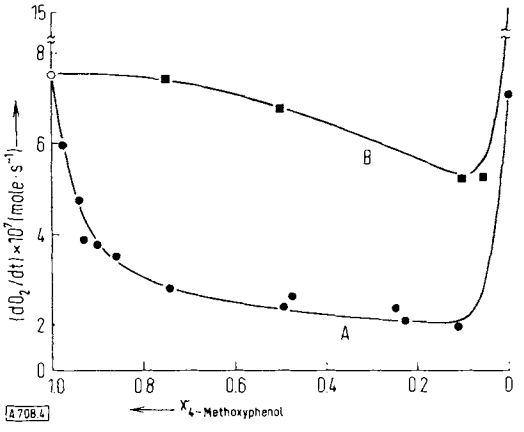
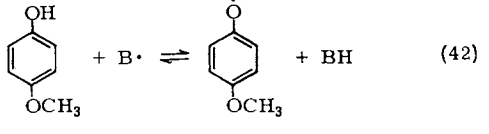


Fig. 4. The rates of oxygen absorption of a chlorobenzene solution of 99 mmoles 9,10-dihydroanthracene at 60 °C containing 31 mmoles 2,2,3,3-tetraphenylbutane, and Curve A: 3,5-di-*tert*-butylphenol + 4-methoxyphenol; Curve B: phenol + 4-methoxyphenol. The total concentrationof the two antioxidants for both curves is equal to 100 mmoles.

An extension of the mechanism which accounts for the synergistic behavior of mixtures of hindered and non-hindered phenols to mixtures where both phenols are non-hindered seems quite logical. For both of the non-hindered mixtures the equilibrium



(42)

where B· is the 3,5-di-*tert*-butylphenoxyl radical or the unsubstituted phenoxyl radical should lie to the right. We come to this conclusion since the values of k_{12}/k_3 which should, in the case of non-hindered phenols, be a measure of the phenoxyl radical stability are 284, 15.0, and 9.8 for 4-methoxyphenol, 3,5-di-*tert*-butylphenol, and phenol respectively. The shape of the oxidation curves A and B will depend upon the relative rates of the termination reactions.

An examination of the kinetic parameters for 3,5-di-*tert*-butylphenol as an antioxidant in the 9,10-dihydroanthracene-tetraphenylbutane (*2*) system strongly suggests that the rates of termination reactions involving the sterically hindered phenoxyl radical derived from it are quite slow.

The values of k_{12}/k_3 for 3,5-dimethylphenol and 3,5-di-*tert*-butylphenol are 10.0 and 15.0 while the values of $k_{15}/(2k_{14})^{1/2}$ are 7×10^{-3} and 40×10^{-3} $l^{1/2} \cdot mole^{-1/2}\ sec^{-1/2}$. Since the rate constant for reactions at the –OH group are very similar, the value of k_{15} for both phenols should be similar, and the value of k_{14} for the 3,5-di-*tert*-butylphenol radical should be small.

In agreement with this view the rates of oxidation manifested by mixtures of 4-methoxyphenol and 3,5-di-*tert*-butylphenol are relatively constant until the mole fraction of 3,5-di-*tert*-butylphenol exceeds 95 mole percent. In contrast, the presence of 5 mole percent phenol strongly reduces the rate of oxidation. This suggests that the cross termination reaction of 4-methoxyphenoxyl and phenoxyl radicals is very rapid compared to the dimerization of 4-methoxyphenoxyl and phenoxyl radicals.

A more detailed analysis of such systems is at present difficult since values for the rate of (30) and/or equilibrium constants (k_{30}/k_{-30}) for non-hindered phenol systems are not yet available.

7. Aromatic Amines as Antioxidants

The mechanism of the antioxidant behavior of aromatic amines has been subjected to considerably less systematic study than that of phenols. The results of study of the deuterium isotope effects are consistent with the peroxyl radical abstracting the amino hydrogen atom [46].

Although the kinetic dependence of the initial rates upon initiator, hydrocarbon, hydroperoxide, and inhibitor concentrations are somewhat complex, the relative effectiveness of substituted diphenylamines and *N*-methylanilines may be correlated with σ^+ values to yield ρ values equal to –0.89 and 1.6 respectively [47] in the styrene system.

In addition to the occurrence of chain restarting reactions of the amino radicals with hydroperoxide and hydrocarbon, a very serious complication encountered in the study of amine antioxidants is that the reaction of a peroxyl radical with an aminyl radical, reaction (43), produces a nitroxide radical and an alkoxyl radical [48].

$$RO_2{\cdot} + {\cdot}NR_2 \rightarrow RO{\cdot} + {\cdot}O{-}NR_2 \qquad (43)$$

The alkoxyl radical will regenerate the peroxyl radical *via* reactions with hydroperoxide and hydrocarbon. The subsequent reactions of the nitroxide radicals are very complex; they are apparently capable of reaction with both R· and RO_2· and also with hydroperoxide as indicated by the effect of oxygen pressure and hydroperoxide upon hydrocarbon oxidation inhibited by stable nitroxides [49].

The author wishes to acknowledge the contributions of his collaborators at the Scientific Laboratory of Ford Motor Company, particularly Dr. Margaret A. DaRooge.

Received: October 17, 1968 [A 708 IE]
German version: Angew. Chem. *81*, 555 (1969)

[46] *I. T. Brownlie* and *K. U. Ingold*, Canad. J. Chem. *44*, 861 (1966).

[47] *I. T. Brownlie* and *K. U. Ingold*, Canad. J. Chem. *45*, 2419 (1967).

[48] *J. Q. Adams, S. W. Nicksic*, and *J. R. Thomas*, J. chem. Physics *45*, 654 (1966), and literature cited therein.

[49] *I. T. Brownlie* and *K. U. Ingold*, Canad. J. Chem. *45*, 2427 (1967).

The Ene Reaction

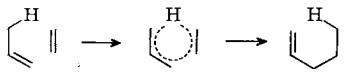
By H. M. R. Hoffmann[*]

The ene reaction is defined as the indirect substituting addition of a compound with a double bond (enophile) to an olefin with an allylic hydrogen (ene). For a long time the reaction has been neglected and has remained overshadowed by the related Diels-Alder addition. It is shown that the ene reaction possesses wide scope and applicability ranging from industrial to biosynthetic processes. Preparative aspects are summarized and current views on the mechanism are discussed.

1. Introduction

Although the ene reaction is one of the most simple and versatile reactions of organic chemistry, it is surprisingly little known and virtually ignored in all textbooks. Isolated examples such as certain reactions of olefins with formaldehyde (Prins reaction; cf. also Section 3.4)[1] as well as retro-ene reactions, *e.g.*, the decarboxylation of β-ketoacids and the formation of olefins by ester pyrolysis have been known at least since the beginning of the century, but many further examples have been buried in the patent literature[2] and in a number of obscure journals. Only after a paper by *Alder*[3] in 1943 did the scope of the ene reaction begin to be recognized. However, until today the "ene synthesis" has remained unfashionable and overshadowed by the related Diels-Alder addition ("diene synthesis"). Furthermore, much of the early work is insecurely based, because the by now common analytical and spectroscopic tools were not available. It is the purpose of this review to discuss what results and mechanistic insight are now available on this reaction.

The ene reaction is the "indirect substituting addition"[3] of a compound with a double bond (enophile) to an olefin possessing an allylic hydrogen (ene) and involves allylic shift of one double bond, transfer of the allylic hydrogen to the enophile and bonding between the two unsaturated termini (Scheme 1). Formally the reaction is not only related to the Diels-Alder addition, but can also be regarded as an intermolecular variant of the symmetry-allowed 1,5-hydrogen shift[4]

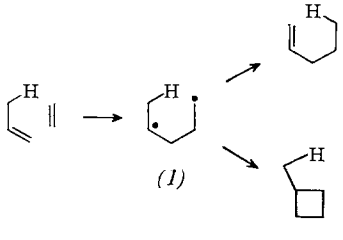


Scheme 1



Scheme 2. $\Delta H^{\ddagger} = 35.4$ kcal/mole, $\Delta S^{\ddagger} = -7.1$ e.u. [6].

(Scheme 2), although the transition state geometry of all three reactions is different (Section 6.5). It must be stressed from the very beginning that the ene reaction need not necessarily proceed in concerted fashion. If, for example, the ene component is so constituted that simultaneous bond-making at its carbon and hydrogen termini is geometrically unfavorable, the stepwise reaction involving a biradical *(1)* may occur (Scheme 3). Such a mechanism will usually betray itself on careful product analysis, since it seems clear from the elegant work of *Bartlett*[5] that a biradical such as *(1)* will at least partly leak into the cyclobutane derivative *(2)*. Conversely, current theory suggests that in the absence of any cyclobutane derivatives the ene reaction is most likely to take a concerted course. The other mechanistic extreme, *i.e.*, formation of an intermediate allylic radical by slow transfer of the hydrogen to the enophile, appears to be extremely rare (Section 6.5).



(1) *(2)*

Scheme 3

2. The Ene Component

2.1. Monoolefins

The most simple ene reaction, that of propylene with ethylene (Scheme 1), appears to be unknown and only the reverse reaction, *i.e.*, decomposition of 1-pentene can be achieved at elevated temperatures[6]. However,

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[1] *H. J. Prins*, Chem. Weekblad *16*, 1510 (1919); see also ref. [83].

[2] See *C. P. A. Kappelmeier*, *J. H. van der Neut*, and *W. R. van Goor*, Kunststoffe *40*, 81 (1950); see also [3], footnotes 1 and 2.

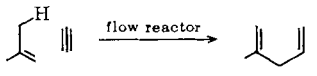
[3] *K. Alder*, *F. Pascher*, and *A. Schmitz*, Ber. dtsch. chem. Ges. *76*, 27 (1943).

[4] *R. B. Woodward* and *R. Hoffmann*, J. Amer. chem. Soc. *87*, 2511 (1965).

[5] *P. D. Bartlett*, Science (Washington) *159*, 833 (1968).

[6] *W. R. Roth*, Chimia *20*, 229 (1966).

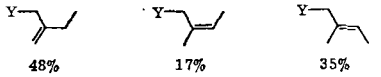
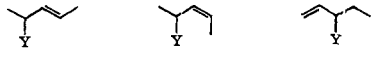
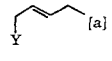
under high pressure acetylene has been proved to react with a number of simple olefins to form 1,4-dienes[7]. For instance, 2-methyl-1,4-pentadiene *(4)* can be isolated in 40% yield when a large excess of isobutylene *(3)* is treated with acetylene in a flow reactor at 170 atm.



(3) *(4)*

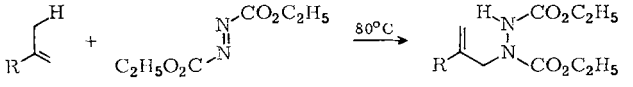
Thaler and *Franzus*[8] have treated a number of isomeric butenes and pentenes with diethyl azodicarboxylate (Scheme 4) and identified the products by NMR spectroscopy and gas-liquid chromatography (Table 1). These data demonstrate that the azo ester

Table 1. Monoadducts, yields, and relative rates of the reaction of diethyl azodicarboxylate with butenes and pentenes; Y = $N(CO_2C_2H_5)$—$NHCO_2C_2H_5$ [8] (cf. Scheme 4).

Entry	Olefin	Monoadducts	Rate Relative to *cis*-But-2-ene
1			17.2
2			3.73
3		 83% 17%	2.57
4			1.00
			Rate Relative to Pent-1-ene
5			4.33
6		 48% 17% 35%	3.64
7			2.13
8		 [a]	1.00
9			slow

[a] Not clear whether *trans* and/or *cis* adduct formed.

attacks the least substituted allylic position preferentially. In other words, a primary hydrogen is abstracted more readily than a secondary and much faster than a tertiary one (entries 1, 3, 9). The thermodynamic stability of the product is not decisive here. 3-Methyl-1-butene (entry 9), which can only donate its crowded isopropyl hydrogen to the enophile, reacts very slowly despite the fact that the abstracted hydrogen is tertiary. In fact, in the latter reaction it is difficult to isolate the monoadduct, which, having six primary hydrogen atoms, forms the bisadduct very smoothly.



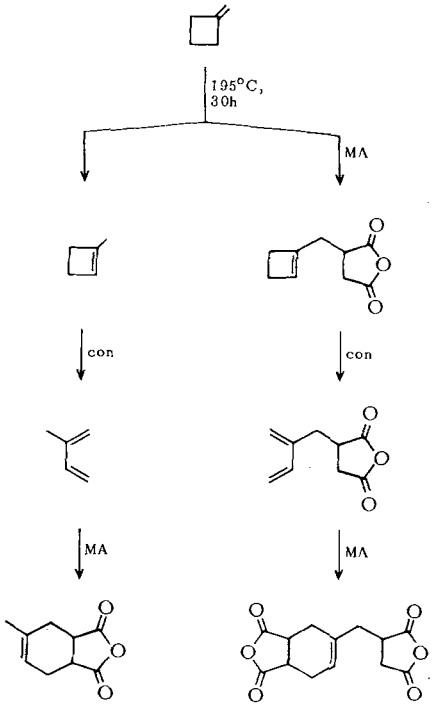
Scheme 4

Substituent effects at the nonterminal vinylic carbon of the ene component have been investigated less thoroughly. However, relative rates obtained from competition experiments indicate that feeding electrons into this position increases rates. Note also that 2-methyl-2-butene forms the adduct in which Y is attached to the secondary but not the tertiary carbon (entry 5) and that *trans*-2-butene reacts faster than the *cis* isomer (entries 2,4).

Substituted allylic compounds such as 1,3-diarylpropenes react with diethyl azodicarboxylate according to Scheme 4[9], and with selenium dioxide in acetic acid[10], but have been claimed not to react with maleic anhydride[11], which admittedly is a less effective enophile.

2.2. Methylenecycloalkanes and 1-Methylcycloalkenes

Methylenecyclobutane affords a 1:2 adduct with maleic anhydride (MA) in easily discernible fashion. The 1:1 adduct which is formed in a side reaction, is visualized



Scheme 5

[7] *N. F. Cywinski*, J. org. Chemistry *30*, 361 (1965).

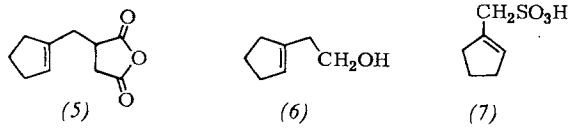
[8] *W. A. Thaler* and *B. Franzus*, J. org. Chemistry *29*, 2226 (1964).

[9] *R. Huisgen* and *H. Pohl*, Chem. Ber. *93*, 527 (1960).

[10] *J. P. Schaefer*, *B. Horvath*, and *H. P. Klein*, J. org. Chemistry *33*, 2647 (1968).

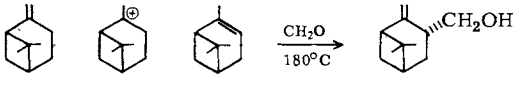
[11] *C. S. Rondestvedt jr.* and *B. H. Wark*, J. org. Chemistry *20*, 368 (1955).

to arise from rearrangement to 1-methylcyclobutene, opening to isoprene, and Diels-Alder trapping (Scheme 5)[12]. Methylenecyclopentane gives rise to *(5)* and *(6)* on heating with, respectively, maleic anhydride and formaldehyde to 200 °C for 2–4 hours. In contrast, the sulfonic acid *(7)* is formed simply on leaving methylenecyclopentane and sulfur trioxide in dioxane at 0 °C[13]. Under the same conditions and with the same reagents methylenecyclohexane forms the adducts corresponding to *(5)*, *(6)*, and *(7)*[14].



(5) *(6)* *(7)*

Naturally-occurring β-pinene *(8)* is particularly reactive towards enophiles. It readily forms adducts with maleic anhydride, dimethyl maleate and fumarate, methylenemalonic ester[15a], formaldehyde[15b], trichloroacetaldehyde[15c], carbonyl cyanide[15d], butyl

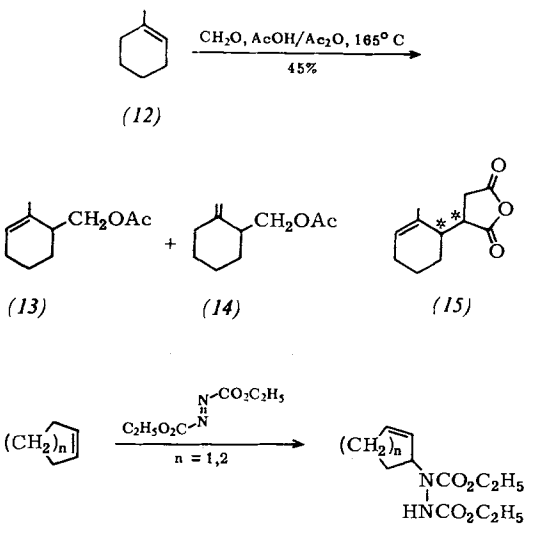


(8) *(9)* *(10)* *(11)*

glyoxylate[15e], and benzyne[15f]. If these reactions were to proceed *via* a carbonium ion such as *(9)* (or the corresponding radical), much rearranged product would arise. In fact, it has been found that the isolated products retain the pinene carbon skeleton. Presumably, in all these reactions the axial hydrogen which is on the more accessible *endo* face, is abstracted from β-pinene. The homologous myrtenol formed from formaldehyde and β-pinene is valued in the perfumery industry under the trivial name of nopol.

Unlike *(8)*, the endocyclic isomer α-pinene *(10)*, which is thermodynamically more stable, reacts not at all or only very reluctantly. For example, the powerful enophile singlet oxygen gives a minor amount of ene adduct only[16], and paraformaldehyde reacts at 180 °C in the absence of solvent to give *(11)* in 12% yield only[17]. In these reactions α-pinene is attacked generally from the less hindered *endo* side.

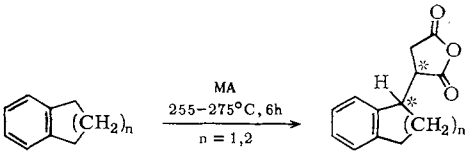
Cyclopentene and cyclohexene react with diethyl azodicarboxylate according to Scheme 6. However, these reactions are abnormal in that they can be catalyzed by radical initiators such as dibenzoyl peroxide and retarded by radical inhibitors (*p*-benzoquinone, acrylonitrile)[8,9] (see also Section 6.5). Indan and tetralin



(12) *(13)* *(14)* *(15)*

Scheme 6

react with maleic anhydride to form diastereomeric 1:1 adducts in which the double bond is unshifted (Scheme 7)[18].



Scheme 7

1-Methylcyclohexene *(12)* reacts with formaldehyde at 165 °C, when acetic acid-acetic anhydride is used as a solvent, to give an approximately equal mixture of acetates *(13)* and *(14)*[17,19]. It has been reported in an earlier paper that *(12)* and maleic anhydride afford *(15)* as a mixture of two diastereoisomers, but not the adduct corresponding to *(14)* with an exocyclic double bond[20]. Recently, *Blomquist* and his co-workers have considerably improved the experimental conditions for inducing ene reactions with formaldehyde. For example, the thermal ene reaction of (+)-limonene *(16)* with formaldehyde in an autoclave at 180–200 °C is completely unsatisfactory. However, if *(16)* is treated with formaldehyde in solvent dichloromethane-acetic anhydride in the presence of boron trifluoride dihydrate, the adduct *(17)* is formed in 69% yield after 70 minutes at autogeneous temperature[21]! Interestingly, the disubstituted double bond of *(16)* is inert to singlet oxygen, which selectively attacks the more electron-rich internal double bond[20a].

[12] *K. Alder* and *H. Dortmann*, Chem. Ber. *85*, 556 (1952).

[13] *R. T. Arnold, R. W. Amidon*, and *R. M. Dodson*, J. Amer. chem. Soc. *72*, 2871 (1950).

[14] *R. T. Arnold* and *J. F. Dowdall*, J. Amer. chem. Soc. *70*, 2590 (1948); see also *K. Alder, H. Söll*, and *H. Söll*, Liebigs Ann. Chem. *565*, 73 (1949).

[15] a) *R. T. Arnold* and *J. S. Showell*, J. Amer. chem. Soc. *79*, 419 (1957); b) *J. P. Bain*, J. Amer. chem. Soc. *68*, 638 (1946); *N. O. Brace, ibid. 77*, 4666 (1955); c) *M. Vilkas, G. Dupont*, and *R. Dulon*, Bull. Soc. chim. France *1955*, 799; d) *G. I. Birnbaum*, Chem. and Ind. (London) *1961*, 1116; e) *E. I. Klimova* and *Y. A. Arbuzov*, Ž. org. Chim. *1968*, 4 (10), 1787; see Chem. Abstr. *70*, 20228d (1969); f) *L. Friedman* and *J. Miller*, private communication.

[16] *C. S. Foote*, Accounts chem. Res. *1*, 104 (1968); and references cited therein.

[17] *A. T. Blomquist, J. Verdol, C. L. Adami, J. Wolinsky*, and *D. D. Phillips*, J. Amer. chem. Soc. *79*, 4976 (1957).

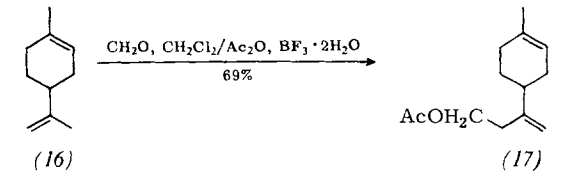
[18] *K. Alder* and *O. Wolff*, Liebigs Ann. Chem. *576*, 182 (1952).

[19] a) *G. Ohloff*, Liebigs Ann. Chem. *627*, 79 (1959), footnote 29; b) Chem. Ber. *93*, 2673 (1960).

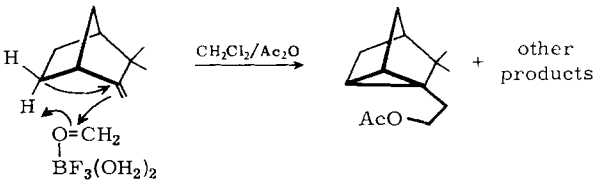
[20] *K. Alder* and *A. Schmitz*, Liebigs Ann. Chem. *565*, 99 (1949).

[20a] *G. O. Schenck, K. Gollnick, G. Buchwald, S. Schroeter*, and *G. Ohloff*, Liebigs Ann. Chem. *674*, 93 (1964).

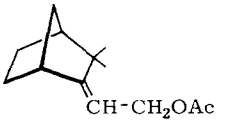
[21] *A. T. Blomquist* and *R. J. Himics*, J. org. Chemistry *33*, 1156 (1968).



(16) (17)



(18) (19)

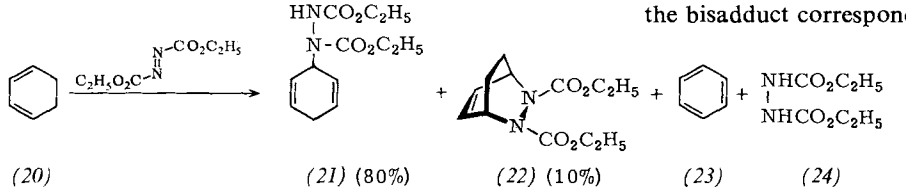


(19a)

On treatment with formaldehyde in dichloromethane containing boron trifluoride dihydrate or, alternatively, stannic chloride, camphene *(18)* forms adduct *(19)* as the main product (57%)[22a]. In contrast, on heating *(18)* to 105 °C with formaldehyde in acetic acid one obtains *(19a)* in 75% yield; *(19a)* is also formed from *(19)* in hot acetic acid[22b]. Consequently, the conversion of *(18)* into *(19)* could represent the first example of a homo-ene reaction as formulated here, although *Blomquist* has suggested a stepwise mechanism *via* a carbonium ion intermediate[22a].

2.3. 1,3-Dienes

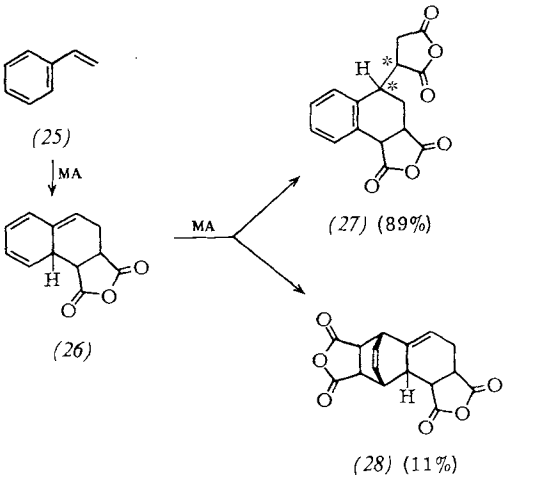
Special factors are required if the ene reaction is to proceed with conjugated dienes in preference to the Diels-Alder addition. It was reported originally that 1,3-cyclohexadiene *(20)* forms exclusively the ene product *(21)* with diethyl azodicarboxylate and no Diels-Alder adduct *(22)*[23]. Reinvestigation revealed that *(22)* is formed albeit in low yields (5–15%)[24]. However, cycloadduct *(22)* may be obtained in 87%



(20) (21) (80%) (22) (10%) (23) (24)

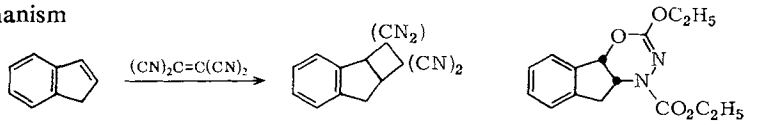
yield without any admixed *(21)* if the reaction solution is irradiated below room temperature[25]. It has been shown that UV irradiation of diethyl azodicarboxylate which normally possesses the more stable *trans* configuration, produces some *cis* isomer in photostationary equilibrium[26]; *cis* azo derivatives are generally much more reactive in both 4 + 2[26,27] and 2 + 2 cycloadditions[28].

A comparison of the benzoannelated dienes *(25)*, *(29)*, and *(32)* is informative. Styrene *(25)* and maleic anhydride first form the Diels-Alder adduct *(26)*, which apparently cannot be isolated, since it possesses a

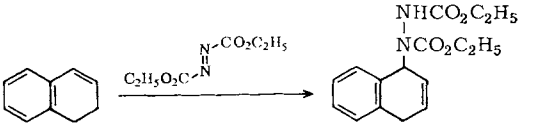


(25) (26) (27) (89%) (28) (11%)

carbon-hydrogen bond weakened by both allyl and pentadienyl resonance. Reaction with a second molecule of maleic anhydride yields the ene product *(27)*



(29) (30) (31)



(32) (33)

and the 4 + 2 adduct *(28)* in a ratio of *ca.* 8:1[29]. In contrast, styrene and diethyl azodicarboxylate form the bisadduct corresponding to *(27)* only[30].

[22] a) *A. T. Blomquist* and *R. J. Himics*, Tetrahedron Letters *1967*, 3947; b) *A. T. Blomquist*, *R. J. Himics*, and *J. D. Meador*, J. org. Chemistry *33*, 2462 (1968).

[23] a) *B. T. Gillis* and *P. E. Beck*, J. org. Chemistry *27*, 1947 (1962); b) *B. Franzus* and *J. H. Surridge*, *ibid.* p. 1951.

[24] *B. Franzus*, J. org. Chemistry *28*, 2954 (1963).

[25] *R. Askani*, Chem. Ber. *98*, 2551 (1965).

[26] *G. O. Schenck*, *H.-R. Kopp*, *B. Kim*, and *E. Koerner von Gustorf*, Z. Naturforsch. *20b*, 637 (1965).

[27] *R. C. Cookson*, *S. S. H. Gilani*, and *I. D. R. Stevens*, J. chem. Soc. (London) *C*, *1967*, 1905; see also Tetrahedron Letters *1962*, 615.

[28] a) *G. O. Schenck* and *N. Engelhard*, Angew. Chem. *68*, 71 (1956); b) *A. H. Cook* and *D. G. Jones*, J. chem. Soc. (London) *1941*, 184.

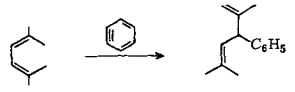
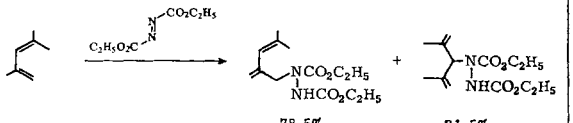
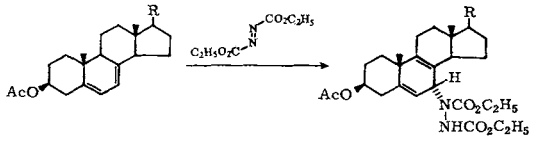
[29] *K. Alder* and *R. Schmitz-Josten*, Liebigs Ann. Chem. *595*, 1 (1955).

[30] *K. Alder* and *H. Niklas*, Liebigs Ann. Chem. *585*, 97 (1954); this paper has been partly criticised by *Huebner et al.* [31a].

Indene *(29)* and tetracyanoethylene afford the 2 + 2 adduct *(30)* [31a]. Originally, the reaction with diethyl azodicarboxylate was assumed to yield the analogous 2 + 2 product [31a], but more recent work has shown that the 4 + 2 adduct *(31)* is formed instead [31b].

1,2-Dihydronaphthalene *(32)* does not undergo a Diels-Alder addition with diethyl azodicarboxylate but forms *(33)* [9]. In this reaction free radical initiators and inhibitors have shown no effect [9]. Not surprisingly, the Diels-Alder addition is completely suppressed for conjugated dienes including a variety of steroidal dienes [34–36], which are highly alkylated at the carbon termini. Apparently, only ene products have been isolated for the reactions listed in Table 2.

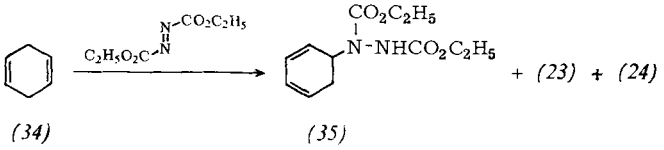
Table 2. Ene reactions of sterically hindered 1,3-dienes.

No.	Reactions	Ref.
1		[32]
2	 78.5% 21.5%	[33]
3		[34]

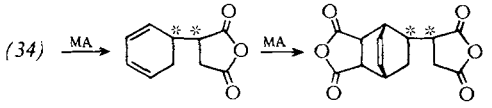
The competition of ene and diene synthesis in the thermal and catalyzed reactions of acyclic 1,3-dienes with carbonyl compounds is described in Section 6.4; see also Table 3.

2.4. 1,4-Dienes

1,4-Cyclohexadiene *(34)* reacts some fifteen times less readily with diethyl azodicarboxylate than 1,3-cyclohexadiene although conjugation energy is gained in the former and lost in the latter reaction. The equilibration of *(34)* and *(20)* with strong base has revealed that the conjugated diene *(20)* is more stable than *(34)* by only 600 cal [24, 36a]. This free energy difference corresponds to a ratio of *(20)*:*(34)* = 2.85:1 at equilibrium!

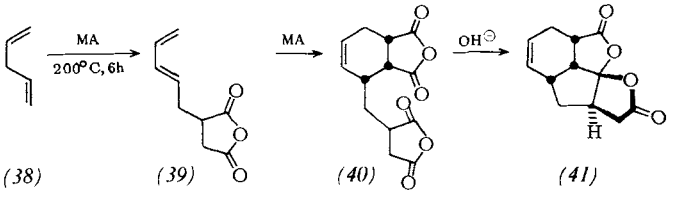


(34) *(35)* + *(23)* + *(24)*



(36) *(37)*

Maleic anhydride is generally less effective as an enophile than diethyl azodicarboxylate, but more efficient as a dienophile. Consistently, the reaction of 1,4-cyclohexadiene *(34)* and maleic anhydride cannot be stopped at the stage of the monoadduct *(36)*, and *(37)* is isolated as the final product [37]. Similarly, heating of 1,4-pentadiene *(38)* with maleic anhydride affords in 40% yield the bisanhydride *(40)*, which is decarboxylated to the spirodilactone *(41)* by traces of alkali [38]. On heating to 120 °C in benzene solvent, maleic anhydride forms the normal ene product with 1,4-dihydronaphthalene [39] and cinnamylsuccinic anhydride



(38) *(39)* *(40)* *(41)*

[31] a) *C. F. Huebner, P. L. Strachan, E. M. Donoghue, N. Cahoon, L. Dorfman, R. Margerison,* and *E. Wenkert,* J. org. Chemistry *32,* 1126 (1967); b) *E. Koerner von Gustorf, D. V. White, B. Kim, D. Hess,* and *J. Leitich,* J. org. Chemistry *1969,* in press; *C. F. Huebener, E. M. Donoghue, C. J. Novak, L. Dorfman,* and *E. Wenkert, ibid.,* in press.

[32] *E. M. Arnett,* J. org. Chemistry *25,* 324 (1960).

[33] *B. T. Gillis* and *P. E. Beck,* J. org. Chemistry *28,* 3177 (1963); see also [23b].

[34] *A. van der Gen, J. Lakeman, M. A. M. P. Gras,* and *H. O. Huisman,* Tetrahedron *20,* 2521 (1964); see also *A. van der Gen, W. A. Zunnebeld, U. K. Pandit,* and *H. O. Huisman, ibid. 21,* 3651 (1965).

[35] *A. M. Lautzenheiser* and *P. W. LeQuesne,* Tetrahedron Letters *1969,* 207.

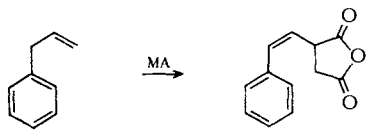
[36] *D. N. Jones, P. F. Greenhalgh,* and *I. Thomas,* Tetrahedron *24,* 5215 (1968).

[36a] *H. Oberhammer* and *S. H. Bauer,* J. Amer. chem. Soc. *91,* 10 (1969).

[37] *K. Alder* and *F. Münz,* Liebigs Ann. Chem. *565,* 126 (1949).

[38] *R. K. Hill* and *H. J. Barjer jr.,* J. org. Chemistry *30,* 2558 (1965).

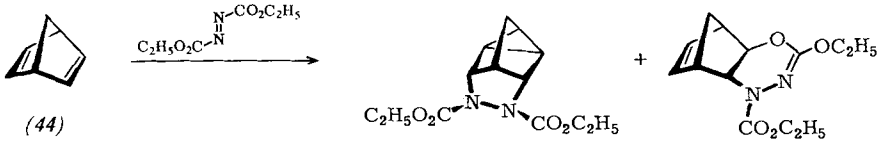
[39] *K. Alder, H. Wollweber,* and *H. Spanke,* Liebigs Ann. Chem. *595,* 38 (1955).



(42) (43)

(43) with allylbenzene (42) [40]. Whether (43) is formed as the *trans* and/or *cis* isomer is unknown.

In norbornadiene (44) a shift of the double bond is forbidden by Bredt's rule. With diethyl azodicarboxylate the 2 + 2 + 2 adduct (44a) and an isomeric compound have been detected in approximately equimolar quantities [41]. Later work has suggested the unusual

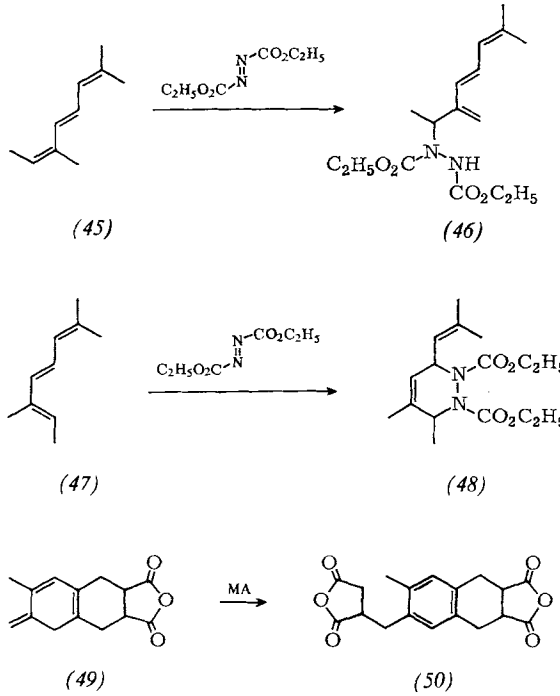


(44) (44a) (44b)

structure (44b) for the second adduct, *i.e.*, the azo ester behaves as a heterodiene [42] analogous to the formation of (31).

2.5. Conjugated Trienes

The allocimene (45) [43], a naturally occurring triene, reacts cleanly with diethyl azodicarboxylate to form (46) under self-heating, while the isomeric triene (47) yields the Diels-Alder adduct (48) only [44a]. Clearly, any cisoid diene component of triene (45) contains at least one terminal *cis* alkyl group, an unfavorable situation in a Diels-Alder addition [45]. On the other hand, the *cis* configuration of the vicinal methyl groups in (47) impedes the ene reaction (Table 1, entry 4), while the methyl and isobutenyl group attached to the reacting cisoid diene system are *trans* and probably promote the cycloaddition. Interestingly, the less hindered and more reactive singlet oxygen gives only one stable ene adduct with either allocimene; cycloperoxides are not formed [44b]. Not surprisingly, triene (49) undergoes the ene rather than diene synthesis [46].



(45) (46) (47) (48) (49) (50)

Cycloheptatriene reacts with a variety of dienophiles such as maleic anhydride [47a,47b], 4-phenyl-1,2,4-triazoline-3,5-dione [27], fumaryl chloride [47a], and dimethyl and diethyl acetylenedicarboxylate [47c] to form Diels-Alder adducts of the general structure (52), in which the cyclopropane ring is oriented *syn* to the double bond. Recently, *Woodward* and *Houk* [48] have concluded that (52) arises from a 2 + 2 + 2 cycloaddition rather than from attack on the norcaradiene valence tautomer as had been frequently suggested [49]. Dimethyl acetylenedicarboxylate does not only form the Diels-Alder product (26% yield); in addition, a minor product (55) (12%) has been observed which seems to arise from an ene reaction followed by electrocyclic closure and a 3,3-sigmatropic process [50]. With diethyl azodicarboxylate [51a,b] and singlet oxygen [51b] cycloheptatriene undergoes the ene reaction exclusively to form adducts (56a) and (56b), respectively. It is of interest how (56a) is actually formed. By using [7-D]-cycloheptatriene, *Koerner von Gustorf* has

[40] *C. S. Rondestvedt jr.*, Org. Syntheses *31*, 85 (1951); see also [11].

[41] *S. J. Cristol, E. L. Allred*, and *D. L. Wetzel*, J. org. Chemistry *27*, 4058 (1962); *R. M. Moriarty, ibid. 28*, 2385 (1963).

[42] *J. J. Tuffariello, T. F. Mich*, and *P. S. Miller*, Tetrahedron Letters *1966*, 2293.

[43] For a discussion of the nomenclature and configuration of the alloocimenes see *K. J. Crowley*, J. org. Chemistry *33*, 3679 (1968).

[44] a) *E. Koerner von Gustorf*, Tetrahedron Letters *1968*, 4693; see also *E. Koerner von Gustorf* and *J. Leitich, ibid. 1968*, 4689; b) *E. Koerner von Gustorf, F.-W. Grevels*, and *G. O. Schenck*, Liebigs Ann. Chem. *719*, 1 (1968).

[45] *J. Sauer*, Angew. Chem. *79*, 76 (1967); Angew. Chem. internat. Edit. *6*, 16 (1967).

[46] *D. T. Longone* and *F.-P. Boettcher*, J. Amer. chem. Soc. *85*, 3436 (1963).

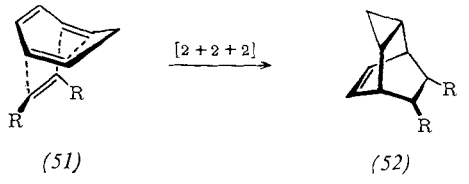
[47] a) *K. Alder* and *G. Jacobs*, Chem. Ber. *86*, 1528 (1953); b) *E. P. Kohler, M. Tishler, H. Potter*, and *H. T. Thompson*, J. Amer. chem. Soc. *61*, 1057 (1939); c) *M. J. Goldstein* and *A. H. Gevirtz*, Tetrahedron Letters *1965*, 4417.

[48] *K. N. Houk*, Ph. D. Thesis, Harvard University, Cambridge, Massachusetts 1968.

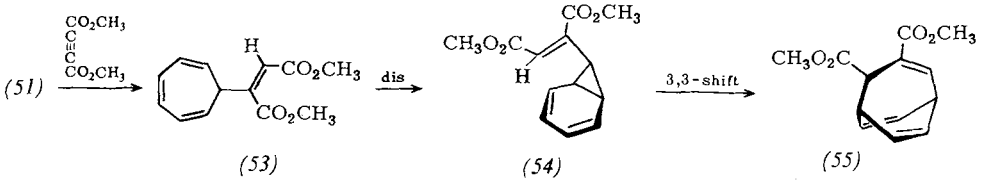
[49] See *G. Maier*, Angew. Chem. *79*, 446 (1967); Angew. Chem. internat. Edit. *6*, 402 (1967).

[50] *M. J. Goldstein* and *A. H. Gevirtz*, Tetrahedron Letters *1965*, 4413.

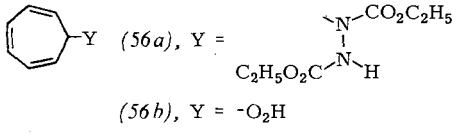
[51] a) *J. M. Cinnamon* and *K. Weiss*, J. org. Chemistry *26*, 2644 (1961); b) *G. O. Schenck, E. Koerner von Gustorf, B. Kim, G. v. Bünau*, and *G. Pfundt*, Angew. Chem. *74*, 510 (1962); Angew. Chem. internat. Edit. *1*, 516 (1962); c) *E. Koerner von Gustorf*, private communication; d) *E. Koerner von Gustorf* and *D. V. White*, unpublished.



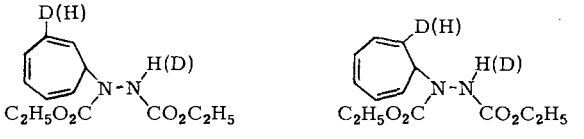
(51) (52)



(53) (54) (55)



(56a), Y = (56b), Y = $-O_2H$

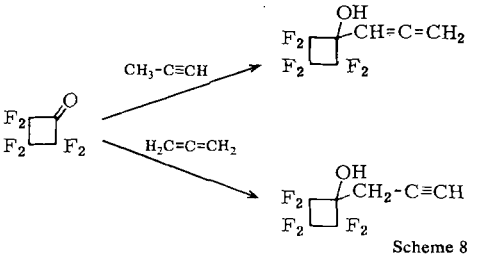


(56c) (56d)

shown recently that *(56c)* and *(56d)* arise in a ratio of 7:1, no deuterium being detectable at the C-3 and C-4 carbon. Apparently, the ene reaction cannot only proceed *via* a 6-membered ring, but also a 10-membered one, provided the loss in entropy is not too high. Clearly both reaction modes are symmetry allowed [51c]. (Cf. also the ene reaction in Scheme 12a, which may be regarded as a 10-electron or even a 14-electron process.)

2.6. Propynes and Allenes

Only the most powerful enophiles react with propynes in the sense of the ene reaction and few examples have been reported. 1-Hexyne *(57)* reacts with benzyne to form the allene *(58)* in less than 4% yield [52], while 1-ethoxypropyne *(59) inter alia* affords *(61)* and *(62)*. The two bis-adducts seem to arise from the reaction of the intermediate allene *(60)* with an excess of benzyne [53]. Whether the allenes *(58)* and *(60)* are formed in a concerted process or not is presently not clear. A further "record enophile" is perfluorocyclobutanone which undergoes the ene reaction with methylacetylene and allene (Scheme 8) [54]. Tetramethylallene reacts

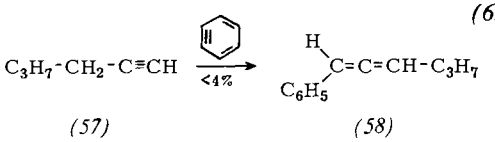


Scheme 8

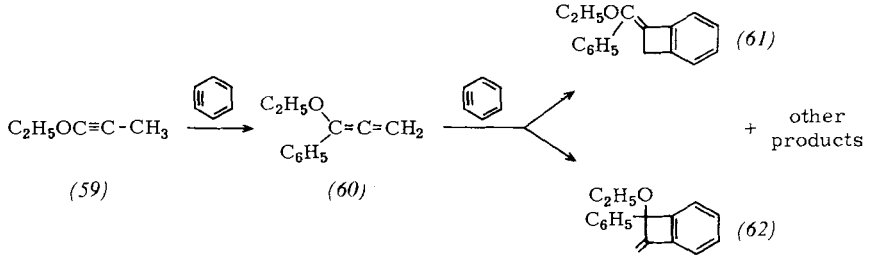
smoothly with azodicarboxylic esters and 5-phenyl-1,2,4-triazoline-3,5-dione to give the corresponding ene adducts at room temperature [51d]; in these reactions the enophile attacks the central carbon of tetramethylallene.

2.7. Strained π- and σ-Bonds

Olefins with strained double bonds seem particularly prone to enter into ene reactions. For example, the naturally occurring sesquiterpene caryophyllene *(63)*, which contains a strained *trans* double bond,



(57) (58)

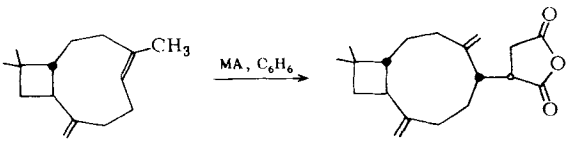


(59) (60) (61) (62)

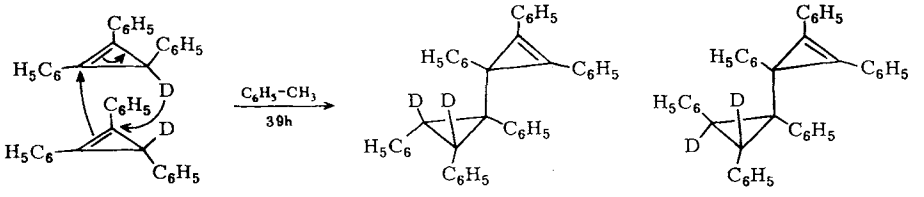
[52] *M. Stiles* and *A. Haag*, private communication to *R. W. Hoffmann*, cited in: Dehydrobenzene and Cycloalkynes. Academic Press, New York 1967, p. 198.

[53] *H. H. Wasserman* and *J. M. Fernandez*, J. Amer. chem. Soc. *90*, 5322 (1968).

[54] *D. C. England*, J. Amer. chem. Soc. *83*, 2205 (1961).



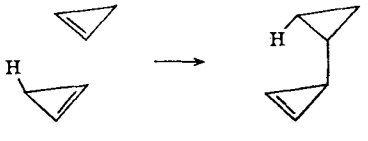
(63) (64)



(65) (66) (67)

reacts smoothly with maleic anhydride in refluxing benzene. Originally the product was formulated as a Diels-Alder adduct[55b,c,d] but after the structure of caryophyllene had been elucidated *Nickon* deduced structure *(64)* for the product[55a]. However, when the comparatively energy rich singlet oxygen is used as the enophile, caryophyllene reacts only about 5–6 times faster than its *cis* isomer (iso-caryophyllene)[55e]. The exocyclic double bond is not attacked by singlet oxygen[55f], although it is more accessible.

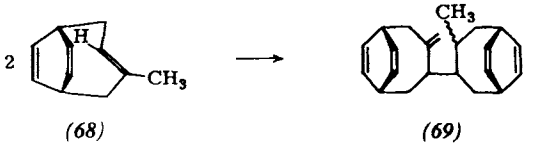
The deuterated triphenylcyclopropene *(65)* dimerizes in 20% yield on heating in toluene; the product has been formulated as the *cis* dimer *(66)* rather than *(67)* because in the formation of *(66)* the deuterium is transferred to the less hindered face of the second cyclopropene system[56]. Even more spectacular is the dimerization of the parent cyclopropene, which has been observed recently by *Dowd* and *Gold*[57]. Such is the reactivity of this hydrocarbon that it polymerizes with explosive violence at room temperature. However, if it is allowed to react in dilute dichloromethane



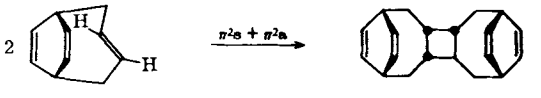
Scheme 9

solution at −25 °C, the extremely labile dimer can be isolated (Scheme 9). This reaction is probably not a free radical process as had been suggested earlier, since neither added nitrobenzene nor *p*-benzoquinone have shown any effect on the rate of dimerization.

The behavior of some bridged *cis,trans*-1,5-cyclooctadienes whose *trans* double bond is considerably twisted is also of great interest. Thus, the photoadduct *(68)* of benzene and isoprene dimerizes to *(69)*, a single compound or a mixture of two stereoisomers being formed below room temperature[58a]! In contrast, olefin *(70)*, which contains a less crowded *trans* double bond, affords *(71)*[58b] in a symmetry-allowed $\pi 2s + \pi 2a$ cycloaddition[59].

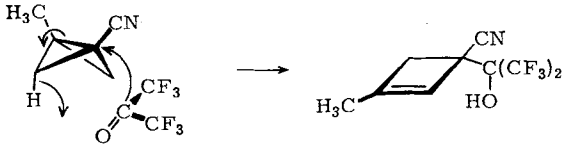


(68) (69)



(70) (71)

Considerable interest has focused recently on reactions of strained hydrocarbons such as bicyclo[1.1.0]-butanes and bicyclo[2.1.0]pentanes, in which the zero bridge exhibits a major degree of unsaturation[60]. 3-Methylbicyclo[1.1.0]butanecarbonitrile *(72)* has



(72) (73) (74)

been treated with a variety of olefins and carbonyl compounds; with hexafluoroacetone in ether solution the cyclobutene derivative *(74)* is formed in 82% yield below room temperature[61a]; dicyanoacetylene

[55] a) *A. Nickon*, J. Amer. chem. Soc. *77*, 1190 (1955); b) *L. Ruzicka, P. A. Plattner*, and *G. Balla*, Helv. chim. Acta *24*, 1219 (1941); c) *L. Ruzicka* and *W. Zimmermann*, *ibid. 18*, 219 (1935); d) *H. N. Rydon*, J. chem. Soc. (London) *1939*, 537; e) *F. A. Litt* and *A. Nickon*, Adv. Chemistry Ser. 77, American Chemical Society 1968, p. 118; f) *K. H. Schulte-Elte* and *G. Ohloff*, Helv. chim. Acta *51*, 594 (1968).

[56] *R. Breslow* and *P. Dowd*, J. Amer. chem. Soc. *85*, 2729 (1963).

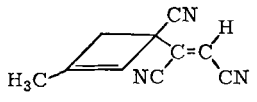
[57] *P. Dowd* and *A. Gold*, Tetrahedron Letters *1969*, 85.

[58] a) *K. Kraft* and *B. Koltzenburg*, Tetrahedron Letters *1967*, 4723; b) *ibid. 1967*, 4357.

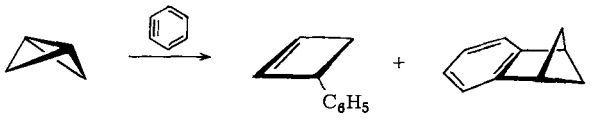
[59] *R. B. Woodward*, Lectures held at the IUPAC Symposium on "Valence Isomerization", Karlsruhe, Sept. 1968, and the Symposium on "Orbital Symmetry Correlations in Organic Reactions", Cambridge, England, January 1969.

[60] *M. Pomerantz* and *E. W. Abrahamson*, J. Amer. chem. Soc. *88*, 3970 (1966).

[61] a) *E. P. Blanchard jr.*, and *A. Cairncross*, J. Amer. chem. Soc. *88*, 487 (1966); b) *P. G. Gassman* and *K. T. Mansfield*, *ibid. 90*, 1517 (1968).

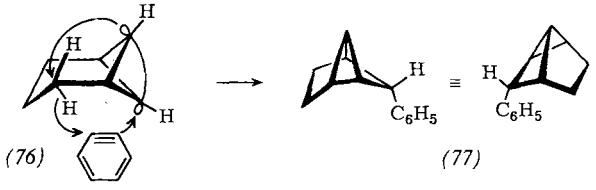


(75)

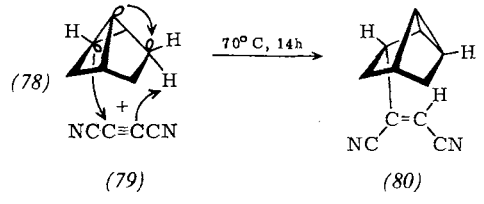


6.5 : 1

Scheme 10



(76) (77)



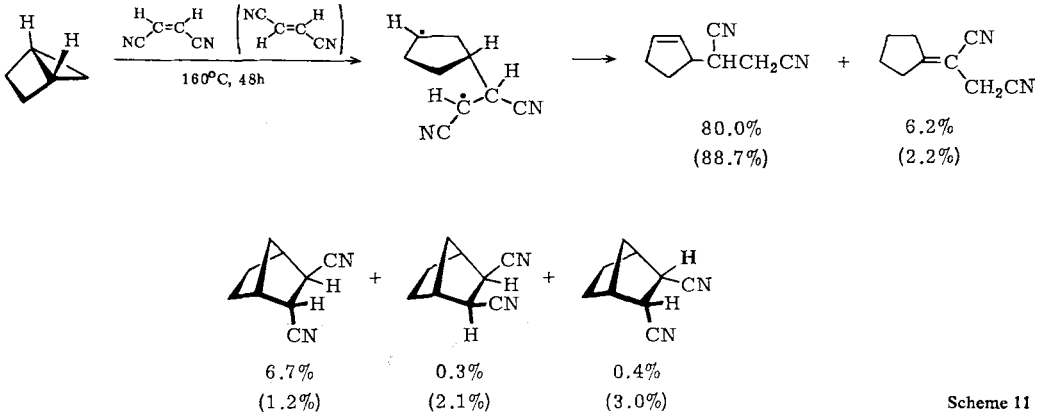
(78) (79) (80)

gives rise to *(75)* and three unidentified very minor by-products [61b].

In analogous fashion 1,3-dimethylbicyclo[1.1.0]butane reacts with dehydrobenzene [62a], hexafluoroacetone [62b], and maleic anhydride [62b]. The propano-bridged bicyclobutane *(76)* and dehydrobenzene afford *(77)* in 61% yield [63] while hydrocarbon *(78)* which contains the structural element of bicyclo[2.1.0]-pentane reacts with dicyanoacetylene *(79)* to form *(80)* in 46% yield [64].

Frequently, bicyclobutanes and bicyclopentanes react with olefins to give not only ene products, but also cycloadducts. In these cases a stepwise mechanism involving biradical intermediates seems assured, at least for the formation of the cycloadducts (cf. also Scheme 3). For example, the reaction of bicyclobutane with dehydrobenzene gives rise to benzobicyclo[2.1.1]-hexene as a by-product [65] (Scheme 10), in contrast to 1,3-dimethylbicyclo[1.1.0]butane, which under the same conditions yields the ene adduct only [62a].

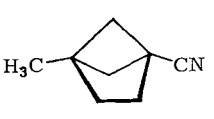
Five of seven products have been identified in the reaction of bicyclo[2.1.0]pentane with maleonitrile and fumaronitrile, respectively (Scheme 11; the yields in brackets refer to the reaction with fumaronitrile). Clearly, the three isomeric 2,3-dicyanonorbornanes are formed in either reaction, and hence rotation about the central bond of maleonitrile and fumaronitrile must have occurred at some stage during the reaction. Since a concerted formation of the cycloadducts is also forbidden by orbital symmetry conservation, the experimental findings are best accommodated by a biradical intermediate, in which rotation about a carbon-carbon single bond may compete with intramolecular radical combination [66]. 1:1 Cycloadducts which are derived from the bicyclo[2.1.1]hexane skeleton *(81)* can also be isolated in reactions of 3-methylbicyclo-[1.1.0]butane-1-carbonitrile *(72)* with ethylene, butadiene, styrene, acrylonitrile, maleonitrile, fumaronitrile, and 1-(*N*,*N*-dimethylamino)cyclopentene [67].



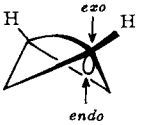
80.0% (88.7%) 6.2% (2.2%)

6.7% (1.2%) 0.3% (2.1%) 0.4% (3.0%)

Scheme 11



(81)



(82)

As regards stereochemistry the enophile could attack the zero bridge from the *exo* or *endo* direction *(82)*. The formation of the *endo* adducts *(77)* and *(80)* demonstrates for two specific examples that it is the backlobe of the zero bridge which is most vulnerable

[62] a) *M. Pomerantz, G. W. Gruber,* and *R. N. Wilke,* J. Amer. chem. Soc. *90,* 5040 (1968); b) *M. R. Rifi, ibid. 89,* 4442 (1967).

[63] *P. G. Gassman* and *G. D. Richmond,* J. Amer. chem. Soc. *90,* 5637 (1968).

[64] *P. G. Gassman* and *G. D. Richmond,* Chem. Commun. *1968,* 1630.

[65] *M. Pomerantz,* J. Amer. chem. Soc. *88,* 5349 (1966).

[66] *P. G. Gassman, K. T. Mansfield,* and *T. J. Murphy,* J. Amer. chem. Soc. *91,* 1648 (1969).

[67] *A. Cairncross* and *E. P. Blanchard jr.,* J. Amer. chem. Soc. *88,* 496 (1966).

to attack from enophiles. In fact, much further work with deuterium labeled substrates suggests that *endo* attack is a general feature of these reactions [68,69] [cf. also the pyrolysis of *(118)*].

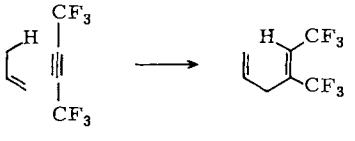
3. The Enophile

3.1. Alkenes

One of the most widely used enophiles of this type is maleic anhydride. In fact, its reactions with caryophyllene [55] and with naturally occurring unsaturated fatty acids and esters [2,3] represent the first recorded examples of ene reactions in all-carbon systems, and much further work has been reported since then [12,14,70]. Typical conditions for reactions of simple allylic compounds are 20 hours and 220 °C, an aromatic solvent generally being used. Trichlorobenzene is a particularly suitable solvent owing to its high boiling point (200–210 °C) which makes an autoclave unnecessary. Polymerization of the reactants and products can be inhibited by adding thionine or phenothiazine. Under these conditions the ene adducts have been isolated in up to 80% yield [71]. Tetracyanoethylene appears to have been used only rarely as an enophile [35,72]. α,β-Unsaturated ketones [73], esters [73], and nitriles [73a], in which the olefinic bond is activated by only one electron-attracting group, are less reactive than maleic anhydride.

3.2. Alkynes

The parent acetylene has been shown to react with isobutene at 350 °C under special conditions [7]. Acetylenedicarboxylic esters [50,73b,74], propiolic ester [73b,74], and dicyanoacetylene [61b,64] generally react below 200 °C, even with unactivated ene components. Hexafluoro-2-butyne readily forms 1,4-dienes with isobutene and 2-butene according to

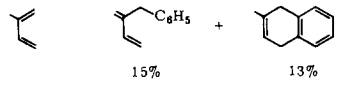
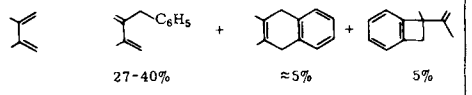
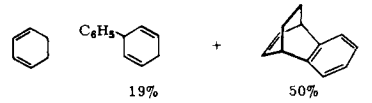


Scheme 12

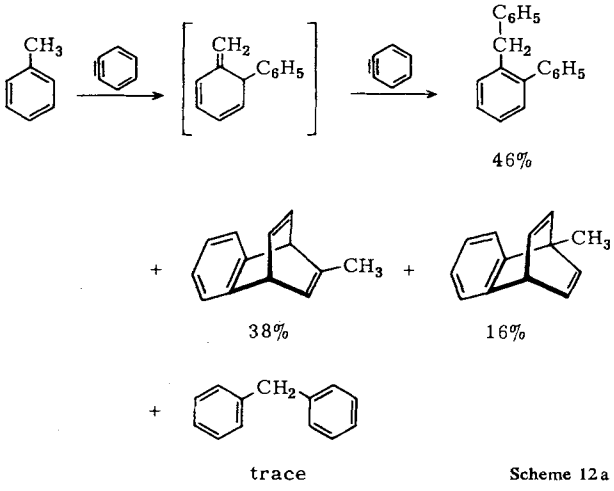
Scheme 12; in fact, it seems somewhat difficult to isolate the monoadduct in these reactions. Trifluoropropyne is less reactive, requiring temperatures of *ca.* 225 °C [74].

Dehydrobenzene is strongly electrophilic and is also one of the most powerful enophiles. Simple olefins such as isobutene [75a], 2,3-dimethyl-2-butene [75b], and cyclohexene [75c] are readily phenylated with shift of the double bond. The ene synthesis can also compete favorably with the Diels-Alder addition in reactions of dehydrobenzene with open-chain dienes, but less so with cyclic dienes, where the cisoid conformation

Table 3. Ene synthesis *versus* Diels-Alder addition in reactions of dehydrobenzene with conjugated dienes.

No.	Olefine	Products	Ref.
1		15% 13%	[75a]
2		27-40% ≈5% 5%	[75a]
3		19% 50%	[75d]

necessary for a 4 + 2 addition is enforced (Table 3). Apparently, in all three reactions listed in Table 3, further as yet unidentified products are formed [75a,75d]. Interestingly, even alkylarenes enter into ene reactions with dehydrobenzene as could be shown recently by *Friedman et al.* For example, the major product (46%) in the reaction of dehydrobenzene with toluene is 1-benzyl-2-phenylbenzene, which is formed in a "double-ene reaction"; Diels-Alder addition and insertion to diphenylmethane (trace) are less important here (Scheme 12a). Ethylbenzene and isopropylbenzene



Scheme 12a

[68] a) *W. R. Roth* and *M. Martin*, Tetrahedron Letters *1967*, 3865, 4695; Liebigs Ann. Chem. *702*, 1 (1967); b) *E. L. Allred* and *R. L. Smith*, J. Amer. chem. Soc. *89*, 7133 (1967).

[69] See also *M. Pomerantz* and *R. N. Wilke*, Tetrahedron Letters *1969*, 463.

[70] *J. Ross*, *A. I. Gebhart*, and *J. F. Gerecht*, J. Amer. chem. Soc. *68*, 1373 (1946); *K. Alder* and *H. Söll*, Liebigs Ann. Chem. *565*, 57 (1949).

[71] *W. Stumpf*, *F. Derichs*, *K. Rombusch*, and *W. Franke*, Liebigs Ann. Chem. *687*, 124 (1965).

[72] *T. L. Cairns* and *B. C. McKusick*, Angew. Chem. *73*, 520 (1961).

[73] a) *C. J. Albisetti*, *N. G. Fisher*, *M. J. Hogsed*, and *R. M. Joyce*, J. Amer. chem. Soc. *78*, 2637 (1956); b) *K. Alder* and *H. von Brachel*, Liebigs Ann. Chem. *651*, 141 (1962).

[74] *J. C. Sauer* and *G. N. Sausen*, J. org. Chemistry *27*, 2730 (1962).

[75] a) *G. Wittig* and *H. Dürr*, Liebigs Ann. Chem. *672*, 55 (1964); b) *G. Wittig* and *R. W. Hoffmann*, Chem. Ber. *95*, 2718 (1962); c) *H. E. Simmons*, J. Amer. chem. Soc. *83*, 1657 (1961); see also *J. A. Kampmeier* and *A. B. Rubin*, Tetrahedron Letters *1966*, 2853; d) *R. Huisgen* and *R. Knorr*, Tetrahedron Letters *1963*, 1017.

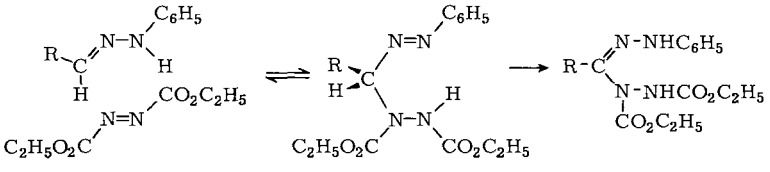
react similarly, but *tert*-butylbenzene, which does not contain an allylic hydrogen, failed to give any ene product, as expected. Tetrafluorobenzyne and tetrachlorobenzyne only yield Diels-Alder adducts with toluene.

1-Methylnaphthalene undergoes (4 + 2) cycloaddition exclusively with preferential attack (63 %) of the methylated ring. In contrast, 2-methylnaphthalene not only forms Diels-Alder adducts, but also the double ene product 2-benzyl-1-phenylnaphthalene in 38 % yield. Apparently, this difference is due to a simple electronic effect, *i.e.*, enophiles, like electrophiles, attack preferentially the more electron-rich α-carbon of naphthalenes [76].

Altogether, alkynes undergo the ene reaction more readily than comparable alkenes (cf. also Section 6.1).

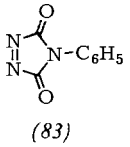
3.3. Azo Compounds

The most widely used derivative is diethyl azodicarboxylate, which reacts under rather mild conditions with ene components, heating to 80 °C for a few hours being sufficient to complete the reaction [8, 77]. The same compound also enters into ene reactions

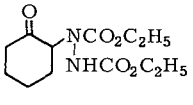


Scheme 13

with conjugated dienes and trienes, 1,4-dienes (see above) and with aldehyde hydrazones (Scheme 13) [78]. If the azo-linkage is present in the *cis*-configuration as in photochemically generated azodicarboxylate [25, 26, 79] and in 4-phenyl-1,2,4-triazoline-3,5-dione *(83)* [27] the dienophilic properties are considerably enhanced. In fact, *(83)* is a "record dienophile" which reacts smoothly with a variety of conjugated dienes [27, 80] and cycloheptatriene [27].



(83)



(84)

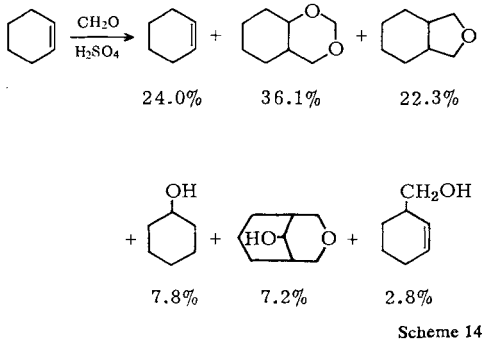
It must be mentioned that diethyl azodicarboxylate has general hydrogen-abstracting properties. For example, it smoothly oxidizes primary and secondary alcohols, thiols, anilines, and hydrazobenzene to aldehydes, ketones, disulfides, azobenzenes, and azobenzene, respectively, while itself being converted into diethyl hydrazodicarboxylate [81a]. Similarly, it abstracts hydrogen α to oxygen in ethers [81b] and α to sulfur in sulfides [81c]. Reaction with cyclohexanone affords *(84)*, the formation of which is weakly catalyzed by free radical initiators but strongly base-catalyzed [81d].

3.4. Carbonyl Compounds

The reaction of formaldehyde with olefins is of industrial interest and has been studied with unusual intensity. When the reaction is carried out thermally in the absence of catalyst, the products are generally those expected from ene reactions. However, there still exists a great deal of mechanistic uncertainty and even confusion about acid-catalyzed reactions ("Prins reactions") [83], which appear to react partly in the sense of the ene reaction, partly *via* an electrophilic addition of protonated formaldehyde (cf. also Section 6.5 and Table 5, No. 5).

The reaction of cyclohexene with aqueous formaldehyde in sulfuric acid may serve as an example for the complexity of the product mixtures (Scheme 14) [82] that may be obtained.

Clearly, the presence of mineral acids makes it difficult to determine the products of kinetic control and only little mechanistic insight can be gained. Investigations with *Blomquist*'s system of catalysts [21] could be of interest.



Scheme 14

[76] *L. Friedman* and *J. M. Brinkley*, private communication.

[77] *O. Achmatowicz* and *O. Achmatowicz jr.*, Roczniki Chem. *37*, 317 (1963).

[78] *B. T. Gillis* and *F. A. Daniher*, J. org. Chemistry *27*, 4001 (1962).

[79] See *B. T. Gillis* in *J. Hamer*: 1,4-Cycloadditions. Academic Press, New York and London, 1967, p. 143 for 1,4-cycloadditions of diethyl azodicarboxylate.

[80] *J. Sauer* and *B. Schröder*, Chem. Ber. *100*, 678 (1967).

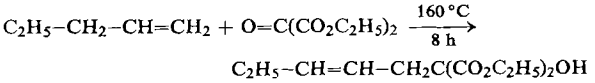
[81] a) *F. Yoneda, K. Suzuki*, and *Y. Nitta*, J. Amer. chem. Soc. *88*, 2328 (1966); b) *R. C. Cookson, I. D. R. Stevens*, and *C. T. Watts*, Chem. Commun. *1965*, 259; c) *R. B. Woodward, K. Heusler, J. Gosteli, P. Naegeli, W. Oppolzer, R. Ramage, S. Ranganathan*, and *H. Vorbrüggen* J. Amer. chem. Soc. *88*, 852 (1966); d) *R. Huisgen* and *F. Jacob*, Liebigs Ann. Chem. *590*, 37 (1954).

[82] *O. Kovacs* and *I. Kovari*, Magyar. kem. Folyóirat *70*, 223 (1964); Chem. Abstr. *61*, 5528b (1964).

[83] *C. W. Roberts* in *G. A. Olah*: Friedel-Crafts and Related Reactions, Interscience, New York 1964, Vol. II, Part 2, p. 1175; *V. I. Isagulyants, T. G. Khaimova, V. R. Melikyan*, and *S. V. Pokrovskaya*, Usp. chim. *37*, 61 (1968); *E. Arundale* and *L. A. Mikeska*, Chem. Reviews *51*, 505 (1952); see also *L. J. Dolby, C. L. Wilkins*, and *R. M. Rodia*, J. org. Chemistry *33*, 4155 (1968); *B. Fremaux M. Davidson, M. Hellin*, and *F. Coussemant*, Bull. Soc. chim. France *1967*, 4250; *M. Hellin, M. Davidson*, and *F. Coussemant, ibid. 1966*, 1890, 3217.

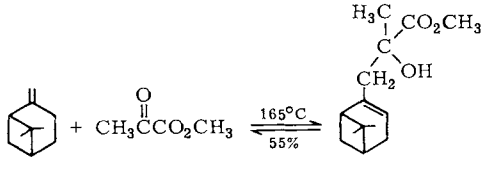
Higher aldehydes react less readily and apparently only if enolization is blocked. Trichloroacetaldehyde[15c] and phenylglyoxal[14] react with monoolefins of the methylenecyclohexane type, but the former has been reported not to react with less active ene components[84], although it does react readily if an electrophilic catalyst such as stannic chloride is present (see Section 6.4).

A variety of ketones has been employed as enophiles. Diethyl mesoxalate reacts with 1-pentene (Scheme 15), cyclohexene, and α-methylstyrene; as an enophile it



Scheme 15

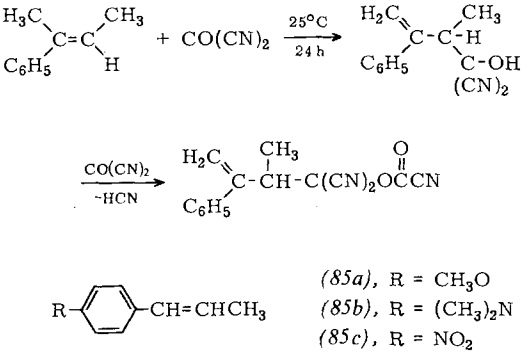
appears to be superior to formaldehyde, but inferior to carbonyl cyanide[85]. Methyl pyruvate and β-pinene form an adduct (55%) in a readily reversible process (Scheme 16)[86] (cf. also Section 5.2).



Scheme 16

Perhaloketones such as hexafluoroacetone and *sym*-dichlorotetrafluoroacetone add to a variety of ene components. The reaction with isobutene, β-pinene, and isopropenyl methyl ether occurs already at room temperature in high yields (80%). It has been asserted on rather little evidence that a stepwise rather than concerted mechanism best accounts for the experimental observations[87]. The most remarkable of all perhaloketones is perfluorocyclobutanone which reacts with alkynes and allenes (Scheme 8)[54].

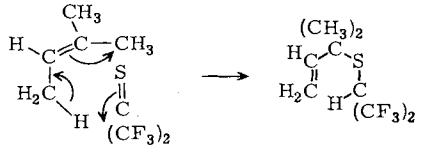
Ene reactions with carbonyl cyanide have been studied in some detail by a Polish group. Generally, the first formed adduct alcohols are not so easy to isolate; as they are fairly acidic, they readily lose hydrogen cyanide and react with a second molecule of carbonyl cyanide[88] (Scheme 17). In analogy to Diels-Alder additions electron-rich ene components such as the *p*-methoxystyrene derivative *(85a)* and, even more so, *(85b)* react readily with carbonyl cyanide[89a], while the electron-deficient *p*-nitro derivative *(85c)* failed to react[89b]. Ene reactions with carbonyl chloride and carbonyl fluoride have to the knowledge of the author not yet been described or have failed[84]. Possibly, the ene components employed have not been sufficiently reactive, or alternatively the first formed adducts liberate acid which destroys reactants and products alike (cf also Scheme 17). The presence of a suitable acid trapping reagent might bring about a change.



(85a), R = CH_3O
(85b), R = $(CH_3)_2N$
(85c), R = NO_2

Scheme 17

Hexafluorothioacetone is not only a highly active dienophile which reacts instantaneously with butadiene at −78 °C, thus allowing a titration of the diene[90], but also forms adducts with ene components under similar conditions. It is worthy of note that the orientation (Scheme 18) is the reverse of that for ene reactions with carbonyl compounds[91] (cf. Section 6.1).



Scheme 18

3.5. Singlet Oxygen

The dye-sensitized photooxygenation of olefins and dienes has long been known[16,92], but only recently *Foote*[16] has shown that the reactive intermediate is the first excited singlet state of molecular oxygen [$O_2(^1\Delta g)$], which is only 22 kcal above the ground state; $O_2(^1\Delta g)$ resembles ethylene electronically, but is more electron-deficient. The reactions with singlet oxygen have contributed substantially to our mechanistic understanding of the ene reaction and lead to allylic hydroperoxides which can be reduced smoothly

[84] *O. Achmatowicz* and *O. Achmatowicz jr.*, Roczniki Chem. *36*, 1812 (1962).

[85] *O. Achmatowicz* and *O. Achmatowicz jr.*, Roczniki Chem. *36*, 1791 (1962).

[86] *R. T. Arnold* and *P. Veeravagu*, J. Amer. chem. Soc. *82*, 5411 (1960).

[87] *R. L. Adelman*, J. org. Chemistry *33*, 1400 (1968).

[88] *O. Achmatowicz* and *K. Belniak*, Roczniki Chem. *39*, 1685 (1965).

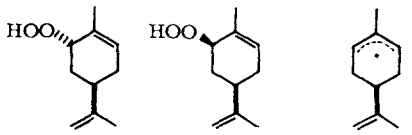
[89] a) *O. Achmatowicz, O. Achmatowicz jr., K. Belniak*, and *J. Wrobel*, Roczniki Chem. *35*, 783 (1961); b) *O. Achmatowicz* and *J. Szychowski, ibid. 37*, 963 (1963).

[90] *W. J. Middleton*, J. org. Chemistry *30* 1390 (1965).

[91] *W. J. Middleton*, J. org. Chemistry *30*, 1395 (1965); *W. J. Middleton, E. G. Howard*, and *W. H. Sharkey*, J. Amer. chem. Soc. *83*, 2589 (1961).

[92] *K. Gollnick* and *G. O. Schenck*, Pure Applied Chemistry *9*, 507 (1964); *K. Gollnick*, Adv. Photochemistry *6*, 1 (1968); for the behavior of singlet oxygen as a dienophile see *K. Gollnick* and *G. O. Schenck* in *J. Hamer*: 1 4-Cycloaddition Reactions, Academic Press, New York, 1967, p. 255.

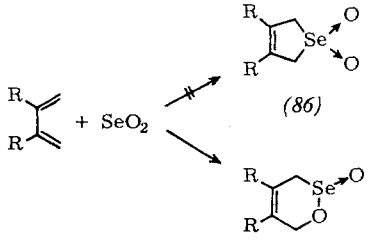
to the allylic alcohols. The alcohols derived from limonene *(16)* are natural products, and in the case of the carveyl alcohols are formed *via* the carveyl hydroperoxides *(85d)* and *(85e)* with complete conservation of chirality at the C-4 carbon, *i.e.*, this reaction does not involve a substituted cyclohexenyl radical intermediate *(85f)* which is symmetrical [20a].



(85d) *(85e)* *(85f)*

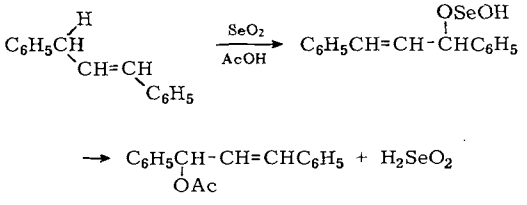
3.6. Sulfur Trioxide and Selenium Dioxide

Sulfur trioxide reacts with a variety of ene components [93] and it has been suggested that the sulfonic acid *(7)* is formed from methylenecyclopentane in concerted fashion [13]. Until recently, selenium dioxide was believed to form cyclic selenones *(86)* with



(86) *(87)*

various substituted butadienes. A reinvestigation has revealed that unlike sulfur dioxide, selenium dioxide possesses dienophilic properties and forms adducts *(87)* instead [94]. Therefore, it seems reasonable to conclude that selenium dioxide also possesses enophilic properties and that allylic oxidations with this compound proceed at least in part by an ene reaction. In fact, *Schaefer* [10] and *Trachtenberg* [95] have proposed an ene type mechanism *via* a hypothetical selenium(II) ester which is solvolyzed to the products



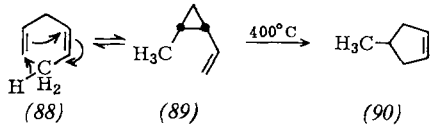
Scheme 19

(Scheme 19). What has been said above for the Prins reaction is even more relevant to this reaction, *i.e.* the products of kinetic control are hard to isolate.

4. Intramolecular Ene Reactions

4.1. 1,3- and 1,4-Dienes

The 1,5-hydrogen shift of *cis*-1,3-pentadienes (Scheme 2) occurs smoothly at about 150–200 °C and may be classified as an intramolecular ene reaction. The most simple homovariant of this reaction is provided

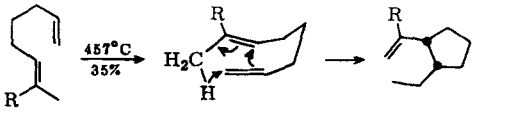


(88) *(89)* *(90)*

by the isomerization of *cis*-1,4-hexadiene *(88)*, which on heating to 400 °C forms *(90)*; a rapid pre-equilibrium of *(88)* and *(89)* is followed by irreversible formation of the product *(90)* [96]. Both 1,5-hydrogen shifts [6,97] and their homocounterpart [6,97,98] have been reviewed. 1,5-Dienes undergo 3,3 shifts (Cope rearrangement).

4.2. 1,6-Dienes

1,6-Octadiene *(91a)* (a mixture of the *cis* and *trans* form being used) has been reported to cyclize at elevated temperatures to the *cis* substituted cyclopentane *(92a)* exclusively; similarly, *(91b)* has been assumed to furnish the *cis* isomer *(92b)* only [99]. In contrast,



(91a), R = H *(92a)*, R = H
(91b), R = CH_3 *(92b)*, R = CH_3

3,7-dimethyl-1,6-octadiene *(94)*, which may be prepared in 90% yield [100] from *cis*-pinane *(93)* *via* a 2+2 cycloelimination, cyclizes under the same conditions to

[93] *F. G. Bordwell, C. M. Suter,* and *A. J. Webber,* J. Amer. chem. Soc. *67,* 827 (1945); for the behavior of sulfur trioxide as a dienophile see *F. G. Bordwell, R. D. Chapman,* and *C. E. Osborne, ibid. 81,* 2002 (1959).

[94] *W. L. Mock* and *J. H. McCausland,* Tetrahedron Letters *1968,* 391.

[95] *E. N. Trachtenberg* in *R. L. Augustine*: Oxidation. Marcel Dekker, Inc., New York 1969; see also *G. Büchi* and *H. Wüest,* J. org. Chemistry 34, 857 (1969).

[96] *W. R. Roth* and *J. König,* Liebigs Ann. Chem. *688,* 28 (1965).

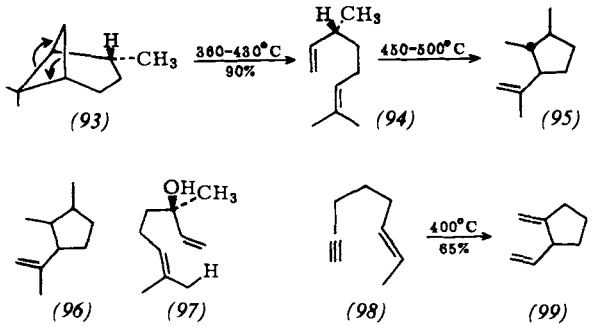
[97] *D. S. Glass, R. S. Boikess,* and *S. Winstein,* Tetrahedron Letters *1966,* 999; *H. M. Frey* and *R. Walsh,* Chem. Rev. *69,* 103 (1969).

[98] *E. N. Marvell, D. R. Anderson,* and *J. Ong,* J. org. Chemistry *27,* 1109 (1962); *A. Habich, R. Barner, R. M. Roberts,* and *H. Schmid,* Helv. chim. Acta *45,* 1943 (1962); *R. M. Roberts* and *R. G. Landolt,* J. Amer. chem. Soc. *87,* 2281 (1965); *R. M. Roberts, R. N. Greene, R. G. Landolt,* and *E. W. Heyer, ibid.,* p. 2282; *A. Habich, R. Barner, W. von Philipsborn,* and *H. Schmid,* Helv. Chim. Acta *48,* 1297 (1965); *G. Fráter* and *H. Schmid, ibid. 49,* 1957 (1966); *R. M. Roberts* and *R. G. Landolt,* J. org. Chemistry *31,* 2699 (1966); *A. Jefferson* and *F. Scheinmann,* Chem. Commun. *1966,* 239, 316.

[99] *W. D. Huntsman, V. C. Solomon,* and *D. Eros,* J. Amer. chem. Soc. *80,* 5455 (1958).

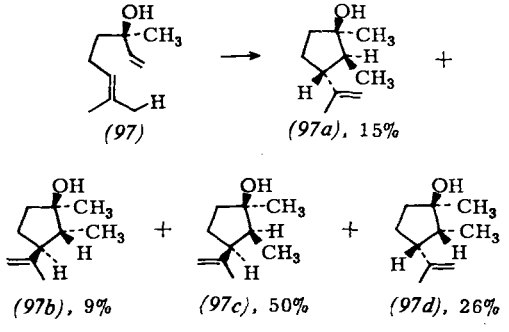
[100] a) *R. Rienäcker,* Brennstoff-Chem. *45,* 206 (1964); b) *R. Rienäcker* and *G. Ohloff,* Angew. Chem. *73,* 240 (1961).

give a mixture of isomeric cyclopentanes considered to be *(95)* (main product) and *(96)* (minor product) [101]. The steric course of the cyclization of linalool



(93) *(94)* *(95)* *(96)* *(97)* *(98)* *(99)*

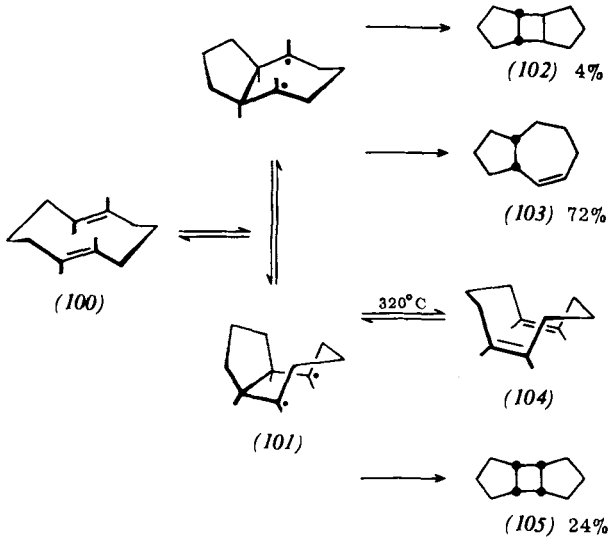
(97) has been investigated in much greater detail and it has been shown that *all four possible* diastereomeric plinols *(97a)–(97d)* are formed. The formation



(97) *(97a)*, 15% *(97b)*, 9% *(97c)*, 50% *(97d)*, 26%

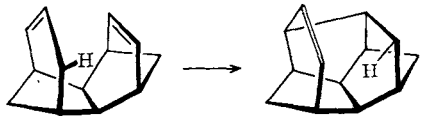
tendency of the four isomers can be related qualitatively to the number of conformations which are favorable and unfavorable for the respective cyclizations [101a].

6-Octen-1-yne *(98)* cyclizes at 400 °C to *(99)* in 65%, yield. Clearly, rupture of an acetylenic π-bond requires less energy than that of an ethylenic π-bond, and the alkenyne is still sufficiently flexible for the reaction to occur [102]. An interesting intramolecular ene reaction of a 1,6-diene has been described by *Roth* [6]. On heating to only 250 °C the strained *trans*, *trans*-1,6-cyclodecadiene *(100)* isomerizes to a mixture of *(102)*, *(103)*, *(105)*, and *cis*,*cis*-1,6-cyclodecadiene *(104)*. A product mixture of identical composition is obtained from *cis*,*cis*-1,6-cyclodecadiene at 320 °C. These findings are best accommodated by the biradical intermediate *(101)*, which not only forms *(103)* (main product), but also collapses to the isomeric cyclobutanes *(102)* and *(105)* (cf. also Scheme 3). Molecular models show that a concerted intramolecular ene reaction of *cis*,*cis*-1,6-cyclodecadiene is geometrically not feasible. The transformations of *(100)* into *(103)* and of *(104)* into *(103)* represent two examples of stepwise ene reactions which are conformationally enforced.



(100) *(101)* *(102)* 4% *(103)* 72% *(104)* *(105)* 24%

The two π-bonds of the birdcage homolog *(105a)* are relatively strain-free, but they are held rigidly in almost parallel planes and separated by only about 2 Å;

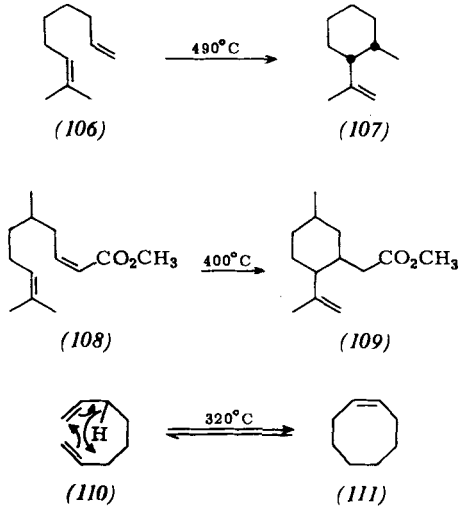


(105a) *(105b)*

(105a) has been found to cyclize to *(105b)* with a half-life of about six hours at 45 °C [102a]! The most simple 1,6-diene, *i.e.*, 1,6-heptadiene does not possess a terminal methyl group and fails to cyclize up to 500 °C [99].

4.3. 1,7-Dienes

A priori, the cyclization of 1,7-dienes can yield either six- or eight-membered rings, and both reactions have been observed. Generally, cyclohexane derivatives are formed less readily than cyclopentanes in intramolecular ene reactions. Thus, 8-methyl-1,7-nonadiene



(106) *(107)* *(108)* *(109)* *(110)* *(111)*

[101] *H. Pines, N. E. Hoffman*, and *V. N. Ipatieff*, J. Amer. chem. Soc. *76*, 4412 (1954); see also *W. D. Huntsman* and *T. H. Curry*, *ibid. 80*, 2252 (1958).

[101a] *H. Strickler, G. Ohloff*, and *E. sz. Kováts*, Helv. chim. Acta *50*, 759 (1967).

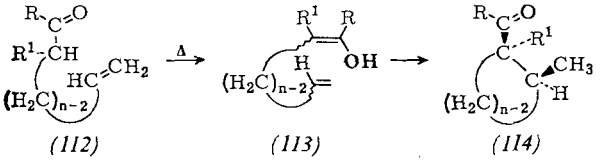
[102] *W. D. Huntsman* and *R. P. Hall*, J. org. Chemistry *27*, 1988 (1962).

[102a] *J. M. Brown*, J. chem. Soc. (B) (London) *1969*, in press.

(106) fails to cyclize at 440 °C, but on raising the temperature to 490 °C an appreciable amount of *(107)* is formed. However, the stereospecific formation of the *cis* derivative could not be confirmed for related examples which were investigated more thoroughly (cf. below). The introduction of a terminal methoxycarbonyl group as in *(108)* facilitates cyclization, as shown by the smooth formation of three diastereomeric menthene acetates *(109)* from *(108)*. Which stereoisomer(s) arise by kinetic control is not clear, since the acetates *(109)* epimerize under the reaction conditions[103]. 1,7-Octadiene *(110)* can be equilibrated with cyclooctene *(111)* above 320 °C. At higher temperature the open chain isomer is favored[6] (cf. also Section 5).

4.4. Unsaturated Carbonyl Compounds

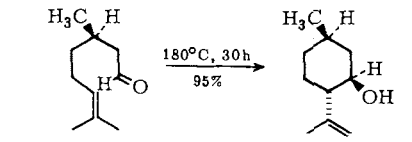
Conia and his co-workers have cyclized a great variety of ethylenic ketones of the general type *(112)* to the corresponding cycloalkyl ketones *(114)*. The



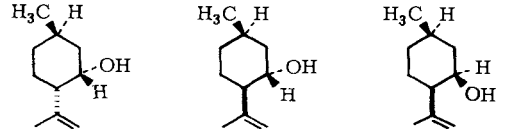
(112) *(113)* *(114)*

reactions proceed under comparatively mild conditions (*ca.* 300 °C, 1 h); cyclopentyl ketones (n = 5) are generally formed quantitatively. Seven- and eight-membered rings (n = 7,8) can also be obtained, albeit in lower yield. On heating to 390 °C for 30 min even 11-dodecen-2-one [*(112)*, R = CH_3, R^1 = H; n = 9] forms the corresponding nine-membered ketone in a respectable yield of 30%[104d]. Of necessity, the cyclization involves enol *(113)*, the formation of which from *(112)* *via* a concerted thermal 1,3-hydrogen shift is forbidden[4]. Interestingly, the formation of the enol and hence cyclization can be accelerated by catalytic amounts of water and by using reaction vessels made of ordinary glass instead of Pyrex[104f].

If $R^1 \neq H$, the product *(114)* cannot epimerize *via* enolization and more detailed investigations have shown very recently that not only the *cis* but also the *trans* isomers are formed[104f].



(+)-ß-Citronellal (−)-Isopulegol (60%)

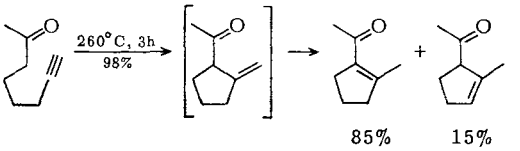


(+)-*neo*-Isopulegol (20%) (+)-*iso*-Isopulegol (15%) (+)-*neoiso*-Isopulegol (5%)

Scheme 19a

Ohloff[105a] has investigated in detail the cyclization of (+)-β-citronellal, an example of a 6-heptenal [Scheme 19a]. All four possible diastereomers are formed in varying amounts. Isopulegol which is formed in 60% yield is an intermediate in the technical synthesis of (−)-menthol.

7-Octyn-2-one cyclizes at 260 °C to give two isomeric cyclopentenes in practically quantitative yield (Scheme 20)[104g,105].



85% 15%

Scheme 20

5. The Retro Ene Reaction

5.1. Acyclic and Cyclic Olefins

On thermodynamic grounds the retro-ene reaction is favored with increasing temperature while the ene reaction is facilitated by increasing pressure. The most simple example, the decomposition of 1-pentene (cf. Scheme 1) has been reported to occur above 400 °C. However, whether the products of this reaction are actually propene and ethylene, has not been investigated[106]. Intramolecular variants of this reaction can be realized more readily, particularly in strained medium-sized cycloalkenes (n = 8–11) which form α,ω-dienes (Scheme 21). For instance, above 320 °C *cis*-cyclooctene *(111)* can be converted into 1,7-octadiene *(110)*[6]. The more strained *trans*-cyclooctene opens more easily, temperatures of *ca.* 250 °C being

[103] *W. D. Huntsman, P. C. Lang, N. L. Madison,* and *D. A. Uhrick,* J. org. Chemistry *27,* 1983 (1962).

[104] a) *F. Rouessac, P. Le Perchec,* and *J.-M. Conia,* Bull. Soc. chim. France *1967,* 818; b) *P. Le Perchec, F. Rouessac,* and *J.-M. Conia, ibid. 1967,* 822; c) p. 826; d) *J.-M. Conia* and *F. Leyendecker, ibid. 1967,* 830; e) *R. Bloch* and *J.-M. Conia,* Tetrahedron Letters *1967,* 3409; f) *J.-M. Conia,* Lecture held at the Symposium on Synthetic Methods and Rearrangements in Alicyclic Chemistry, Oxford, July 1969, and personal communication of August 7, 1969; g) a good review has been written by *J.-M. Conia,* Bull. Soc. chim. France *1968,* 3057; for a description of the general technique, see *F. Leyendecker, G. Mandville,* and *J.-M. Conia, ibid.,* in press.

[105] *F. Rouessac, P. LePerchec, J.-L. Bouket,* and *J.-M. Conia,* Bull. Soc. chim. France *1967* 3554; *R. Bloch P. LePerchec, F. Rouessac,* and *J.-M. Conia,* Tetrahedron *24,* 5971 (1968).

[105a] *G. Ohloff,* Tetrahedron Letters *1960,* 11, 10; for the experimental part see *K. H. Schulte-Elte* and *G. Ohloff,* Helv. chim. Acta *50,* 153 (1967).

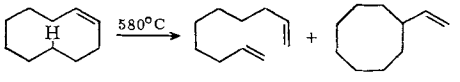
[106] *J. F. Norris* and *G. Thomson,* J. Amer. chem. Soc. *53,* 3108 (1931); see also ref. [6].



n = 8-11

Scheme 21

sufficient to observe the diene. Pure *trans*-cyclononene forms 1,8-nonadiene (85%) and *cis*-cyclononene (15%) on heating to 500 °C, while under the same conditions *cis*-cyclononene yields only *ca.* 20% diene, 80% of the starting material remaining unchanged[107]. In contrast, *cis*-cyclodecene does not only afford 1,9-decadiene, but also vinylcyclooctane (5%) in a side reaction[100] (Scheme 22) (see also Section 6.5). It is advantageous to pyrolyze the cycloalkenes in a cyclic



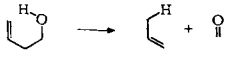
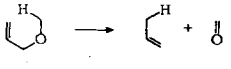
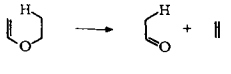
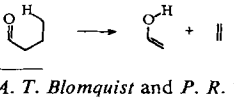
Scheme 22

reactor, in which the dienes are removed immediately as they are formed and the starting material can be recycled continuously[100b]. Since the alkadienes boil about 20 °C lower than the corresponding cycloalkenes, the product can be distilled off readily. Thus, under reduced pressure and at temperatures around 600 °C it has been possible to isolate the α,ω-dienes in yields up to 90% and higher[100]!

5.2. Heteroatom Analogs

Numerous heteroatom analogs of retro ene reactions have been reported over a span of a hundred years or so, and Table 4[107a] summarizes the reaction types generated by permutation of one oxygen atom. The cleavage of γ,δ-unsaturated alcohols represents the reverse of the formation of unsaturated alcohols from ene components and carbonyl compounds (see Section 3.4) and proceeds in the vicinity of 500 °C, unless

Table 4. Retro-ene reactions of systems containing one oxygen atom.

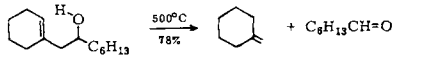
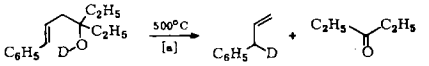
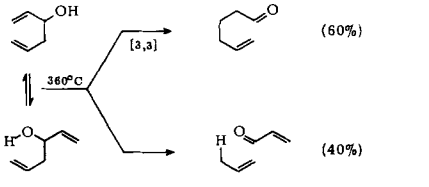
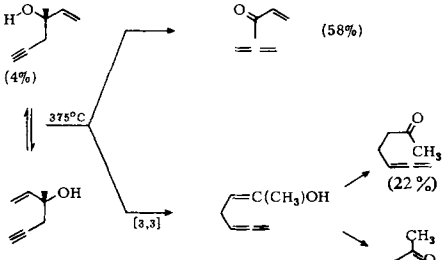
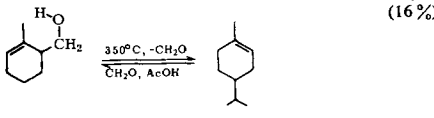
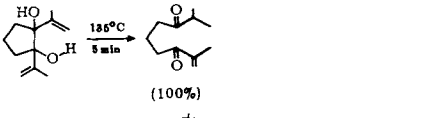
Entry	Reactions
1	
2	
3	
4	

[107] *A. T. Blomquist* and *P. R. Taussig*, J. Amer. chem. Soc. *79*, 3505 (1957).

[107a] For further examples, see *A. T. Balaban*, Revue roum. Chim. *12*, 875 (1967).

extra allylic resonance or other factors facilitate the breaking of the C–C bond (Table 5). The first two reactions in Table 5 are clearly kinetically controlled, while reactions 3 and 4 exemplify the competition of the retro-ene reaction and the 3,3-shift (Cope rearrangement).

Table 5. Retro-ene reactions of γ,δ-unsaturated alcohols.

Entry	Reaction	Ref.
1		[108]
2		[109]
3		[110]
4		[111]
5		[19b]
6		[111a]

[a] E_a = 41.8 kcal/mole; $\Delta S^{\neq} = -4.8$ e.u.

Presumably, the ene cleavage in entry 5 is facilitated by the rigidity of the allylic system, which allows the transition state to be reached more readily (cf. also Section 6.5). The retro-ene reaction in Scheme 16 could be favored for the same entropy reasons as well as by the methoxycarbonyl group which generates a retro-Claisen-like system. The smooth ene cleavage of *trans*-1,2-divinylcyclopentane-1,2-diol (Table 5, entry 6) is of interest. However, with increasing ring size the retro-

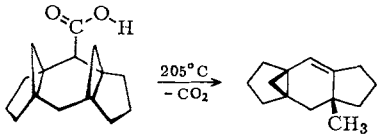
[108] *R. T. Arnold* and *G. Smolinsky*, J. Amer. chem. Soc. *81*, 6443 (1959); *ibid. 82*, 4918 (1960); cf. also *K. J. Voorhees*, *G. G. Smith*, *R. T. Arnold*, *R. R. Covington*, and *D. G. Mikolasek*, Tetrahedron Letters *1969*, 205.

[109] *R. T. Arnold* and *G. Smolinsky*, J. org. Chemistry *25*, 129 (1960); see also *G. G. Smith* and *R. Taylor*, Chem. and Ind. (London) *1961*, 949.

[110] *A. Viola*, *E. J. Iorio*, *K. K. Chen*, *G. M. Glover*, *U. Nayak*, and *P. J. Kocienski*, J. Amer. chem. Soc. *89*, 3462 (1967).

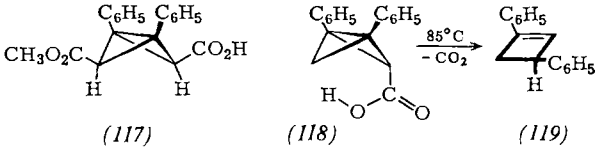
[111] *J. W. Wilson* and *S. A. Sherrod*, Chem. Commun. *1968*, 143; see also *A. Viola* and *J. H. MacMillan*, J. Amer. chem. Soc. *90*, 6141 (1968).

ene reaction is completely suppressed in favor of the 3,3-shift [111a]. The decarboxylation of β,γ-unsaturated acids requires temperatures in the range of 250–300 °C [112]. A more recent variant is the decarboxylative opening of cyclopropaneacetic acids. For example, on heating above its melting point carboxylic



(115) (116)

acid *(115)* smoothly loses carbon dioxide to form *(116)* with introduction of an angular methyl group [113]. The steric requirements for decarboxylation of bicyclobutanecarboxylic acids (cf. also Section 2.7) are demonstrated nicely by the relative stability of the



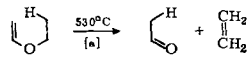
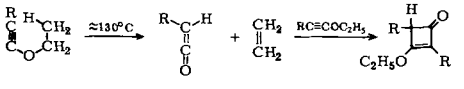
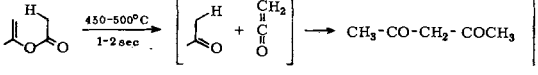
(117) (118) (119)

exo acid *(117)* (no reaction up to 200 °C), whereas the structurally related *endo* acid *(118)* affords 1,3-diphenylcyclobutene *(119)* quantitatively on heating to only 85 °C [114].

The ene cleavage of allyl ethers (Table 4, entry 2) constitutes the microscopic reverse of the "wrongly oriented" addition of a carbonyl compound to an ene component and has been investigated and discussed recently by *Cookson* and *Wallis* [115].

The retro-ene reaction of vinyl ethers (Table 4, entry 3 and Table 6, entry 1) proceeds at temperatures [116]

Table 6. Pyrolysis of vinyl ethers.

Entry	Reaction	Ref.
1		[116]
2		[117]
3		[118]

[a] E_a = 43.8 kcal/mole; $\Delta S^{\ddagger}$ = −10.2 e.u. at 530 °C.

comparable to those required for unactivated analogs (*ca.* 500 °C), while acetylenic ethers break up under rather mild conditions (*ca.* 130 °C) to form aldoketenes which are trapped by the starting material to give ethoxycyclobutenones (Table 6, entry 2).

The well-known pyrolysis of esters [119] and xanthates [120] is related to the ene cleavage of carbonyl compounds (Table 4, entry 4).

6. Reaction Mechanisms

6.1. Bond Energies and Reactivity

For a discussion of reactivities it is useful to consider the change in bond energy during an ene reaction. In the generalized Scheme 23 the debit side contains the energy required for breaking the C_3–H σ-bond and the X=Y π-bond, while energy is gained by making



Bond energy expended	Bond energy gained
$D(C_3–H)$	$D(X–H)$
$D_\pi(X=Y)$	$D(C_1–Y)$
$D_\pi(C_2=C_1)$	$D_\pi(C_2=C_3)$

$\Delta F = \Delta H - T\Delta S$;
$\Delta H = D(X–H) + D(C_1–Y) - D(C_3–H) - D_\pi(X=Y)$

Scheme 23

the X–H and C_1–Y bonds; the last items in each column cancel on balance unless one of the two double bonds is particularly strained (see below). Provided that steric and solvent effects remain constant in a series of related reactions (as is indeed frequently the case; cf. Section 6.3) then

$$\delta_R \Delta S = 0 \text{ [*]}.$$

Hence,

$$\delta_R \Delta F = \delta_R \Delta H$$

i.e., the difference in free energy of two reactions is equal to the corresponding differential heat of reaction [121]. One now assumes that the calculated ground state energy term $\delta_R \Delta F$ is proportional to the differential free energy of activation $\delta_R \Delta F^{\ddagger}$. Such an

[111a] *P. Leriverend* and *J.-M. Conia*, Tetrahedron Letters *1969*, 2681; see also *E. N. Marvell* and *T. Tao*, *ibid. 1969*, 1341; for retro-ene reaction of 1-vinylcycloalkane-1,2-diols see *J.-M. Conia* and *J.-P. Barnier*, *ibid. 1969*, 2679.

[112] *R. T. Arnold*, *O. C. Elmer*, and *R. M. Dodson*, J. Amer. chem. Soc. *72*, 4359 (1950); see also *K. Mackenzie* in *S. Patai*: The Alkenes. Wiley, New York, 1964, p. 457.

[113] *T. Hanafusa*, *L. Birladeanu*, and *S. Winstein*, J. Amer. chem. Soc. *87*, 3510 (1965); see also *J. J. Sims*, *ibid.*, p. 3511.

[114] *S. Masamune*, Tetrahedron Letters *1965*, 945.

[115] *R. C. Cookson* and *S. R. Wallis*, J. chem. Soc. (London) *B 1966*, 1245; see also *J. A. Berson* and *E. J. Walsh jr.*, J. Amer. chem. Soc. *90*, 4730 (1968), and [104b].

[116] *A. T. Blades* and *G. W. Murphy*, J. Amer. chem. Soc. *74*, 1039 (1952); *A. T. Blades*, Canad. J. Chem. *31*, 418 (1953).

[117] *R. H. Hasek*, *P. G. Gott*, and *J. C. Martin*, J. org. Chemistry *29*, 2510 (1964); *J. Nieuwenhuis* and *J. F. Arens*, Recueil Trav. chim. Pays-Bas *77*, 761 (1958).

[118] *H. J. Hagemeyer jr.*, and *D. C. Hull*, Ind. Engng. Chem. *41*, 2920 (1949).

[119] *C. H. DePuy* and *R. W. King*, Chem. Reviews *60*, 431 (1960).

[120] *H. R. Nace*, "Organic Reactions" Vol. *12*, 57, New York 1962.

[*] The reaction operator δ_R denotes the change of a thermodynamic quantity when two reactions are compared; see *J. E. Leffler* and *E. Grunwald*: Rates and Equilibria of Organic Reactions, Wiley, New York, 1963, p. 26.

[121] *M. J. S. Dewar*, Adv. Chem. Phys. *8*, 65 (1965); see also *R. Huisgen*, Angew. Chem. *75*, 742 (1963); Angew. Chem. internat. Edit. *2*, 641 (1963).

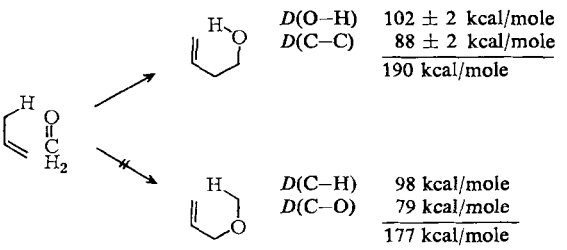
approximation is more drastic, but presumably not bad, if bond-making and bond-breaking, respectively, have proceeded to about the same extent in the transition states of the reactions to be compared. Clearly, this approximation allows that the new σ-bonds are formed with considerable asymmetry within one reaction class (see Section 6.2).

Several conclusions follow: First, the dependence of the reactivity of the ene component on $D(C_3-H)$ has been obvious throughout Section 1 and needs no more comment. Further, the enhanced reactivity of acetylenic *vis-à-vis* olefinic enophiles can be seen to be not only the consequence of the reduced π-bond energy of the triple bond, but also of the increased energy of the vinylic carbon-hydrogen bond [$D(C_2H_3-H) = 104 \pm 2$ *versus* $D(C_2H_5-H) = 98 \bullet 1$ kcal/mole][122].

The distinction of enophilic and dienophilic reactivity now emerges also more clearly. For instance, it has been seen that cycloheptatriene forms a 4 + 2 adduct with maleic anhydride[47a,47b], while in the reaction with acetylenedicarboxylic ester an ene adduct is formed as a by-product[50]. Since D_π (C≡C) enters the energy balance of both diene and ene synthesis, but a new carbon-hydrogen bond is only made in the ene reaction, alkynes are expected to be relatively more enophilic than dienophilic when compared with alkenes. That dehydrobenzene is such an efficient enophile should be the consequence of internal strain and, possibly, of a steric effect. Similarly, the quite remarkable reactivity of ene components with strained or "soft" π-bonds (Section 2.7) appears to be primarily the consequence of a lowering of $D_\pi(C_2 = C_1)$ (Scheme 23).

[122] All bond energies are taken from *J. A. Kerr*, Chem. Rev. 66, 465 (1966).

Bond energies are also useful for predicting the orientation of enophilic attack. For instance, the exclusive formation of the alcohol rather than the ether when carbonyl compounds are used as enophiles (Scheme 24) can be rationalized by the greater gain in bond energy for the observed reaction. Similarly, the reversal in orientation with thioketones[91] as enophiles is probably partly due to the fact that $D(C-H) = 98$, while $D(S-H) = 90$ kcal/mole only [$D(C-S)$ appears to be unknown][122].

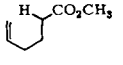
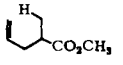
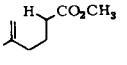
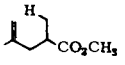
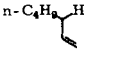
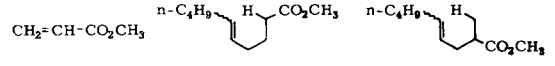
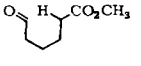
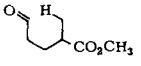
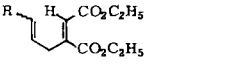
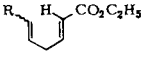
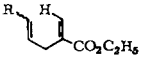


Scheme 24

6.2. Orientation Phenomena

Little work has been reported here and the few observations of *Alder* and *von Brachel*[73b] on propiolic and acrylic ester are compiled in Table 7. Apparently,

Table 7. Orientation phenomena in ene reactions [73b].

Entry	Ene	Enophile	Products	
1		$CH_2=CH-CO_2CH_3$	 88%	 12%
2		$CH_2=CH-CO_2CH_3$	 95%	 5%
3		$CH_2=CH-CO_2CH_3$	75%	 25%
4		$CH_2=CH-CO_2CH_3$	 60%	 40%
5		$C_2H_5O_2CC{\equiv}CCO_2C_2H_5$		
6		$HC{\equiv}CCO_2C_2H_5$	 80%	 20%

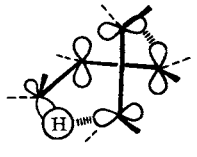
the linear isomer, in which the position of the ester grouping is "*para*" with respect to the vinylic carbon C_2 (cf. Scheme 23), predominates over the branched or "*meta*" isomer. Thus, in contrast to an earlier report[73a], a mixture of isomers rather than a single product appears to be formed generally. The preferred formation of the linear isomer suggests that bond-

making in the transition state is somewhat more efficient between the unsaturated termini than between the allylic hydrogen and the corresponding carbon atom of the enophile; or to rephrase, a double bond is a better Michael-type donor than an allylic carbon-hydrogen bond. Note that the analogy to the Michael addition is purely formal, since, *e.g.*, ene reactions are not catalyzed by bases. Furthermore, while the clean orientation with carbonyl enophiles (Scheme 24) is consistent with advanced bond-making between the unsaturated termini, the observed opposite orientation with hexafluorothioacetone probably indicates that the transition state may by variable.

6.2.1. The *cis*-Principle

The Diels-Alder addition entails stereospecific *cis*-addition. Likewise, the adducts of 1-hexene and 1-heptene with acetylenedicarboxylic ester have been found to be derivatives of maleic rather than fumaric esters (Table 7, entry 5), and the linear isomer formed in the reaction of ethyl propiolate with ene components is a derivative of acrylic ester containing a *trans* double bond (Table 7, entry 6) [see also Scheme 12 and the formation of *(53)*].

It is worthy of mention that the *anti,anti* ene reaction [*anti* with respect to the ene and enophile; cf. *(119c)*] is also symmetry-allowed. Obviously, such a transition state is far less likely than *(122)* for steric reasons, but



(119c)

it remains an interesting speculation for special cases such as ene components containing twisted double bonds and enophiles which are sterically readily accessible. In any case, such a reaction mode seems more probable here than for the related and better investigated Diels-Alder addition, where, as implied above, the *anti, anti* attack has never been observed.

6.3. Solvent Effects and Activation Parameters

In analogy to other "no mechanism" reactions [123] the ene synthesis is little affected by solvent changes. *Huisgen* and *Pohl* [9] have measured the rate of reaction of 1,3-diarylpropenes with diethyl azodicarboxylate. On changing the solvent from cyclohexane to nitrobenzene the rate increases by a factor of 4 only (Table 8).

For the ene reaction of diethyl azodicarboxylate with some cyclic dienes *Franzus* [24] has found a highly negative entropy of activation ($\Delta S^{\neq}$ = −30 to −40 e.u.) similar to Diels-Alder additions. As expected, $\Delta S^{\neq}$ is less negative for intramolecular ene reactions, since less molecular motion has to be frozen in the transition state (cf. Table 5, entry 2, Table 6 entry 1, and Scheme 2).

Table 8. Solvent effect on the ene reaction of diethyl azodicarboxylic ester with 1-phenyl-3-(*p*-tolyl)propene [9].

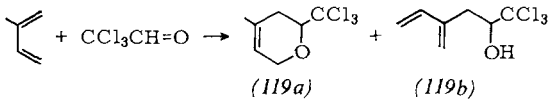
Solvent	Rate constant $10^4\,k_2$ [l mole^{-1} sec^{-1}] at 50 °C
cyclohexane	1.02
dioxane	1.12
dimethylformamide	2.0
acetonitrile	2.2
1,2-dichloroethane	3.2
nitrobenzene	4.0

6.4. Catalysis of Ene Reactions

The facilitation of intermolecular ene reactions by an increase in pressure and that of the retro-ene reaction by high temperatures needs no comment. Likewise, the enhanced reactivity of certain enophiles in the presence of organic and aqueous mineral acids is familiar.

Attention is drawn to the catalyst system CH_2Cl_2/Ac_2O/$BF_3 \cdot 2H_2O$ [21,22], in which the boron trifluoride dihydrate is present presumably as $\overset{\oplus}{H}\overset{\ominus}{B}F_3OAc + 3\,AcOH$, as well as stannic chloride [21,22,124,125] and aluminum chloride, which has been used as such and as the etherate [125c]. With these catalysts the reaction times can be shortened dramatically, and it would be of preparative interest to know whether allylic oxidations by selenium dioxide can be catalyzed similarly.

The reaction of isoprene with trichloroacetaldehyde in dichloromethane affords 5% Diels-Alder *(119a)* and 95% ene adduct *(119b)*, if the reaction is run at room temperature in the presence of stannic chloride. In the absence of catalyst, however, the reaction requires temperatures around 150 °C, and the ratio of *(119a)*: *(119b)* is reversed completely, being 90:10. A similarly characteristic reversal in the composition of products has been observed for other catalytic and thermal reactions of isoprene and 2,3-dimethylbutadiene with carbonyl compounds [125a]. As one possible reason for this remarkable observation it should be considered that the proportion of the cisoid diene conformer is greater at higher temperature so that the cycloaddition is preferred.



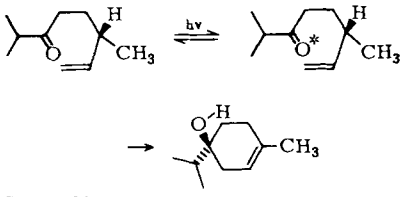
(119a) *(119b)*

[123] *W. von E. Doering* and *W. R. Roth*, Tetrahedron *18*, 67 (1962).

[124] *N. C. Yang, D.-D. H. Yang*, and *C. B. Ross*, J. Amer. chem. Soc. *81*, 133 (1959).

[125] a) *E. I. Klimova, E. G. Treshchova*, and *Y. A. Arbuzov*, Dokl. Akad. Nauk SSSR *180*, 865 (1968); see Chem. Abs. *69*, 67173b (1968); formula (II) in this abstract needs revision; b) *E. I. Klimova* and *Y. A. Arbuzov*, Dokl. Akad. Nauk SSSR *173*, 1332 (1967); see Chem. Abs. *67*, 108156c (1967); c) *E. I. Klimova* and *Y. A. Arbuzov*, Dokl. Akad. Nauk SSSR *167*, 1060 (1966); see Chem. Abs. *65*, 3736h (1966).

The interesting case of a photo-ene reaction has been described for 2,6-dimethyl-7-octen-3-one, which on irradiation with ultraviolet light forms terpinen-4-ol (2.5%) amongst other products. Although the yield is low the terpinen-4-ol arises with complete transfer of chirality, suggestive of a concerted transformation of the excited ketone into the product (Scheme 24a) [126a].



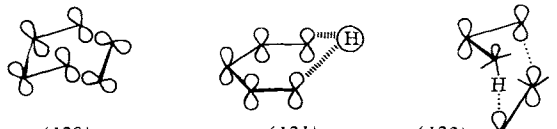
Scheme 24a

The reverse reaction proceeds thermally and also entails complete induction of chirality [126b].

To summarize, ene reactions proceed most readily if the ene is electron-rich and the enophile electron-deficient. Ene reactions with inverse electron demand have not yet been described.

6.5. The Geometry and Timing of Bond Changes in the Transition State

The Diels-Alder addition, 1,5-hydrogen shift, and the ene reaction are structurally related cyclic six-electron processes, although bonding in the transition state is maximized in each reaction in a different way. The transition state of the Diels-Alder reaction is boat-like [127], *i.e.*, the π-orbitals of the reactants overlap partly π-wise, partly σ-wise *(120)*.



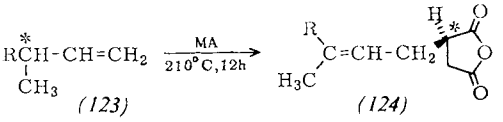
(120) *(121)* *(122)*

The optimum geometry for a 1,5-hydrogen shift involves a planar carbon framework with a suprafacial [4] placement of the hydrogen *(121)*, while a concerted ene reaction maximizes allylic resonance by turning the axis of the breaking carbon-hydrogen bond parallel to the p-orbitals of the neighboring double bond *(122)*.

The ene cleavage of (−)-6-hydroxymethyl-Δ^1-*p*-menthene smoothly forms (+)-Δ^1-*p*-menthene with 100% conservation of chirality (Table 5, entry 5). If this retro-ene reaction were to proceed *via* a substituted cyclohexenyl radical intermediate, much racemic menthene would have to be formed [cf. also the formation of *(85d)* and *(85e)*].

Microscopic reversibility demands that the reverse reaction is also completely stereospecific. While the reaction of (+)-Δ^1-*p*-menthene with formaldehyde requires acid catalysis, the γ,δ-unsaturated alcohol is formed with more than 98% retention of configuration at the C-4 carbon [19b]. Thus, it is proven that the Prins reaction may proceed *via* a concerted ene reaction (cf. also Section 3.4).

The reaction of maleic anhydride with optically active olefin *(123)* has been shown to give optically active adduct *(124)*; however, it is unknown to what extent precisely chirality is preserved during this reaction [128].



(123) *(124)*

The ene reaction of cyclopentene and cyclohexene with diethyl azodicarboxylate can be catalyzed by free radical initiators and retarded by free radical inhibitors [8,9]. However, whether cyclopentenyl and cyclohexenyl radicals are actually intermediates in these reactions has not yet been shown clearly. Since one would expect that shift of the double bond is incomplete if a free allylic radical is involved, experiments with cycloalkenes possessing a positional or radioactive label might provide further clues.

Molecular models show that cyclopentene and cyclohexene are relatively rigid and that it may be difficult to achieve the optimum geometry *(122)*. Alternatively, one could argue that the relative stability of the cyclopentenyl and cyclohexenyl radicals [129] favors a stepwise process. However, 1,2-dihydronaphthalene *(32)* and the 1,4-dihydro isomer seem to react in concerted fashion [9] although any potential intermediate radical would be even more stable. Models suggest a greater flexibility for these two compounds so that the *p*-orbitals of the developing double bond can become coaxial in the transition state.

A concerted mechanism is geometrically impossible for the pyrolysis of *trans,trans*-1,6-cyclodecadiene *(100)* and of *(104)*. Presumably, cyclodecene rearranges also at least in part *via* a biradical, which would account for the formation of vinylcyclooctane (Scheme 22). In any case, the thermal formation of vinylcyclooctane from cyclodecene by a concerted suprafacial 1,3-carbon shift is forbidden [4]. The twisted bicyclobutane and bicyclopentanes enter into stepwise ene reactions also. However, to conclude that *all* bicyclobutanes and bicyclopentanes react in a stepwise manner may be premature, since these compounds appear to form

[126a] *K. H. Schulte-Elte* and *G. Ohloff*, Tetrahedron Letters *1964*, 1143; a related reaction has been described by *N. C. Yang, A. Morduchowitz*, and *D.-D. H. Yang*, J. Amer. chem. Soc. *85*, 1017 (1963); however, these authors postulated a unified stepwise mechanism *via* free radicals; cf. also *N. J. Turro*: Molecular Photochemistry. Benjamin, New York 1965, p. 155; for the photo-ene reaction of methyl- and dimethylmaleic anhydride with α-cedrene see *C. H. Krauch* and *H. Küster*, Chem. Ber. *97*, 2085 (1964).

[126b] *G. Ohloff*, private communication.

[127] *H. M. R. Hoffmann* and *D. R. Joy*, J. chem. Soc. (London) *B 1968*, 1182.

[128] *R. K. Hill* and *M. Rabinovitz*, J. Amer. chem. Soc. *86*, 965 (1964).

[129] *C. Walling* and *W. Thaler*, J. Amer. chem. Soc. *83*, 3877 (1961).

exclusively the ene adduct without any admixed 2 +2 product in a number of reactions.

It should be borne in mind that the initial rate-limiting abstraction of an allylic hydrogen (possibly followed in certain reactions of cyclopentene and cyclohexene; cf. also Scheme 7) and the similarly rate-limiting formation of the biradical (Scheme 3) represent but two mechanistic extremes which demarcate a broad spectrum of *concerted* ene reactions.

A useful criterion forprobing the timing of bond changes is the deuterium isotope effect k_H/k_D, which has been measured for a few ene reactions. For the reaction of 1,4-dihydronaphthalene *(32)* with diethyl azodicarboxylate $k_H/k_D = 2.8–4.1$ between 60 and 80 °C[9], and for the benzylic oxidation of 1,3-diphenylpropene with selenium dioxide in acetic acid at 115 °C k_H/k_D = 3.2[10]. By comparison, for the intramolecular 1,5-hydrogen shift in *cis*-1,3-pentadiene (Scheme 2) k_H/k_D is greater, being 12.2 at 25 °C, suggestive of a highly symmetric transition state with a half-transferred hydrogen in this case[6]. Clearly, carbon-hydrogen bond-breaking is energetically costly and presumably not fully compensated by formation of the new H–X bond, at least when X = carbon (cf. Scheme 23). The limited data on orientational phenomena discussed above (Section 6.2) seem to reinforce this conclusion and suggest that within the province of concerted ene reactions involving all-carbon systems, the making of the new carbon-carbon bond may well be in the lead in many cases.

For the reaction of two conformationally defined 1-methylcyclohexene systems with singlet oxygen *Nickon* has shown recently that k_H/k_D is also rather low (1.1–2.4); chemical studies indicate that neither C–H bond breaking nor C–O bond making have advanced very far, *i.e.* the transition state is reactant-like in this particular reaction[131].

The few isotope effects measured for the retro-ene reaction again seem to suggest a variable transition state. For example allyl α-deuteriodiphenylmethyl ether undergoes cleavage at 430 °C only about 10% more slowly than the undeuterated compound (k_H/k_D = 1.1)[115]. On the other hand, $k_H/k_D \approx 2$ at 400–500 °C for the pyrolysis of acetates. The latter value appears to be close to the theoretical maximum of 2.1 at this temperature[119].

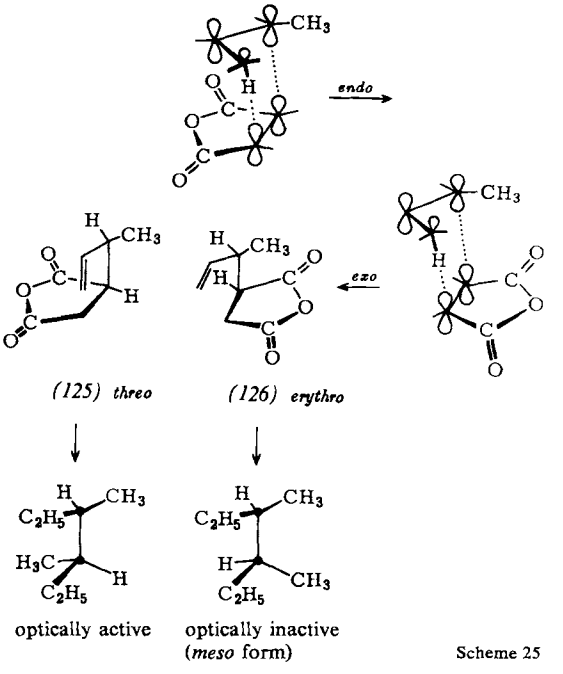
In summary, ene reactions may proceed by a broad spectrum of transition states. While most Diels-Alder additions are considered to be concerted[45], the mechanism of the ene reaction is janus-faced in that both concerted and stepwise routes may be followed. A concerted course is generally preferred, but the stepwise process may occur, provided the optimum geometry of the transition state is inaccessible and, perhaps less urgently, the intermediate radical or biradical is stabilized.

[130] *J. A. Berson, R. G. Wahl,* and *H. D. Perlmutter,* J. Amer. chem. Soc. *88*, 187 (1966).

[131] *A. Nickon, V. Chuang, P.J.L.Daniels, J. B. DiGiorgio, H. G. Vilhuber,* and *E. Werstiuk,* to be published.

6.6. *endo* or *exo* Transition State?

Since the ene reaction does not lead to cyclic adducts, a distinction of *endo* and *exo* transition states is more difficult than in the Diels-Alder addition. Only three ene reactions have so far been scrutinized from this point of view, and all three examples are due to the work of *Berson* and his collaborators[130]. *cis*-2-Butene has been shown to react with maleic anhydride to give two diastereomeric 3-(1-butenyl)succinic anhydrides *(125)* and *(126)* in a ratio of 80–85% to 15–20%. *trans*-2-Butene and maleic anhydride, on the other hand, afford 43% *(125)* and 57% *(126)*. The configurational assignments have been reached by a six-step degradation to 3,4-dimethylhexane: (i) hydrogenation, (ii) hydrolysis, (iii) reaction with 2 CH_2N_2, (iv) reaction with $LiAlH_4$, (v) reaction with 2 *p*-$CH_3C_6H_4$–SO_2Cl in pyridine, and (vi) further reaction with $LiAlH_4$. (see Scheme 25). Clearly, the selectivity



Scheme 25

is considerably reduced with *trans*-2-butene, yet the *endo* preference is qualitatively preserved, because the major diastereomer from *cis*-2-butene is the minor one from the *trans* isomer. For the ene reaction of cyclopentene with maleic anhydride there exists a 3.5:1 preference for the *endo* transition state[130]. The *endo*/*exo* ratio in another ene reaction amounts to either 29:23 or 23:29[36]. Apparently the *endo* selectivity is not particularly striking and is sensitive to steric effects (see below); any generalization on the preferred steric course must be regarded with caution.

6.7. Steric Effects

Ene reactions are notoriously sensitive to steric effects, just like cycloadditions[45]. For example, the reduced *endo* selectivity (57%) for the reaction of *trans*-2-butene with maleic anhydride as compared with more

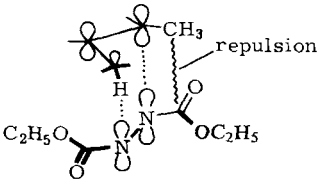
than 80% selectivity for the reaction with *cis*-2-butene (cf. Scheme 25) is probably the consequence of nonbonded repulsion between the nonreacting methyl group of *trans*-2-butene and the opposing carbonyl grouping in the *endo* transition state. Similarly, the formation of the *endo* adducts from α-pinene [cf. *e.g. (11)*], the considerably enhanced reactivity of the parent cyclopropene (Scheme 9) *vis-à-vis* its triphenyl counterpart *(65)*, the formation of the *cis* dimer *(66)* from *(65)*, and the different reactions of *(68)* and *(70)* attest to the importance of steric effects.

In the ene reaction of dehydrobenzene with 1-octene the *trans* isomer has been reported to be formed as the major product (Scheme 26), although the other products were not identified. It has been suggested that the bulky and flexible *n*-pentyl chain prefers to be oriented away from the attacking dehydrobenzene[75c] (cf. also Table 1, entry 3 for the *trans/cis* ratio with a *trans* enophile).



Scheme 26

Steric effects are also manifest in the data of Table 1 which suggest that the enophile attacks the least crowded olefinic terminus preferentially and abstracts the least crowded hydrogen most readily. Interestingly, *trans*-2-butene reacts about 3.7 times faster than the *cis*-isomer with diethyl azodicarboxylate. As can be seen in Scheme 27, one ethoxycarbonyl grouping of the azo ester (which is usually present in its more stable *trans* form) and the opposing methyl group of the *cis*-2-butene clash in the transition state[8]. In



Scheme 27

contrast, no such repulsion is present in the reaction of *trans*-2-butene so that the situation is exactly reversed to that for the reactions with maleic anhydride, which is a *cis*-enophile and would be expected to react more readily with *cis*-2-butene than with the *trans* isomer.

A distinction of *endo* and *exo* transition state is no longer possible when alkynes and dehydrobenzenes act as enophiles. It has been found that *trans* as well as *cis*-alkoxypropenes and dehydrobenzenes afford 2 + 2 cycloadducts and also ene products. In all the reactions studied the *trans* propene derivative enters the ene reaction more readily than the *cis* isomer. Furthermore, the ene reaction is inhibited more with *cis*-ethoxypropene[132a] than with *cis*-methoxypropene[132b]. That all these differences are probably of steric origin is suggested by an inspection of models.

7. Outlook

Much further work is needed before we may claim to understand the ene reaction. On the preparative side further heteroatom analogs await discovery, and new enophiles should be found which react in the presence or absence of electrophilic catalysts. Much of what has been said about the mechanism and particularly the reactivity of the ene reaction has been based on fragmentary data and perhaps even some speculation. Future work will have to explore in a more quantitative way the reactivities, orientation phenomena, and steric effects as well as the variable transition state and its geometry.

I thank Prof. R. B. Woodward for his hospitality at Harvard University, where much of the work on this paper was done, Prof. L. Friedman and Dr. G. Ohloff for stimulating discussions, and Drs. O. Achmatowicz, Jr., R. Alder, J. M. Brown, Prof. J.-M. Conia, Dr. P. Dowd, Dr. E. Koerner von Gustorf, Prof. A. Nickon, Prof. E. Trachtenberg, and Prof. M. C. Whiting for personal communications regarding the manuscript. The support given by the Penrose Fund of the American Philosophical Society is gratefully acknowledged.

Received: May 19, 1969 [A 717 IE]
German version: Angew. Chem. *81*, 597 (1969)

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[132] a) *H. H. Wasserman, A. J. Solodar*, and *L. S. Keller*, Tetrahedron Letters *1968*, 5597; b) *L. Friedman, R. J. Osiewicz*, and *P. W. Rabideau, ibid.* p. 5735.

Chemical Investigations of the Molecular Origin of Biological Radiation Damage

By E. Fahr[*]

The radiation damage observed when UV and ionizing radiations react on biological objects is caused in many cases by changes in the nucleic acids. Exposure of these compounds to UV radiation in vitro and in vivo leads, inter alia, to dimerization of the pyrimidine bases with formation of cyclobutane derivatives, and to addition of water to the 5,6-double bond of the pyrimidine bases to form derivatives of the 6-hydroxyhydropyrimidine system. The structure of the irradiation products has been established. The dimerization prevents the reduplication of the DNA, and the addition of water appears to be the cause of UV mutations. Ionizing radiation in aqueous solution results e.g. in addition of H and/or HO radicals to the 5,6-double bond of the pyrimidine bases and cleavage of the imidazole ring of the purine bases. The mutations caused by ionizing radiation are probably also due, in part, to the formation of 6-hydroxydihydropyrimidine derivatives.

1. Introduction

The first scientifically based observations on the biological effects of radiation were made in the second half of the last century. It was found that UV radiation from a mercury lamp can not only tan the skin, but can also cause burns, skin cancer, mutations, and the death of microorganisms. The very pronounced biological effects of ionizing radiation were discovered immediately after the discovery of radioactivity and X radiation in the last decade of the 19th century, but their danger was not fully appreciated at once. Detailed information about the biological and medicinal effects of UV and ionizing radiation was gained during the first few decades of the present century, after the medical world had at first greeted radium and its radiation as a sort of "miracle drug".

After the second world war, the dropping of the first atomic bombs, the atomic bomb tests, and the use of radioactive material in research and industry, the question of the biological effects of radiation, and particularly that of genetic effects, became of pressing importance.

Though these effects of UV and ionizing radiations have been known for more than a century, knowledge of the chemical processes involved was relatively sparse up to about 20 years ago, since radiation-biologists and biophysicists confined their investigations mainly to the relations between radiation dose and other physical parameters and the biological (and medicinal) effect. The study of the chemical processes that occur when radiation acts on biological material has been made possible only by the methods developed in the last few decades for the separation of substances in mixtures. Since deoxyribonucleic acid (DNA) is the carrier of genetic information, the mutations caused by radiation should be traceable to chemically detectable changes in the DNA; since, moreover, the spectrum of action for the destruction of microorganisms by UV radiation coincides very closely with the absorption spectrum of the nucleic acid, special attention has been given to the action of radiation on nucleic acids and their components.

Exposure of biological objects to UV and ionizing radiation (X rays, γ rays, corpuscular radiation) leads to a number of successive processes that depend on the nature of the radiation, the radiation dose, the nature of the biological object, and other factors. These processes are:

a) The primary physical interaction between the radiation and the molecular components of the biological object.

b) The radiation-chemical process of the high-energy molecule resulting from interaction with the radiation, which leads to specific chemical reactions (photochemical processes on irradiation with UV and/or visible light, formation of ions and/or radicals by ionizing radiation).

c) The actual biological effect that results from these processes.

The present discussion is confined mainly to the radiation-chemical processes[1].

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[1] We have recorded 520 articles dealing with the action of UV and ionizing radiations on nucleic acids and on pyrimidine and purine derivatives. Understandably it has not been possible to cite all of these references in the present review.
The following aspects have not been covered in this article: a) physical primary processes in the action of UV and ionizing radiation on nucleic acids and their components; b) investigations on the mechanism of the photochemical addition of water and dimerization; c) photochemical dimerization in non-aqueous solvents; d) sensitized photochemical processes; e) behavior of pyrimidine and purine derivatives that do not occur in natural nucleic acids toward UV and ionizing radiations.
Information on these topics may be obtained from the following articles, which refer to earlier literature: On (a) *P. J. Wagner* and *D. J. Bucheck*, J. Amer. chem. Soc. *90*, 6530 (1968); *J. Eisinger*, Photochem. and Photobiol. *7*, 597 (1968). On b) *S. Y. Wang*, Photochem. and Photobiol. *1*, 135 (1962); *A. Wacker*, *A. Kornhauser*, and *L. Träger*, Z. Naturforsch. *20b*, 1043 (1965); *S. Y. Wang* and *J. C. Nnadi*, Chem. Commun. *1968*, 1160; *A. A. Lamola*, Photochem. and Photobiol. *7*, 619 (1968); *A. A. Lamola* and *J. Eisinger*, Proc. nat. Acad. Sci. USA *59*, 46 (1968); *J. G. Burr*, *B. R. Gordon*, and *E. H. Park*, Photochem. and Photobiol. *8*, 73 (1968). On c) see [1a] and *H. Morrison* and *R. Kleopfer*, J. Amer. chem. Soc. *90*, 5037 (1968). On d) *J. D. Spikes* and *R. Straight*, Annu. Rev. physic. Chem. *18*, 409 (1967). On e) see [2a, b].

2. Action of UV Radiation on Nucleic Acids and their Components[2]

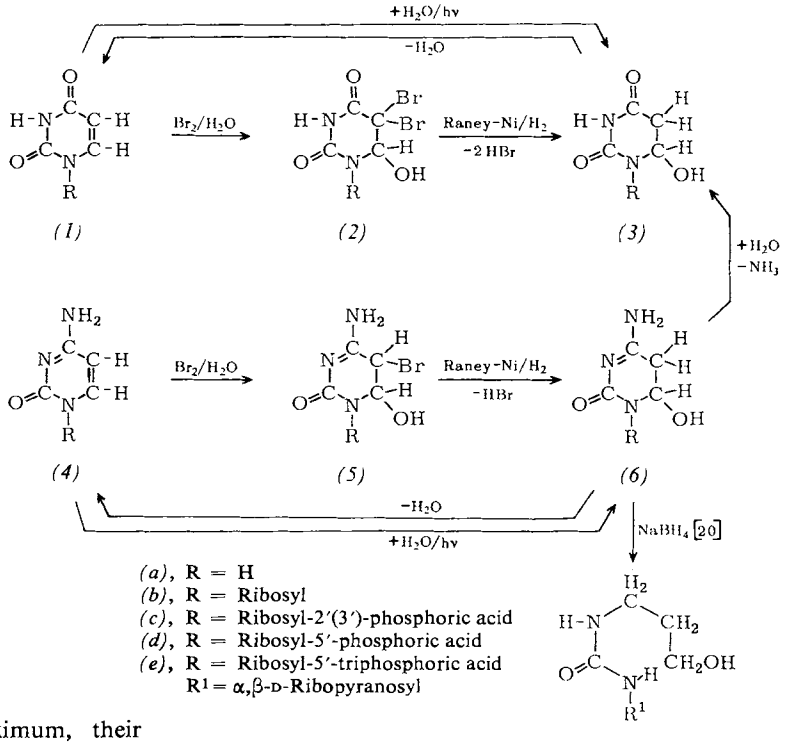
2.1. "Reversible" Irradiation Products

In 1949, *Sinsheimer* and *Hastings*[3] reported that UV irradiation of uracil *(1a)* and uridine *(1b)* in aqueous solution leads to products that change back into the starting materials on standing, or more rapidly when heated. These substances are therefore known as *reversible irradiation products*. Since they do not absorb in the region around 260 nm, where uracil and uridine have a characteristic absorption maximum, their formation and their conversion back into the starting materials can be followed quantitatively. The structure of these compounds has been investigated by *Moore* and *Thomson*[4] and by *Wang*[5,6]. These authors have shown that the formation of the reversible irradiation products probably involves the addition of water to the 5,6-double bond of the uracil system; the reversible irradiation products of the bases occurring in the nucleic acids were not isolated.

We have prepared the reversible irradiation products of *(1a)–(1e)* by UV irradiation of aqueous solutions of these compounds and separated them from the solutions[8].

If the irradiation is carried out with cooling in ice and using low pressure mercury lamps to suppress the thermal back-reaction[7b], chromatography of the irradiation solution on a column is unnecessary in the case of the uridylic acids *(1c)–(1e)*. The reversible irradiation products *(3c)–(3e)* are obtained in purities of about 90% on freeze-drying of the solution[8c].

The 6-hydroxydihydrouracil structure *(3)* of the reversible irradiation products has been proved by chemical synthesis[8] *(1a)→(2a)→(3a)*. The resulting compound *(3a)*, according to its IR spectrum and chromatographic data, is identical with the reversible irradiation product of uracil. We also prepared *(3b)* to *(3e)* in a similar manner.



Scheme 1.

The behavior of cytosine *(4a)*, cytidine *(4b)*, and cytidylic acid *(4c)* on UV irradiation in aqueous solution has been discussed in several publications[6]. Cytosine

[2] *D. Shugar* in *E. Chargaff*, and *J. N. Davidson*: The Nucleic Acids. Academic Press, New York 1960, Vol. 3; *A. Wacker* in *J. N. Davidson*, and *W. E. Cohn*: Progress in Nucleic Acid Research. Academic Press, Inc., New York 1963, Vol. 1; *E. Fahr*, Biophysik *5*, 2 (1968); and [104].

[3] *R. L. Sinsheimer* and *R. Hastings*, Science (New York) *110*, 525 (1949).

[4] *A. M.Moore* and *C. H. Thomson*, Science (Washington) *122*, 594 (1955); Canad. J. Chem. *35*, 163 (1957); *36*, 281 (1958).

[5] *S. Y. Wang*, *M. Apicella*, and *B. R. Stone*, J. Amer. chem. Soc. *78*, 4180 (1956); *S. Y. Wang*, *ibid. 80*, 6196 (1958).

[6] For further articles on the photochemical addition of water to uracil and cytosine derivatives, see [8c] and [9b].

[7] The following lamps produced by Original Hanau Quarzlampengesellschaft, Hanau, were used for the UV irradiations: a) Low pressure mercury lamp, NK 25/7; b) low pressure mercury lamp, NK 6/20; c) Low pressure mercury lamp of the special analytical lamp (without filter).

[8] a) *H. Gattner* and *E. Fahr*, Liebigs Ann. Chem. *670*, 84 (1963); b) Z. Naturforsch. *19b*, 74 (1964); c) *E. Fahr*, *H. Gattner*, *G. Dörhöfer*, *R. Kleber*, and *H. Popp*, Z. Naturforsch. *22b*, 1256 (1967).

[9] a) *R. Kleber*, *E. Fahr*, and *E. Boebinger*, Naturwissenschaften *52*, 513 (1965); b) *E. Fahr*, *R. Kleber*, and *E. Boebinger*, Z. Naturforsch. *21b*, 219 (1966).

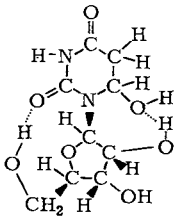
and cytidylic acid form very unstable reversible irradiation products, for which some authors, by analogy with uracil, have assumed a 6-hydroxydihydrocytosine structure, whereas *Wang* [10] believes that photoisomerization of the cytosine ring occurs. By means of a special irradiation apparatus [7a,9b], we obtained the reversible irradiation products of *(4a)–(4c)* in such high concentrations that it was possible to study the thermal back-reaction and to separate the reversible irradiation product of cytidylic acid by thin layer chromatography on cooled polyethyleneiminecellulose [9]. *Johns et al.* [11–13] separated the same irradiation product from the solution by paper electrophoresis. The 6-hydroxydihydrocytosine structure *(6)* of these irradiation products was demonstrated by the reaction sequence *(4c)*→*(5c)*→*(6c)* [9].

The products *(6)* undergo deamination on standing (dark reaction) to form the compounds *(3)*, so that the cytosine system can be converted into the uracil system by the path *(4)*→*(6)*→*(3)* [9, 11–14, 15].

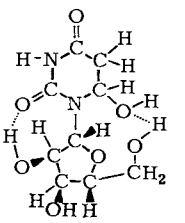
It is not yet certain whether thymine, thymidine, and thymidylic acid *(7)* can form a reversible irradiation product *(8)*. On UV irradiation of thymine in aqueous solution we were able to detect a very unstable reversible irradiation product (half life about 1–2 min) [9b,22]. Our attempts to synthesize a 6-hydroxydihydrothymine *(8)* by the method used for uracil, cytosine, and their derivatives were unsuccessful. *Nofre* [16], on the other hand, obtained *(8)* by debromination of the corresponding thymine compound with Zn/glacial acetic acid [17].

On column-chromatographic separation of the products resulting from the UV irradiation of uridine in frozen aqueous solution, we obtained two reversible irradiation products of uridine [21e]. It is not yet certain whether these are two isomers differing in their H-bonding in accordance with formulations *(9a)* and *(9b)* [18] or the diastereoisomers *(10)* [19].

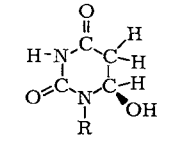
The detailed kinetic investigation [8b,8c,9b,21a–21d] of the decomposition of the reversible irradiation products *(3a)–(3e)* and *(6a)–(6c)* showed that the stability of the 6-hydroxydihydropyrimidine system is



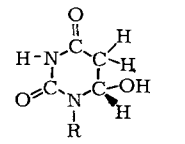
(9a)



(9b)



(10a)



(10b)

R = D-Ribosyl

very strongly influenced by the sugar or sugar phosphate residue on N-1, and increases in the order base→nucleoside→nucleotide. Investigations by *Logan* and *Whitmore* [23] show that this effect does not end with the nucleotide, but that the stability of the 6-hydroxydihydrouracil system in polynucleotides increases with increasing chain length, *i.e.* toward the nucleic acid. This influence on the reactivity of the pyrimidine system, which has also been observed in other investigations [24, 123b], is presumably due to H bonds between parts of the pyrimidine ring and the OH groups of the sugar residue, to "steric screening" of the reactive centers of the pyrimidine ring by the phosphate group(s), and to electrostatic interactions between the pyrimidine ring or individual parts of rings and the phosphate group(s) [24]. In polynucleotides and nucleic acids, other steric effects (*e.g.* the screening of the base by individual parts of the macromolecule) and electrostatic effects of the electric field of the nucleic acid on attacking ionic reactants also occur. These effects can influence the reactivity of a pyrimidine base [25] to such an extent that it reacts quite differently as the free base than it does in the form of its nucleotide or when it is incorporated into a nucleic acid. Thus an effect observed with a pyrimidine base [25] cannot be immediately assumed to be applicable also to the corresponding nucleoside or nucleotide, or even to a nucleic acid [26].

[10] *S. Y. Wang*, Nature (London) *184*, 184 (1959).

[11] *H. E. Johns, J. C. LeBlanc*, and *K. B. Freeman*, J. molecular Biol. *13*, 849 (1965).

[12] *K. B. Freeman, P. V. Hariharan*, and *H. E. Johns*, J. molecular Biol. *13*, 833 (1965).

[13] *H. Becker, J. B. LeBlanc*, and *H. E. Johns*, Photochem. and Photobiol. *6*, 733 (1967).

[14] *H. Schuster*, Z. Naturforsch. *19b*, 815 (1964).

[15] A direct photochemical deamination of cytosine has been discussed by *M. Daniels* and *A. Grimison*, Biochem. biophysic. Res. Commun. *16*, 428 (1964).

[16] *C. Nofre*, Dissertation, University 1968.

[17] Photochemical addition of water to thymine and debromination of the corresponding thymine derivative may lead to different isomers of *(8)*; see *I. Pietrzykowska* and *D. Shugar*, Science (Washington) *161*, 1248 (1968), reference 9.

[18] See [8c].

[19] *W. J. Wechter* and *K. C. Smith*, Biochemistry *7*, 4064 (1968).

[20] For mechanism see *N. Miller* and *P. Cerutti*, Proc. nat. Acad. Sci. USA, *59*, 34 (1968); *(3b)* was also broken down in a similar manner.

[21] a) *H. Gattner*, Dissertation 1964; b) *R. Kleber*, Dissertation 1966; c) *G. Dörhöfer*, Dissertation 1966; d) *H. Popp*, qualifying Thesis 1966; e) *G. Fürst*, Dissertation 1968; f) *B. Sojka*, Dissertation 1969; g) *R. Pastille*, qualifying Thesis; h) *P. Richter*, qualifying Thesis, all Universität Würzburg; i) unpublished results as well as *K.-H. Dönges* and *E. Fahr*, Z. Naturforsch. *21b*, 87 (1966).

[22] The behavior of thymidine on reduction with $NaBH_4$ in the presence of UV radiation suggests the intermediate formation of *(8)*, see *Y. Kondo* and *B. Witkop*, J. Amer. chem. Soc. *90*, 764 (1968), and [20].

[23] *D. M. Logan* and *G. F. Whitmore*, Photochem. and Photobiol. *5*, 143 (1966).

[24] See [8c].

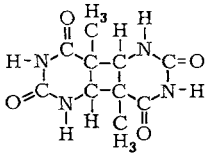
[25] Preliminary experiments indicate that the above assumptions are also valid for purine bases.

[26] Effects of this type are probably responsible for the unusual behavior of free radicals produced by ionizing radiation in nucleic acids [77b] as compared with "normal" organic free radicals.

2.2. Dimeric Irradiation Products

2.2.1. Structure of the Dimeric Irradiation Products

In 1958–1960, *Rörsch, Beukers, Ijlstra,* and *Berends* [27] and *Wang* [28] reported observations according to which a *thermally irreversible* irradiation product is formed on UV irradiation of thymine in frozen aqueous solution (referred to hereafter as ice matrix). The authors suggested (without providing further evidence) that photochemical dimerization had occurred, with formation of a tricyclic cyclobutane derivative [*(11)*



(11)

according to the formulation of [27c, 28c]]. The choice of irradiation in the ice matrix was based on observations by *A. v. Szent-Györgyi*, according to which the ice matrix should correspond more closely to the biological conditions than an aqueous solution [27, 28]. The discovery of these irreversible irradiation products, the formation of which has also been observed with other pyrimidine derivatives, immediately led to very intensive investigation of this field. The following questions had to be answered:

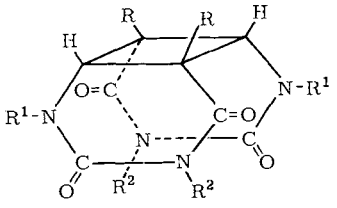
(i) Are these irradiation products really cyclobutane derivatives in accordance with the formulation *(11)*?

(ii) If so, which of the four possible isomers *(12)* to *(15)* are formed?

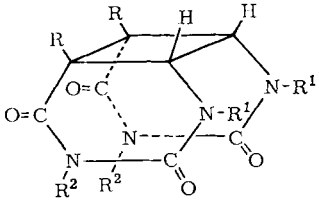
(iii) Are similar irradiation products formed on UV irradiation of nucleic acids?

The cyclobutane structure of the irreversible irradiation products has been demonstrated by several research groups. *Anet* [29] and *Blackburn* and *Davies* [30a] showed by NMR spectroscopy and with the aid of a novel degradation (see Section 2.2.2) that the dimeric thymine formed in the ice matrix has the *cis/syn* structure *(13a)*. The structure *(13b)* of the dimeric uracil has been proved by us by degradation [21i], by NMR spectroscopy (*Blackburn* and *Davies*) [30b], and by X-ray analysis (*Adman, Gordon,* and *Jensen*) [31]. Several research groups (see Section 4) have shown that the ice-matrix dimers of thymine and uracil are also formed on UV irradiation of nucleic acids.

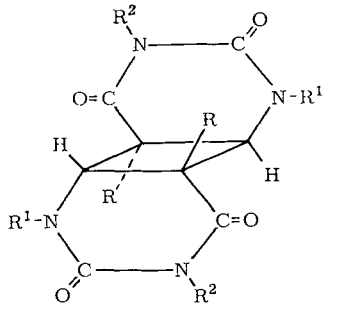
It is much more difficult to establish whether the UV irradiation of thymine and uracil, as well as of nucleosides, nucleotides, and nucleic acids, leads only to the *cis/syn*-isomer *(13)* or also to the other isomers *(12)*, *(14)*, and *(15)*. Some authors assumed that the four isomers of dimeric thymine and of dimeric uracil can



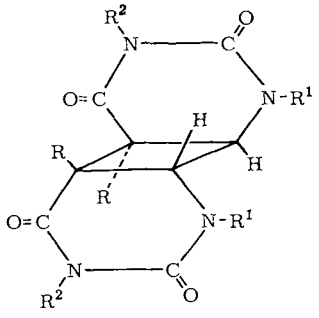
(12)



(13)



(14)



(15)

(a), R = CH_3, R^1 = R^2 = H
(b), R = R^1 = R^2 = H
(c), R = CH_3, R^2 = H, R^1 = Deoxyribosyl
(d), R = R^2 = H, R^1 = Ribosyl
(e), R = R^1 = H, R^2 = CH_3

be distinguished by thin layer or paper chromatography. However, we have shown with mixtures of these isomers [21e, 21f] that this is not necessarily so. Furthermore, the isomers cannot be reliably separated from one another by fractional recrystallization and similar operations. Other methods are therefore necessary to distinguish them.

Mass spectrometry, which is particularly suitable for the identification of small quantities of material, is completely unsuccessful in this case. The dimers are broken down in the ion chamber both thermally and by the electrons [121] from the ion source. Experiments with various mass spectrometers and under various sets of conditions gave only the mass spectra of the monomers.

Though the dimers can be distinguished and hence identified by *NMR spectroscopy* [21f], this method requires at least mg quantities of the substance, whereas such quantities are generally not available on isolation of the dimers from biological systems.

A reliable identification of the dimers is possible by *IR spectroscopy* [32, 33, 59], which can be used without serious technical difficulties even in the μg range. As little as 10% of one isomer can be detected in a mixture of two isomeric dimers [21f, 32].

The dimers required as reference substances can be prepared in the following way: Dimerization of

[27] a) *A. Rörsch, R. Beukers, J. Ijlstra,* and *W. Berends*, Recueil Trav. chim. Pays-Bas *77*, 423 (1958); b) *R. Beukers, J. Ijlstra,* and *W. Berends, ibid. 78*, 883 (1959); *79*, 101 (1960); c) *R. Beukers,* and *W. Berends*, Biochim. biophysica Acta *41*, 550 (1960).

[28] a) *S. Y. Wang*, Nature (London) *184*, BA 59 (1959); b) *188*, 844 (1960); c) *190*, 690 (1961).

[29] *R. Anet*, Tetrahedron Letters *1965*, 3713.

[30] a) *G. M. Blackburn* and *R. J. H. Davies*, Chem. Commun. *1965*, 215; b) Tetrahedron Letters *1966*, 4471.

[31] *E. Adam, M. P. Gordon,* and *L. H. Jensen*, Chem. Commun. *1968*, 1019.

[32] See *E. Fahr* and *W. Rohlfing*, Z. analyt. Chem. *243*, 43 (1968).

[33] To increase the identification capacity, it is recommended that measurements be carried out up to about 35 μm [32].

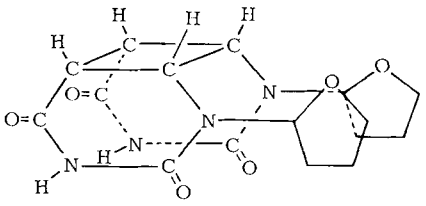
thymidine in the ice matrix followed by chromatographic separation of the irradiation products on a column gives the three dimeric thymidines *(12c)*, *(13c)*, and *(14c)* [34]. Hydrolysis of these compounds yields the dimeric thymines *(12a)*, *(13a)*, and *(14a)* [35]. The fourth dimeric thymine *(15a)* was prepared by *Weinblum* and *Johns* [35] by UV dimerization of thymidyl-(3′–5′)-thymidine followed by hydrolysis [36].

Dimerization of thymidine in *tert*-butanol with acetone as a sensitizer led to the four dimeric thymidines *(12c)* to *(15c)* [37]. The dimeric thymines *(14a)* and *(15a)* were formed on irradiation of thymine in the presence of acetone, benzophenone, and other ketones as sensitizers [38].

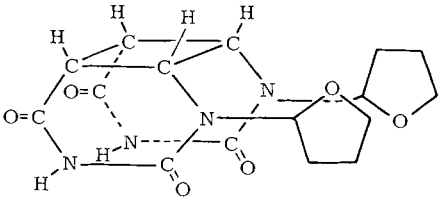
We obtained the dimeric uracil *(12b)* in the two optically active forms by UV irradiation of uridine in the ice matrix [7c], separation of the irradiation solution by column chromatography, and hydrolysis of the corresponding dimeric uridines [21e, 39]. We have been able to obtain all four dimeric uracils by total synthesis (see Section 2.2.3) [21h, 40].

On separation of the irradiation products of uridine (ice matrix), we obtained two fractions which gave the same dimeric uracil *(13b)* on hydrolysis. Examination of molecular models [41] showed that in the *cis/syn* dimeric uridine *(13d)*, rotation of the ribose residue about the N-1/C-1′ axis, which is restricted in any case by H bonding between the 2-C=O groups and the HO groups of the sugar residue, must be prevented by the bulk of the two neighboring ribose residues. Three isomers, corresponding to the formulas *(16)*, *(17)*, and *(18)* can be formed, though the formation of *(18)*, with the *trans/trans* arrangement of the ribose O atoms in relation to the H atoms of the cyclobutane ring is opposed by steric factors. We believe that the two fractions mentioned above are the uridine dimers *(16)* and *(17)* [21e].

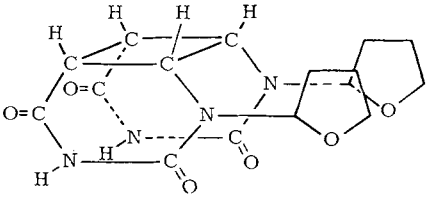
Detailed investigation of the dimerization showed that it is not confined to the ice matrix, or to the solid state in general [50], but also occurs in solution, though in a poorer yield. The yield depends on the wavelength of the radiation used [47]; a photochemical equilibrium is established with a maximum dimer content at about 275 nm. Even cyclobutane derivatives containing only one dihydropyrimidine ring, *e.g. (26)*, are broken down into the monomer by short-wave UV radiation (about 230 nm).



(16)



(17)



(18)



The stability of the cyclobutane ring in the dimers is influenced by the sugar or sugar phosphate group on N-1 in the same way as in the case of the 6-hydroxydihydropyrimidine ring systems *(3)* and *(6)* (see Section 2.1). Whereas the dimeric uracil *(13b)* is perfectly stable towards 6 N HCl, the dimeric uridine *(13d)* yields not only the dimeric uracil *(13b)* by loss of the sugar residue, but also forms uracil [21e]; thus as in the case of the 6-hydroxydihydropyrimidine derivatives, no direct conclusions concerning the behavior of a nucleoside, nucleotide, or base segment in the nucleic acids can be drawn from the behavior of the corresponding base.

Investigations by several research groups on the quantitative relation between the radiation dose received and the quantity of dimer *(13a)* or *(13b)* obtained by acid hydrolysis must be regarded as uncertain, since the quantity of *(13a)* and *(13b)* isolated does not correspond to the quantity of dimer formed in the nucleic acid, since part of the dimer formed may be broken down into monomer or destroyed in some other way during isolation [43].

The identification of the dimers isolated from nucleic acids purely on the basis of their chromatographic behavior must always be regarded as uncertain. IR spectroscopy must also be used to check that the isolated irradiation product does not contain other dimers as well as *(13a)* or *(13b)* [21e, 21f].

[34] The dimers *(12a)* and *(12b)* and *(15a)* and *(15b)*, which have the symmetry group C_2, must be capable of being resolved into optical antipodes. The dimerization of thymidine and uridine accordingly yields the dimers *(12c)* and *(12d)* in two diastereoisomeric forms, which give the dimers *(12a)* and *(12b)* in optical antipodes on hydrolysis.

[35] *D. Weinblum* and *H. E. Johns*, Biochim. biophysica Acta *114*, 450 (1966).

[36] For determination of the structures of the dimeric thymines, see [35] and a) *D. Weinblum, F. P. Ottensmeyer*, and *G. F. Wright*, Biochim. biophysica Acta *155*, 24 (1968); b) *D. P. Hollis* and *S. Y. Wang*, J. org. Chemistry *32*, 1620 (1967).

[37] *E. Ben-Hur, D. Elad*, and *R. Ben-Ishai*, Biochim. biophysica Acta *149*, 355 (1967).

[38] *I. v. Wilucki, H. Matthäus*, and *C. H. Krauch*, Photochem. and Photobiol. *6*, 497 (1967).

[39] *E. Fahr, G. Fürst*, and *R. Pastille*, Z. Naturforsch. *23b*, 1387 (1968).

[40] a) *P. Richter* and *E. Fahr*, Angew. Chem. *81*, 188 (1969); Angew. Chem. internat. Edit. *8*, 208 (1969); b) *G. Dörhöfer* and *E. Fahr*, Tetrahedron Letters *1966*, 4511.

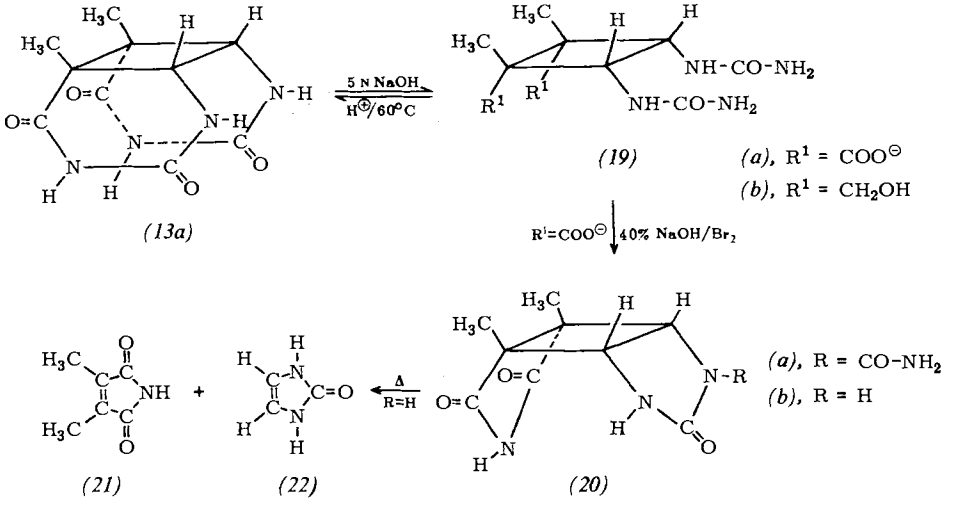
[41] Stuart-Briegleb models [42] calculated and constructed by us from the X-ray structural data of [31] (see [21g]).

[42] *G. Briegleb*, Fortschr. chem. Forsch. *1*, 642 (1950).

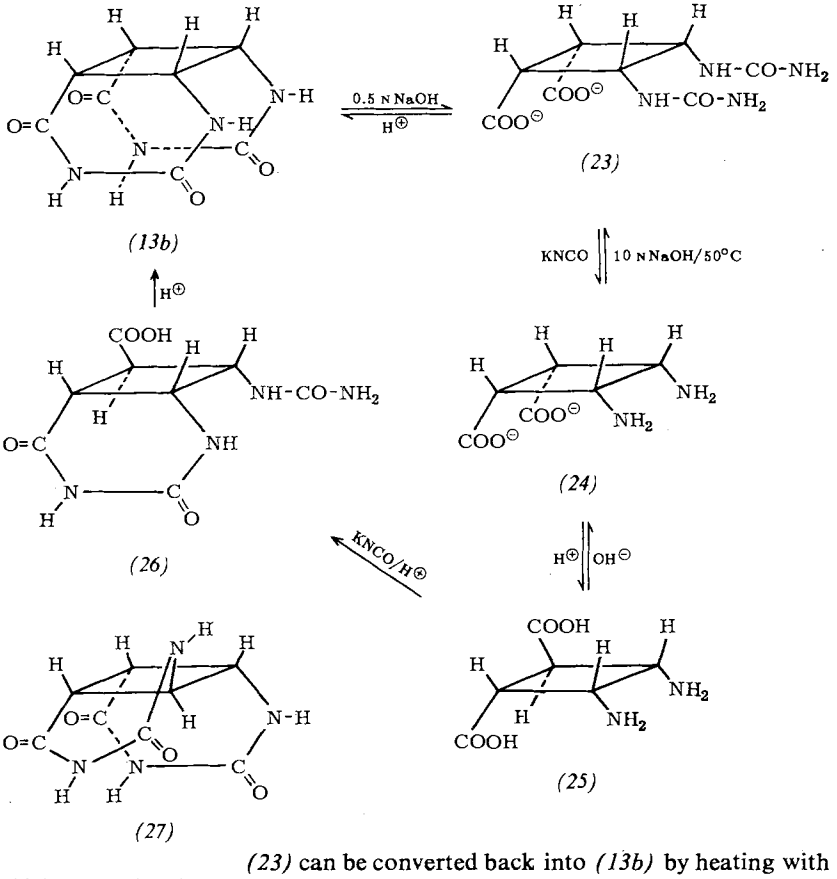
[43] The dimers *(12b)* and *(14b)* [21e, 21h] and *(12a)* and *(14a)* [21f, 35, 37] are unstable towards acids.

2.2.2. Reactions of the Dimeric Thymines and Dimeric Uracils

When dissolved in 0.1 N NaOH, the dimeric thymine *(13a)* forms a disodium salt, which changes into the diureido compound *(19a)* when heated at 60 °C with 5 N NaOH [21f,30a,44a,44b]. Similar diureido compounds are formed by the dimers *(12a)* and *(14a)* [38,44a]. Treatment of *(19a)* with 40% NaOH and bromine yields the compound *(20a)*, which reacts with HNO_2 to form *(20b)*. When heated to 240 °C, *(20a)* and *(20b)* give *(21)* and *(22)* [30a,44b]. The conversion of *(13a)* into *(21)* and *(22)* was taken by *Blackburn* and *Davies* [30,44b] as evidence of the structure of *(13a)*. Unlike the dimeric uracils (Section 2.2.3), the dimeric thymines can be converted into the tetramethyl derivatives by reaction with dimethyl sulfate [36a,44c,44d]. The reaction of *(13a)* with $NaBH_4$ yields *(19b)*, which gives *(19a)* on reaction with $KMnO_4$ [44a]. The dimers *(12a)* and *(14a)* behave similarly with $NaBH_4$.



The dimeric uracil *(13b)* also dissolves in dilute NaOH to give a disodium salt, which forms the diureido compound *(23)* when heated at 50 °C in 0.5 N NaOH; *(23)* can be converted back into *(13b)* by heating with dilute acid [21e,30b].



The reaction sequences *(13a)*→*(19a)*→*(13a)* and *(13b)*→*(23)*→*(13b)* conclusively rule out the otherwise conceivable

[44] a) *B. Witkop*, Photochem. and Photobiol. *7*, 813 (1968); b) *G. M. Blackburn* and *R. J. H. Davies*, J. chem. Soc. (London) *C 1966*, 2239; c) *1966*, 1342; d) *R. Beukers* and *W. Berends*, Biochim. biophysica Acta *49*, 181 (1961).

possibility of *trans* linkage of the heterocyclic rings [*e.g. (27)*]. A ring system as strained as this could be formed in the photochemical dimerization[45], but not on addition of acid to *(19a)* or *(23)*.

When heated at 50 °C with 10 N NaOH, *(23)* and *(13b)* are converted into a complex mixture of products, which include the diamino dicarboxylic acids *(24)* and *(25)*[46]. On reaction with potassium cyanate, the mixture gives some dimer *(13b)*, probably together with the compound *(26)*, which can be converted into *(13b)* by prolonged heating with concentrated hydrochloric acid[21e]. On methylation of *(13b)* with dimethyl sulfate, we obtained some trimethylated dimeric uracil[21e] as well as the dimethyl dimer *(13e)*[30b]. The tetramethylated dimer could not be obtained even with diazomethane.

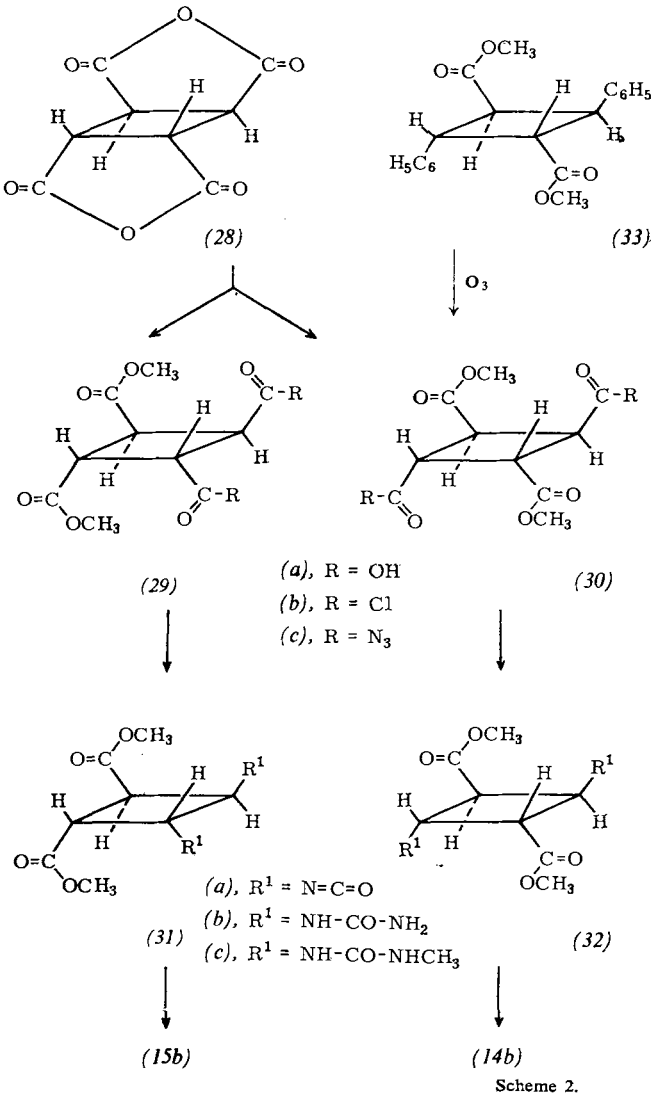
2.2.3. Total Synthesis of the Dimeric Uracils[21h,40]

We were able to prepare all four dimeric uracils by sterically comprehensive syntheses.

On boiling in methanol, the dianhydride *(28)* forms a mixture of the two isomeric half-esters *(29a)/(30a)*, which can be separated by fractional crystallization. The structure of *(30a)* was proved by ozonolysis of the α-truxillic acid ester *(33)*. *(29a)* and *(30a)* are converted *via* the acid chlorides *(29b)* and *(30b)* into the azides *(29c)* and *(30c)*, the Curtius degradation of which yields the isocyanates *(31a)* and *(32a)* respectively.

The reaction of *(31a)* and *(32a)* with NH_3 leads to the diureido components *(31b)* and *(32b)*, which are converted by acid into the dimeric uracils *(15b)* and *(14b)* respectively. Reaction of *(31a)* and *(32a)* with methylamine leads to *(31c)* and *(32c)*, which yield the methylated dimers *(14e)* and *(15e)* on ring closure.

The *cis* dimeric uracils *(12b)* and *(13b)* were synthesized by a similar route. When the dianhydride *(70)* is boiled with methanol, it forms a mixture of the half-esters *(71a)* and *(72a)* which were converted into the *cis* dimeric uracils *(12b)* and *(13b)* by the following reaction steps *(71a)*→*(71b)*→*(71c)*→*(73a)*→*(73b)* or *(72a)*→*(72b)*→*(72c)*→*(74a)*→*(74b)*[*]. The resulting *cis/anti* dimeric uracil *(12b)* is identical with the dimer that we obtained from uridine by UV irradiation[21e,39] (see Section 2.2.1), and thus confirms its structure.



Scheme 2.

2.2.4. Dimeric Cytosines and Mixed Dimers

The questions whether cytosine, as a base or as a component of nucleic acids, is capable of dimerizing and which of the four possible dimers are formed have not yet been finally settled. The experimental results suggest that dimerization is possible in dinucleotides[12,51,105] and nucleic acids[52–55], *e.g.* to form the dimer *(34)*, which, as a derivative of dihydrocytosine, readily undergoes thermal deamination to form *(13b)*. In no case was dimeric cytosine isolated. UV irradiation of cytosine, cytidine, and cytidylic acid in the ice matrix yields either no dimeric uracil deriv-

[45] See the formation of a *trans*-linked cyclobutane ring observed by *E. J. Corey, J. D. Bass, R. LeMahieu*, and *R. B. Mitra*, J. Amer. chem. Soc. *86*, 5570 (1964), on UV irradiation of a mixture of 2-cyclohexenone and isobutylene.

[46] The formation of *(25)* and *(26)* and the conversion of *(26)* into *(13b)* require the isomerization of a COOH group on the cyclobutane ring. Isomerizations of this type have been described by *E. R. Buchman, A. O. Reims, T. Skei*, and *M. J. Schlatter*, J. Amer. chem. Soc. *64*, 2696 (1942).

[*] Additional material inserted during checking.

[47] a) *R. B. Setlow*, Biochim. biophysica Acta *49*, 237 (1961) and [2a, 2b]; b) *H. E. Johns, S. A. Rapaport*, and *M. Delbrück*, J. molecular Biol. *4*, 104 (1962).

[48] *K. C. Smith*, Photochem. and Photobiol. *2*, 503 (1963).

[49] *H. L. Günther* and *W. H. Prusoff*, Biochim. biophysica Acta *149*, 361 (1967).

[50] *H. Ishihara*, Photochem. and Photobiol. *2*, 455 (1963).

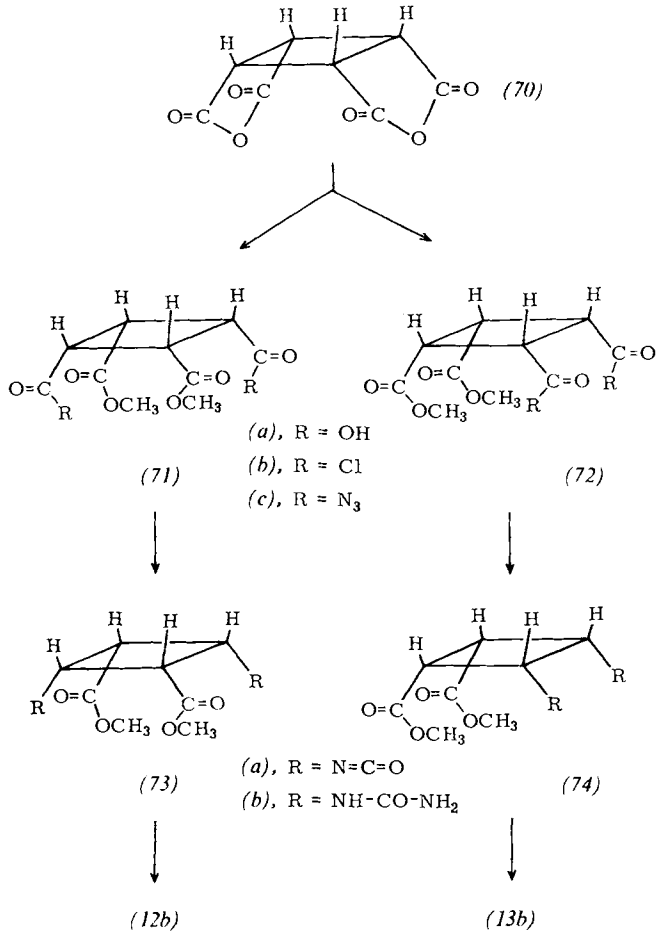
[51] *P. V. Hariharan* and *H. E. Johns*, Canad. J. Biochem. *46*, 911 (1968).

[52] a) *R. B. Setlow* and *W. L. Carrier*, Nature (London) *213*, 906 (1967); b) *J. K. Setlow, M. E. Boling*, and *F. J. Bollum*, Proc. nat. Acad. Sci. USA *53*, 1430 (1965).

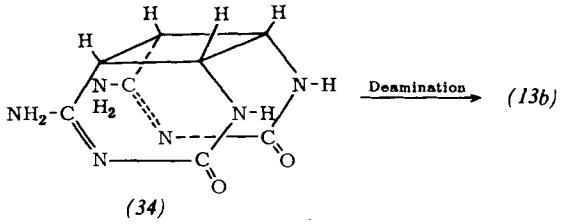
[53] *H. Dellweg* and *A. Wacker*, Z. Naturforsch. *17b*, 827 (1962).

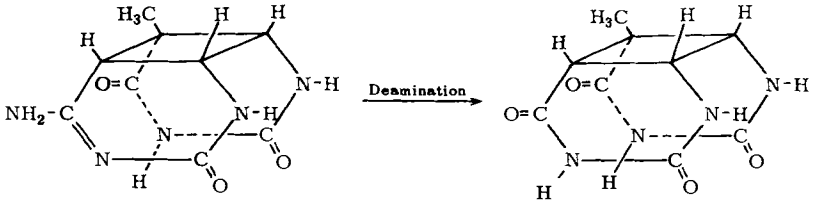
[54] *V. Merriam* and *M. P. Gordon*, Photochem. and Photobiol. *6*, 309 (1967).

[55] *R. B. Setlow* and *W. L. Carrier*, J. molecular Biol. *17*, 237 (1966).



atives[21f,14,50] or so little[48,49] that direct photochemical deamination followed by dimerization must also be taken into account in these cases[15].

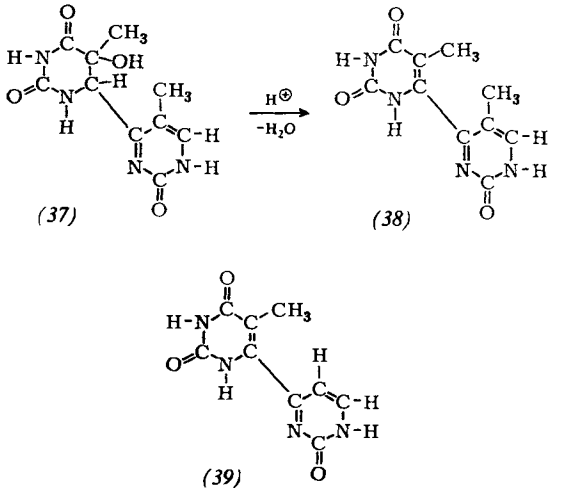




On exposure of thymine/uracil mixtures in the ice matrix to UV radiation, a mixed uracil/thymine dimer is obtained as well as dimeric thymine *(13a)* and dimeric uracil *(13b)*[21f,27c,48,56–58]. This mixed dimer is identical with that obtained on irradiation of DNA[59], which presumably results from deamination of a mixed cytosine/thymine dimer[52,55,59–64,105]. *Weinblum*[59] has suggested the structure *(36)* for the mixed uracil/thymine dimer, so that the mixed cytosine/thymine dimer should have the structure *(35)*. On UV irradiation of a mixture of uridine and thymidine in the ice matrix we obtained, in addition to the dimeric uridines and thymidines, several mixed thymidine/uridine dimers, which gave three other mixed thymine/uracil dimers as well as *(36)* on hydrolysis[21f,21g].

2.3. Other Photochemical Reactions[65]

Several authors have found evidence that other photochemical reactions occur as well as the photochemical addition of water to the 5,6-double bond and the for-



mation of dimers on UV irradiation of nucleic acids. On irradiation of DNA, dinucleotides and thymine in the ice matrix, photoproducts having a specific absorp-

[56] *K. C. Smith*, Biochem. biophysic. Res. Commun. *25*, 426 (1966).

[57] *A. Wacker, D. Weinblum, L. Träger*, and *Z. H. Moustafa*, J. molecular Biol. *3*, 790 (1961).

[58] *K. C. Smith* [48] described the formation of two mixed dimers.

[59] *D. Weinblum*, Biochem. biophysic. Res. Commun. *27*, 384 (1967).

[60] *A. Wacker, H. Dellweg*, and *E. Lodemann*, Angew. Chem. *73*, 64 (1961).

[61] *G. M. Blackburn* and *R. J. Davies*, J. Amer. chem. Soc. *89*, 5941 (1967).

[62] *G. L. Whitson, A. A. Francis*, and *W. L. Carrier*, Biochim. biophysica Acta *161*, 285 (1968).

[63] *A. J. Varghese* and *S. Y. Wang*, Science (Washington) *156*, 955 (1967).

[64] *K. C. Smith, B. Hodgkins*, and *M. E. O'Leary*, Biochim. biophysica Acta *114*, 1 (1966).

[65] Purines are much more resistant to UV radiation than pyrimidines. No specific reactions have been found; see *J. S. Connolly* and *H. Linschitz*, Photochem. and Photobiol. *7*, 791 (1968).

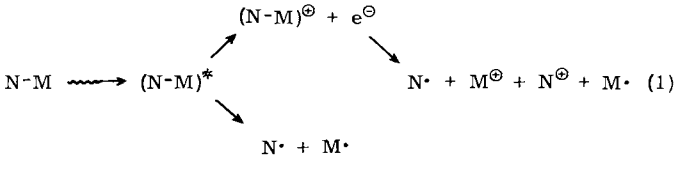
tion maximum at about 320 nm are formed [48,66–70]. *Wang* and *Varghese* [67,68] proposed the structure *(37)* for the product (λ_{max} = 316 nm) obtained on UV irradiation of thymine in the ice matrix [71]. When heated with acid, *(37)* is converted into *(38)*. A similar product having the structure *(39)* was obtained by these authors [68] on hydrolysis of UV-irradiated DNA. The uracil residue of the substance is presumably derived from the cytosine part of the DNA [68].

It is possible that we have obtained a product of uracil analogous to *(38)* on dimerization of uridine in the ice matrix [21e, 76]. On UV irradiation of thymine, the formation of dihydrothymine [73] and the oxidation of the CH_3 group [74, 75] were observed.

3. Action of Ionizing Radiation on Nucleic Acids and their Components [77]

Unlike the processes brought about by UV radiation, which are selectively influenced by the wavelength of the radiation used, the processes caused by ionizing radiation are much more complex. Several reaction possibilities must be considered:

The direct interaction of the radiation with the nucleic acid (N–M), which produces a positive charge on the nucleic acid strand at or near the point of impact, and leads to the formation of free radicals [eq. (1)].



(1)

The nature and the chemical behavior of the reaction products $(N-M)^{\oplus}$, N·, M·, $N^{\oplus}$, and $M^{\oplus}$ depend on the point of impact on the nucleic acid, *i.e.* the nucleic acid macromolecule can yield many different species $(N-M)^{\oplus}$, N·, M·, $N^{\oplus}$, and $M^{\oplus}$. The reaction is further complicated by the liberated electrons, which can reattack the nucleic acid.

The interaction between the radiation and the other cell components. Corresponding to equation (1), free-radical and ionic particles are formed, and these can again attack the nucleic acid.

The interaction between the radiation and the water. This leads to a small extent directly to HO and H radicals [78], but mainly to $H_2O^{\oplus}$ and electrons [equations (2) and (3)]. The electrons can now form further $H_2O^{\oplus}$ particles, whereupon they themselves are converted into electrons of lower energy ($e_p^{\ominus}$) and liberate further electrons ($e_s^{\ominus}$). The interaction between the ionizing radiation and the water thus leads to an avalanche of $H_2O^{\oplus}$ particles and electrons having various energies. The reaction sequence ends when the energy of the electrons has fallen below about 30 eV. The electrons are then "trapped" and stabilized as thermal electrons by hydration ($e^{\ominus}_{Hydr.}$). Their energy is dissipated *e.g.* in the formation of H radicals [eq. (6)] [79].

$$H_2O \rightsquigarrow H_2O^* \longrightarrow HO\cdot + H\cdot \quad (2)$$

$$H_2O \rightsquigarrow H_2O^* \longrightarrow H_2O^{\oplus} + e_p^{\ominus} \quad (3)$$

$$e_p^{\ominus} + H_2O \rightarrow \begin{cases} H_2O^* + e_p^{\ominus\prime} \\ H_2O^{\oplus} + e_p^{\ominus\prime} + e_s^{\ominus} \end{cases} \longrightarrow HO\cdot + H\cdot \quad (4)$$

$$H_2O^{\oplus} + H_2O \rightleftarrows HO\cdot + H_3O^{\oplus} \quad (5)$$

$$e^{\ominus}_{Hydr.} + H_3O^{\oplus} \rightleftarrows H\cdot + H_2O \quad (6)$$

If the irradiated systems contain oxygen, the reactions formulated in equations (7) to (9) also take place.

$$e^{\ominus}_{Hydr.} + O_2 \longrightarrow O_2^{\ominus} \quad (7)$$

$$H\cdot + O_2 \longrightarrow HO_2\cdot \quad (8)$$

$$HO_2\cdot + H_2O \rightleftarrows O_2^{\ominus} + H_3O^{\oplus} \quad (9)$$

The processes that can occur on irradiation of nucleic acids with ionizing radiation are as follows:

a) The "direct hit" on the nucleic acid in accordance with equation (1), which is difficult to detect chemically because of the many possibilities.

b) Reactions of the nucleic acid with the particles H·, HO·, $H_2O^{\oplus}$, and $e^{\ominus}_{Hydr.}$ formed from water and with reactive particles obtained from other cell components in accordance with eq. (1).

[66] *M. L. Pearson, F. P. Ottensmeyer,* and *H. E. Johns,* Photochem. and Photobiol. *4,* 739 (1965).

[67] *A. J. Varghese* and *S. Y. Wang,* Science (Washington) *160,* 186 (1968).

[68] *S. Y. Wang* and *A. J. Varghese,* Biochem. biophysic. Res. Commun. *29,* 543 (1967).

[69] *A. Haug,* Photochem. and Photobiol. *3,* 207 (1964).

[70] *H. E. Johns, M. L. Pearson, C. W. Helleiner,* and *D. M. Logan,* Symp. Fundamental Cancer Res. *18,* 29 (1964); Chem. Abstr. *63,* 3213 (1965).

[71] See [72].

[72] *H. E. Johns, M. L. Pearson, J. C. LeBlanc,* and *C. W. Helleiner,* J. molecular Biol. *9,* 503 (1964).

[73] *T. Yamane, B. J. Wyluda,* and *R. G. Shulman,* Proc. nat. Acad. Sci. USA *58,* 439 (1967).

[74] *R. Alcántara* and *S. Y. Wang,* Photochem. and Photobiol. *4,* 473 (1965).

[75] *S. Y. Wang* and *R. Alcántara,* Photochem. and Photobiol. *4,* 477 (1965).

[76] The possibility of formation of dimers with no cyclobutane ring has also been discussed by *P. V. Hariharan* and *H. E. Johns,* Photochem. and Photobiol. *8,* 11 (1968).

[77] a) See *J. J. Weiss* in *J. N. Davidson* and *W. E. Cohn:* Progress in Nucleic Acid Research. Academic Press, New York 1964, Vol. 3; b) The irradiation of nucleic acids and their components in the dry state or in the ice matrix at low temperatures and the ESR-spectroscopic study of the irradiation products have not been discussed here; see *A. Müller:* Progress in Biophysics and Molecular Biology. Pergamon Press, Oxford 1967, Vol. 17, p. 99; *A. D. Lenherr* and *M. G. Ormerod,* Biochim. biophysica Acta *166,* 298 (1968); *W. Bernhard* and *W. Snipes,* Proc. nat. Acad. Sci. USA *59,* 1038 (1968); J. chem. Physics *46,* 2848 (1967).

[78] See *E. J. Hart,* Science (Washington) *146,* 19 (1964); *D. C. Walker,* Quart. Rev. (chem. Soc., London) *21,* 79 (1967).

[79] Simplified description; for review of the primary processes and references to further literature, see *H. Heusinger,* Chimia *22,* 277 (1968).

The action of ionizing radiation on aqueous solutions of nucleic acids thus leads to a number of reactions that also depend on other factors such as the nature of the radiation, the radiation dose and its time distribution, the concentration, and the pH value of the solution, and that become increasingly complicated on irradiation of cells and larger biological objects. We have concentrated our investigations mainly on the chemical processes that take place on irradiation of nucleic acid components in aqueous solution [2c, 80]. Investigations by other workers had shown that large radiation doses (more than 10^6 rad) are required to obtain mg quantities of irradiation products. ^{60}Co sources and X-ray tubes, however, seldom yield more than 1000 rad/min, so that long irradiation times are necessary to obtain the quantities of substances required for the structure investigations. The result is that the thermally unstable irradiation products decompose during irradiation and cannot be isolated. The processes that occur in accordance with equations (4) to (6) on irradiation in aqueous solution can also be initiated independently of processes (2) and (3) by direct injection of electrons into the aqueous system [primary process corresponding to eq. (4)] [81].

We therefore carried out the irradiation as follows (see Fig. 1) [80]:

The electrons are accelerated in an accelerator tube by the voltage of an electrostatic generator (approx. 1 MV) and focused in a system of magnetic lenses. At the end of the system they emerge through an Al window (about 0.33 mm thick) into the air (energy of the electrons on emerging approx. 800 keV; diameter of the beam about 1—2 mm). The irradiation cell, situated a few centimeters behind the exit window is made of apparatus glass (3.5 × 4.5 × 10 cm) and has an Al window (0.02 mm thick and 2.8 cm in diameter) in its broad side; this window acts as a collecting electrode for the injected charges. The window is connected to an electronic current integrator, by means of which the number of electrons injected can be determined. We generally used doses of 8000 to 9000 rad/sec (irradiation times of about 1 to 3 min). The solutions were vigorously agitated with a magnetic stirrer during the irradiation, and were frozen immediately after irradiation. The solutions were then separated by thin layer, paper, or column chromatography; the products were generally identified by IR and UV spectroscopy, and in some cases also by NMR and mass spectroscopy.

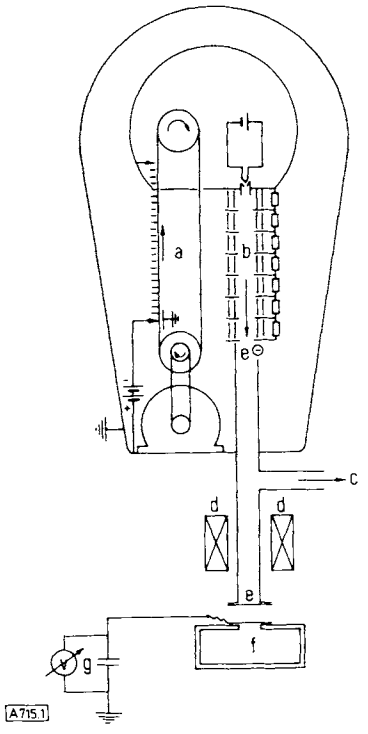


Fig. 1. Schematic drawing of the irradiation apparatus (Physikalisches Institut der Universität Würzburg). Drawing not to scale.

a: band generator, b: accelerator tube, c: vacuum pumps, d: magnetic beam guide elements, e: exit window, f: cell, g: current integrator.

3.1. Uracil, Thymine, and Cytosine

Irradiation of aqueous solutions of uracil, thymine, and cytosine in the absence of oxygen leads to the formation of the products indicated in Schemes 3 and 4, which result mainly from the attack of H and/or HO radicals and of $e^{\ominus}_{Hydr.}$ on the 5,6-double bond of the pyridine system [16,80,83–90].

Since the formation of the reactive particles and the reactivity of the pyrimidines used toward the radicals and $e^{\ominus}_{Hydr.}$ depend on the pH value of the solution, some of the reaction courses shown in Schemes 3 and 4 are also strongly influenced by the pH value [91]. These reactions can theoretically be formulated as proceeding both by attack of H or HO radicals and with the participation of $e^{\ominus}_{Hydr.}$. Since no systematic studies allowing a distinction between the two possibilities in every case have yet been reported, we have formulated both possibilities for uracil and thymine, whereas only the reaction involving free radicals is shown in the case of cytosine for the sake of clarity.

The irradiation of uracil leads by formal addition of two H radicals to dihydrouracil *(47a)* [92], by formal

[80] a) *B. Lösche*, Diplomarbeit, Universität Würzburg 1966; b) *G. Roos*, Diplomarbeit, Universität Würzburg 1967; c) *E. Fahr, W. Rohlfing*, and *B. Leitermeier*, unpublished results.

[81] Detailed differences in action may be due to the differences in the spectral distribution of the electrons in electron, X, and γ radiation. As was shown by calculation of the electron spectra by *D. Harder*, Intern. atomic Energy Agency, Vienna, Techn. Rep. Ser. *58*, 140 (1966), the differences between irradiation with electrons having an initial energy of 1 MeV and with ^{60}Co-γ radiation are very small. On the other hand, distinct differences are found in the electron spectra of X radiation for tube voltages of 100 and 200 kV.

[82] Schemes 3 and 4 show the most important substances formed on irradiation; for other irradiation products, see *R. Pleticha-Lansky* and *J. J. Weiss*, Analyt. Biochem. *16*, 510 (1966); *K. C. Smith* and *J. E. Hays*, Radiat. Res. *33*, 129 (1968).

[83] *G. Scholes* and *R. L. Willson*, Trans. Faraday Soc. *63*, 2983 (1967).

[84] *M. N. Khattk* and *J. H. Green*, Int. J. Radiat. Biol. *11*, 131 (1966); Chem. Abstr. *65*, 20476 (1966); *ibid. 11*, 137 (1966); Chem. Abstr. *65*, 20476 (1966); *ibid. 11*, 577 (1966); Chem. Abstr. *67*, 50837 (1967).

[85] *C. Nofre* and *A. Cier*, Bull. Soc. chim. France *1966*, 1326.

[86] *B. Ekert*, Nature (London) *194*, 278 (1962).

[87] *B. Ekert* and *R. Monier*, Nature (London) *188*, 309 (1960).

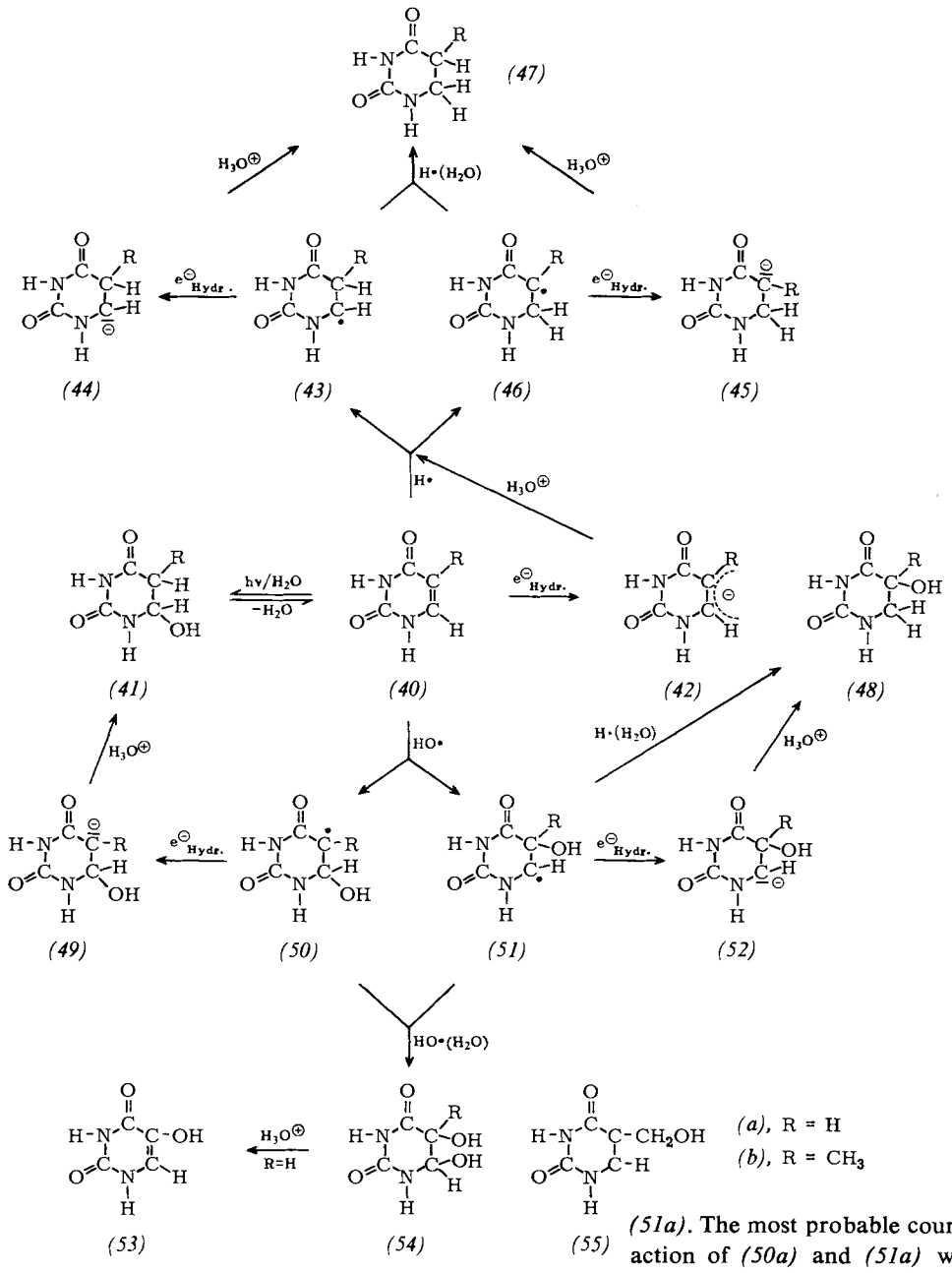
[88] *G. Scholes* and *J. Weiss*, Nature (London) *185*, 305 (1960).

[89] *N. P. Krushinskaya*, Radiobiologiya *5*, 645 (1965); Chem. Abstr. *64*, 3939 (1966).

[90] *S. Apelgot, B. Ekert*, and *A. Bouyat*, J. Chim. physique Physicochim. biol. *60*, 505 (1963).

[91] See *C. L. Greenstock, M. Ng*, and *J. W. Hunt*, Advances Chem. Ser. *1968*, No. 81, 397; *D. Heitkamp* and *O. Merwitz*, Z. Naturforsch. *23b*, 579 (1968).

[92] On irradiation of dihydrouracil in aqueous solution with ^{60}Co-γ radiation in the presence of air, the formation of uracil and of the uracil irradiation products *(41a)*, *(48a)*, *(53)* and *(54a)* was observed; see *G. Vincendon, A. Cier*, and *C. Nofre*, Bull. Soc. chim. France *1965*, 1997; *W. Snipes* and *W. Bernhard*, Radiat. Res. *33*, 162 (1968).



Scheme 3. Reactions occurring on irradiation of uracil and thymine [96] with ionizing radiation in deaerated aqueous solution [82].

addition of two HO radicals to the unstable uracil glycols *(54a)*, which readily change into isobarbituric acid *(53)*, and by addition of H and HO to 5- or 6-hydroxydihydrouracil *(48a)* or *(41a)*.

The mechanism of the formation of the hydroxy compounds *(48a)* and *(41a)* [93] has not been established. Simultaneous addition of H· and HO· seems unlikely, while successive addition of the two radicals is opposed by their short lives. A reaction in accordance with

$$(43a)/(46a) + H_2O \rightarrow (41a)/(48a) + H\cdot$$

and

$$(50a)/(51a) + H_2O \rightarrow (41a)/(48a) + H\cdot$$

should scarcely be possible, in view of the resonance stabilization of the radicals *(43a)/(46a)* and *(50a)/(51a)*. The most probable course in our view is the reaction of *(50a)* and *(51a)* with $e^{\ominus}_{Hydr.}$ to form the anions *(49a)* and *(52a)*, which then give *(41a)* and *(58a)* by protonation.

The reactions in the thymine system proceed similarly. In this case the stable *cis*- and *trans*-thymine glycols *(54b)* can be detected. The formation of *(55)* predominates at very high pH values, presumably because the resonance-stabilized system of the thymine dianion present at such pH values escapes the attack on the 5,6-C=C bond [94].

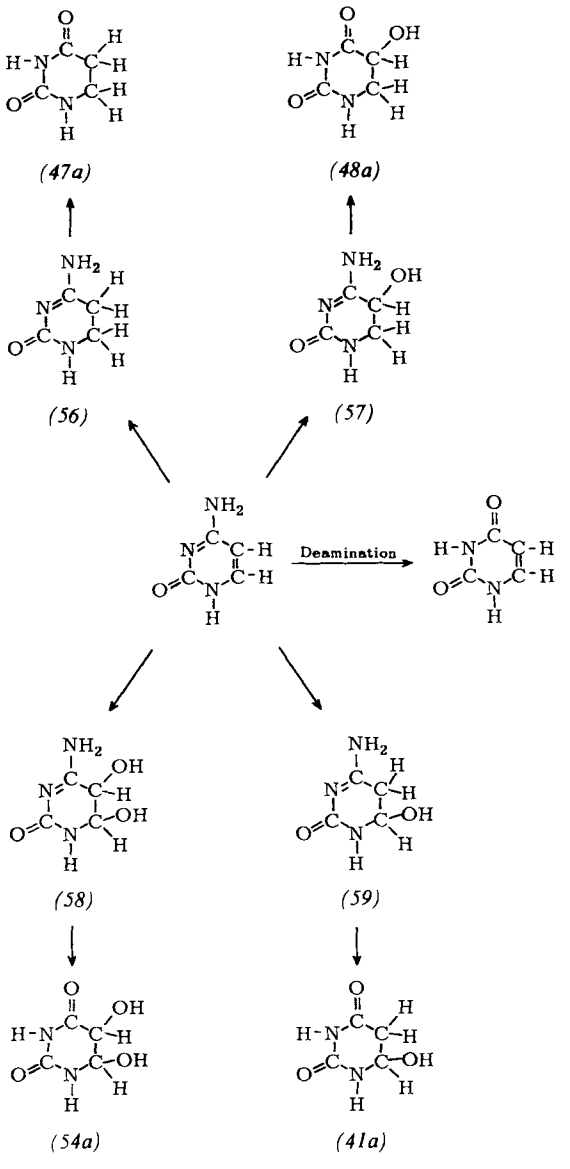
In the case of cytosine, the addition of H and/or HO radicals leads to derivatives of the unstable 5,6-dihydrocytosine system *(56)–(59)*, which undergo deamination to give the corresponding dihydrouracil derivatives *(41a)*, *(47a)*, *(48a)*, and *(54a)*.

If the irradiation is carried out in the presence of oxygen, peroxides are formed [86–90,95]. Thymine gave the peroxides *(60)* and *(61)*, the structures of which were

[93] The same is true of the corresponding compounds of thymine and cytosine.

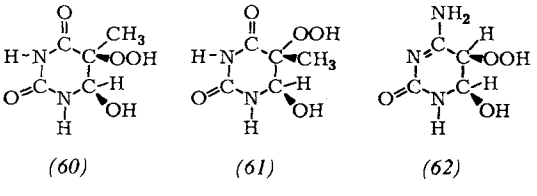
[94] *L. S. Myers jr., J. F. Ward, W. T. Tsukamoto*, and *D. E. Holmes*, Nature (London) *208*, 1086 (1965).

[95] *B. Ekert* and *R. Monier*, Nature (London) *184*, BA 58 (1959).



Scheme 4. Reactions in the irradiation of cytosine [96] with ionizing radiation in degassed aqueous solution [82].

proved by independent synthesis[95]. Similarly, cytosine gives the peroxide *(62)*, which decomposes into cytosine and uracil glycols[87]



3.2. Purines

Purines are more stable towards ionizing radiation than are pyrimidines[98a,99]. The attack by the radicals takes place at the imidazole ring and leads to the formation of the triamino derivatives *(63)* (R^2 = H)[98,99,101] (see Scheme 5). Deamination has also been observed.

In the irradiation of purine nucleosides and nucleotides the radicals partly attack the sugar residue[97–100,102b] – the purine base being released – but mainly attack the purine system with formation of the pyrimidine derivatives *(63)*[98,102b]. *(63b)* could be detected during irradiation of DNA. Peroxides were not found in the irradiations carried out in the presence of oxygen.

Keck and *Hagen* found that the radicals *(65)*, *(66)*, and *(67)* are formed during the irradiation of purine nucleotides[102] as a result of a primary attack by H or HO radicals on the C-5′ or C-8′ atom. Both *(66)* and *(67)* disproportionate to give *(68)* and *(69)*; *(69)* is converted into *(63)* (see Scheme 5).

4. Discussion of the Molecular Origin of Biological Radiation Damage[103]

The observations described in Sections 2 and 3 were obtained from the bases as well as their nucleosides and nucleotides, and we assume that they are not immediately applicable to nucleic acids (Section 2.1). We are therefore faced with the following questions:

(i) Are the photochemical and radiation-chemical findings for bases and their nucleosides and nucleotides valid only for these, or do these reactions also occur on irradiation of the nucleic acids?

(ii) Can definite types of biological damage be attributed to these photochemical and radiation-chemical reactions?

Both questions have been extensively studied[104], mainly for UV radiation, and very definite answers can be given in some respects. The question of the effects of ionizing radiation, on the other hand, is still largely unanswered.

[96] The reaction courses indicated here are also valid for the corresponding nucleosides and nucleotides [80]; as with the purine nucleosides and nucleotides, however, the sugar or sugar phosphate residue is again split off [97].

[97] The ribose residue is more sensitive than the deoxyribose residue [94]

[98] a) *G. Hems*, Nature (London) *186*, 710 (1960); b) *181*, 1721 (1958).

[99] *J. J. Conlay*, Nature (London) *197*, 555 (1963).

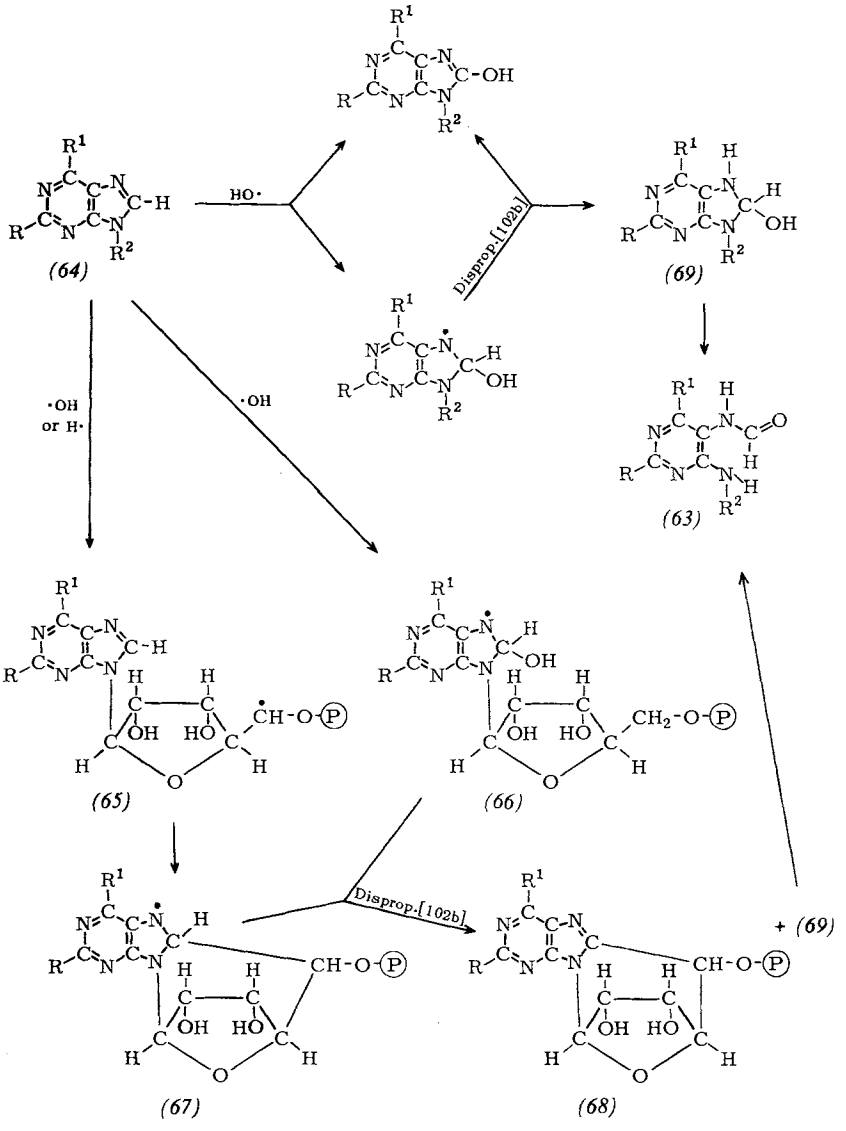
[100] *G. Scholes*, *R. L. Willson*, and *M. Ebert*, Chem. Commun. *1969*, 17.

[101] *C. A. Ponnamperuma*, Dissertation, University of California, 1962, cited in [102b].

[102] a) *K. Keck* and *U. Hagen* as well as *H. Friebolin*, Naturwissenschaften *53*, 304 (1966); b) *K. Keck*, Z. Naturforsch. *23b*, 1034 (1968).

[103] Abbreviations used: dimers are denoted by an arc [*e.g.* $\overset{\frown}{UU}$ = dimeric uracil (no information on the steric structure of the dimer)], and water addition products by * (*e.g.* C*); poly-U = polyuridylic acid, poly-C = polycytidylic acid, UpU = uridylyl-(3′-5′)-uridine, TpT = thymidylyl-(3′-5′)-thymidine, CpC = cytidylyl-(3′-5′)-cytidine; ATP, GTP = adenosine and guanosine triphosphates.

[104] See also [2, 134] and a) *E. M. Witkin*, Science (Washington) *152*, 1345 (1966); b) *K. C. Smith*, Proc. 3. Intern. Congr. Radiat. Res. Cortina d'Ampezzo, p. 756 (1966); c) *K. C. Smith*, Radiat. Res. Suppl. *6*, 54 (1966); d) *S. Y. Wang*, Federat. Proc. *24*, 71 (1965); e) *R. B. Setlow*, Science (Washington) *153*, 379 (1966); f) *D. Shugar*, Israel J. med. Sci. *1*, 1347 (1965); g) *W. Szybalski*, J. Arkansas med. Soc. *62*, 488 (1966).



(a), R = H, $R^1 = NH_2$,
R^2 = Ribosyl(deoxyribosyl) or Ribosyl(deoxyribosyl)phosphate
(b), R = NH_2, R^1 = OH,
R^2 = Ribosyl(deoxyribosyl) or Ribosyl(deoxyribosyl)phosphate

Scheme 5. Reactions in the irradiation of purine nucleotides with ionizing radiation in aqueous solution.

The observation that isolated bases dimerize on UV irradiation of DNA[105] *in vitro* and *in vivo* was made immediately after the discovery of the dimerization in the ice matrix. Thus *Wacker*, *Dellweg*, and *Weinblum*[107], as well as other workers[53,108,109], were able to show that a substance in the DNA hydrolyzate of UV-irradiated bacteria has the same chromatographic properties as dimeric thymine.

A mixed dimer $\widehat{UT}$, which is thought to result from the deamination of $\widehat{CT}$, has also been detected on irradiation of bacteria[60,61].

The dimerization that occurs between two adjacent bases of the same single strand to form the *cis/syn* dimer *(13a)* causes inhibition of the reduplication of the DNA[111] and alters the behavior of the nucleic acid on enzymatic hydrolysis. This leads to oligonucleotides containing the dimer, which cannot be further broken down by enzymes[111–113,123a], and the nature of which depends on the base composition

[105] The processes that occur on UV irradiation of dinucleotides have been studied by *H. E. Johns et al.* [12, 72, 51, 66, 76, 106] and supported by detailed kinetic measurements. These authors showed that TpT [103] forms two dimers. For UpU and CpC, addition of water (*e.g.* to form C*pC, CpC*, and C*pC*) and dimerization occur simultaneously. The $\widehat{CpC}$ dimers undergo deamination to give $\widehat{UpU}$ dimers.

[106] *I. H. Brown, K. B. Freeman*, and *H. E. Johns*, J. molecular Biol. *15*, 640 (1966).

[107] *A. Wacker, H. Dellweg*, and *D. Weinblum*, Naturwissenschaften *47*, 477 (1960).

[108] a) *D. L. Wulff*, J. molecular Biol. *7*, 431 (1963); b) *E. Ben-Hur* and *R. Ben-Ishai*, Biochim. biophysica Acta *166*, 9 (1968); c) *A. Wacker, H. Dellweg*, and *D. Jacherts*, J. molecular Biol. *4*, 410 (1962); d) *A. J. Varghese* and *S. Y. Wang*, Nature (London) *213*, 909 (1967).

[109] *E. Ben-Hur* and *R. Ben Ishai* [108b] found that some *trans/anti*-dimeric thymine *(14a)* is also formed on UV irradiation of DNA; see *G. M. Blackburn* and *R. J. H. Davies*, Biochem. biophysic. Res. Commun. *22*, 704 (1966).

[110] *M. Pearson, D. W. Whillans, J. C. LeBlanc*, and *H. E. Johns*, J. molecular Biol. *20*, 245 (1966).

[111] *P. Howard-Flanders*, Idengaku Zasshi, Suppl. *40*, 256 (1965); Chem. Abstr. *65*, 12536 (1966).

[112] *R. B. Setlow, W. L. Carrier*, and *F. J. Bollum*, Biochim. biophysica Acta *91*, 446 (1964).

[113] *H. Dellweg*, Strahlentherapie *135*, 504 (1968); Chem. Abstr. *69*, 8449 (1968).

of the DNA and on the wavelength and dose of the radiation used.

The formation of dimers in the DNA permits an interpretation of the well known reactivation of UV-damaged microorganisms (reactivation by short-wave UV radiation, enzymatic "dark reactivation", photo-reactivation) [114].

On *reactivation by irradiation with short-wave UV radiation* (about 230 nm), the dimers are broken down into monomers [115]; the quantity of dimeric thymine formed in DNA on UV irradiation accordingly depends on the wavelength of the radiation [116, 132e] (see Section 2.2.1).

The *enzymatic reactivation* (also called "*dark reactivation*" to distinguish it from photo-reactivation) is one of the most interesting reactivation phenomena known [117] (Fig. 2). Attack by one enzyme results in cleavage of a phosphate linkage of the DNA double strand that was damaged by the dimerization [(a) and (b)]. Another enzyme cuts out the dimeric portion, starting at the dimeric nucleotide, together with a few other attached nucleotides [(c)]. The portion removed is replaced by resynthesis (DNA polymerase) with the undamaged DNA strand as a pattern [(d)]. Another enzyme (polynucleotide ligase) then closes the 3′/5′ bond.

The enzymatic dark reactivation also explains the widely differing resistances of bacteria to UV radiation. The radiation-resistant bacteria contain enzymes that can repair the damage caused by UV radiation by the above or similar mechanisms.

In *photo-reactivation*, the radiation damage is repaired by irradiation with visible light (350–420 nm) [118]; photo-reactivating enzymes act as sensitizers and bring about the photochemical cleavage of the dimer into monomer [119].

According to *Wacker et al.*, similar reactivations occur with visible light and uranyl acetate or H_2O_2 [120]. Poly-U can also be reactivated [121] with H_2O_2 or uranyl acetate in the absence of visible light [120b].

It is not certain whether and to what extent photochemical addition of water occurs on UV irradiation of nucleic acids [122]. It appears to take place only in nucleic acids that do not consist of double strands [110, 123], but also appears to be possible to a small extent in DNA [124] by local cleavage of the double strand and dimerization (cleavage of the double strand at the dimerization site, followed by addition of water to adjacent cytosine molecules) [123a].

The possible biological importance of the photochemical addition of water has been studied by *Grossman*,

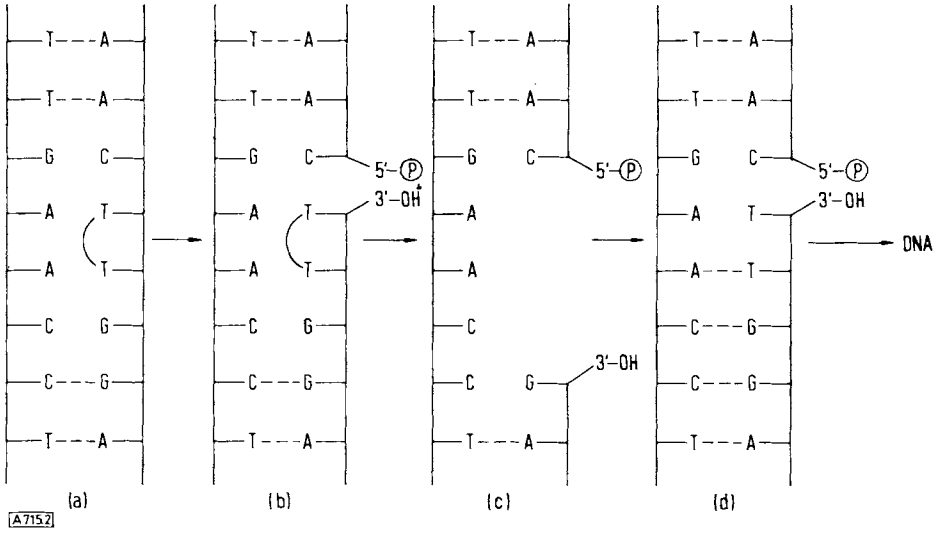


Fig. 2. Scheme of enzymatic dark reactivation [for explanation of (a)–(d) see text].

[114] Reactivation by simply raising the temperature has been described by *I. Pietrzykowska* and *D. Shugar*, Acta biochim. polon. *11*, 79 (1964).

[115] *R. B. Setlow* and *J. K. Setlow*, Proc. nat. Acad. Sci. USA *48*, 1250 (1962).

[116] *D. L. Wulff*, Biophysic. J. *3*, 355 (1963).

[117] a) *W. L. Carrier* and *R. B. Setlow*, Biochim. biophysica Acta *129*, 318 (1966); b) *M. E. Boling* and *J. K. Setlow*, *ibid. 123*, 26 (1966); c) *R. Elder* and *R. F. Beers jr.*, Federat. Proc. *23*, 373 (1964); d) *S. Aoki*, *R. P. Boyce*, and *P. Howard-Flanders*, Nature (London) *209*, 686 (1966); e) *P. T. Emmerson* and *P. Howard-Flanders*, Biochim. biophysic. Res. Commun. *18*, 24 (1965).

[118] See *A. A. Lamola*, J. Amer. chem. Soc. *88*, 813 (1966), and further literature cited there.

[119] The *cis/syn* dimer *(13a)* is broken down into the monomer, whereas the dimer *(14a)* is not [108b].

[120] a) *A. Wacker* and *A. Gerstenberger*, Angew. Chem. *75*, 916 (1963); Angew. Chem. internat. Edit. *2*, 689 (1963); b) *A. Wacker* and *P. Chandra*, Studia biophysica *3*, 239 (1967).

[121] The cleavage of dimers *in vitro* and *in vivo* by fast electrons or γ radiation has been detected by: *V. Greulich*, *D. Hartmann*, and *B. Schmidt*, Z. Naturforsch. *23b*, 755 (1968); *D. Barszcz*, *Z. Tramer*, and *D. Shugar*, Acta biochim. polon. *10*, 9 (1963); *B. Schmidt*, *D. Hartmann*, *K. Grossgebauer*, and *W. Schumacher*, Nature (London) *199*, 504 (1963); Naturwissenschaften *50*, 473 (1963); *E. R. Lochmann*, *ibid. 50*, 474 (1963); *R. A. Deering* and *W. Snipes*, Biophysic. J. *8*, 326 (1968).

[122] See the discussions in a) *L. Grossman*, Photochem. and Photobiol. *7*, 727 (1968); b) *G. D. Small*, *M. Tao*, and *M. P. Gordon*, J. molecular Biol. *38*, 75 (1968).

[123] a) *M. Pearson* and *H. E. Johns*, J. molecular Biol. *20*, 215 (1966); b) *P. V. Hariharan* and *H. E. Johns*, Photochem. and Photobiol. *7*, 239 (1968).

[124] Since segments of single strands occur for short periods during reduplication of DNA, there is a possibility of addition of water during this phase.

Ono, and *Wilson* [125], *Ottensmeyer* and *Whitmore* [126b], and *Wacker et al.* [126a]. The results can be partly interpreted by assuming that 6-hydroxydihydrouracil (U*), as a component of an RNA codon, behaves as cytosine in the enzymatic protein synthesis *in vitro* [126c]. In agreement with this, the incorporation of GTP as well as ATP has been observed in the enzymatic synthesis of polyadenylic acid with UV-irradiated poly-U as the pattern [125b] (see Fig. 3).

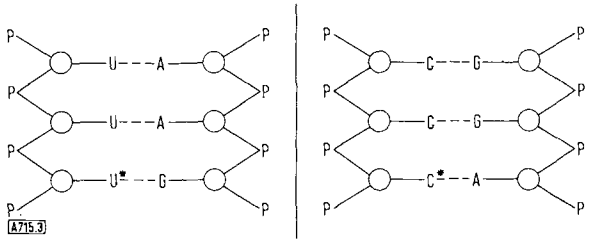


Fig. 3. Scheme of the effect of addition of water to uracil and cytosine in the nucleic acid double strand.

Similarly, the 6-hydroxydihydrocytosine part (C*) [125b, 125c] of UV-irradiated polycytidylic acid causes the incorporation of ATP in the enzymatic synthesis of polyguanylic acid, *i.e.* the C* part codes in the same way as uracil. This effect is not due to conversion of cytosine into uracil in accordance with the reaction sequence *(4)→(6)→(3)→(1)* (Section 2.1), as is shown by the reversibility of the findings; on heating at 37 °C, the poly-C* is converted back into poly-C [127], which causes the incorporation of GTP only.

These results indicate that any 6-hydroxydihydrocytosine parts formed in the DNA cause the incorporation of adenine instead of guanine into the complementary strand, and so lead to "error signals"* in the reading of the genetic code [128].

Several experimental observations indicate that in addition to dimerization and the addition of water UV radiation also causes other effects in nucleic acids, the nature of which is still largely unknown. Some of the effects observed were the breakdown of the nucleic acid strand, breakdown of the intermolecular and intramolecular main valence bridges between nucleic acid strands, and changes in the secondary structure [129]. Whereas breaks in one strand of a DNA double strand can presumably be repaired as in dark reactivation, breaks in the double strand and main valence bridges between the strands are probably irreparable.

The photochemical addition of amino acids to the pyrimidine parts of nucleic acids has been investigated by *K. C. Smith et al.* [64, 130]. The results show that photochemical crosslinking between the nucleic acid and the protein must also be taken into account in the interpretation of UV-radiation damage [131]. The formation of UV products having the characteristic maximum at about 320 nm (see Section 2.3) on irradiation of nucleic acids has been observed by various authors. Bacterial spores give only a little dimer on UV irradiation [132a,b]. Irradiation products of unknown structure are formed that correspond in their chromatographic behavior to those obtained on UV irradiation of DNA in the dried state or in the ice matrix [132].

All the available chemical, physical, and biological evidence on the molecular interpretation of UV-radiation damage adds up to give the following picture:

i) Dimerization and the addition of water play a decisive role in many cases. The contributions of these processes to radiation damage depends on the nature of the nucleic acid, the irradiation conditions, and the wavelength and dose of the radiation [133]. Apart from these two processes, it is also necessary to consider photochemical chain cleavage, main-valence crosslinking between nucleic acid strands, reactions between nucleic acids and proteins, and other, as yet unknown reactions of the pyrimidine bases.

ii) The dimerization prevents reduplication of the DNA; addition of water (and possibly also dimerization [134]) leads *inter alia* to the UV mutations.

Knowledge of the molecular causes of the biological damage caused by ionizing radiation is still far from complete, since ionizing radiation can lead simultaneously to various types of damage [135]. The observations

[125] a) *L. Grossman*, Proc. nat. Acad. Sci. USA *50*, 657 (1963); b) *J. Ono*, *R. G. Wilson*, and *L. Grossman*, J. molecular Biol. *11*, 600 (1965); c) *L. Grossman*, *J. Ono*, and *R. Wilson*, Symp. Fundamental Cancer Res. *18*, 107 (1964); Chem. Abstr. *63*, 3221 (1965), Federat. Proc. *24*, p. 80 (1965).

[126] a) *A. Wacker*, *M. Ishimoto*, *P. Chandra*, and *R. Selzer*, Z. Naturforsch. *19b*, 406 (1964); see also *A. Wacker*, *P. Chandra*, *P. Mildner*, and *H. Feller*, Biophysik *4*, 283 (1968); b) *F. P. Ottensmeyer* and *G. F. Whitmore*, J. molecular Biol. *38*, 1 (1968); *ibid.* *38*, 17 (1968); c) the $\widehat{UU}$ codes in the same way as the base pair GU and unmodified UU.

[127] An alternative interpretation of the above observations is that C* is deaminated on heating to give the thermally very stable U* [8, 9], which codes in the same way as cytosine.

[128] The direct photochemical deamination of cytosine to form uracil [15] should, in principle, also be considered here.

[129] a) *D. M. Logan* and *G. F. Whitmore*, J. molecular Biol. *21*, 1 (1966); b) *P. S. Sarin* and *H. E. Johns*, Photochem. and Photobiol. *7*, 203 (1968).

[130] a) *K. C. Smith* and *R. T. Aplin*, Biochemistry *5*, 2125 (1966); b) *K. C. Smith* and *D. H. C. Meun*, *ibid.* *7*, 1033 (1968); c) *K. C. Smith*, Photochem. and Photobiol. *7*, 651 (1968).

[131] *J. Goddard*, *D. Streeter*, *C. Weber*, and *M. P. Gordon*, Photochem. and Photobiol. *5*, 213 (1966), *ibid.* *8*, 81 (1968), observed the bonding of protein subunits to RNA on UV irradiation of tobacco mosaic virus.

[132] a) *J. E. Donellan jr.* and *R. B. Setlow*, Science (Washington) *149*, 308 (1965); b) *K. C. Smith* and *H. Yoshikawa*, Photochem. and Photobiol. *5*, 777 (1966); c) *R. S. Stafford* and *J. E Donnellan jr.*, Proc. nat. Acad. Sci. USA *59*, 822 (1968), see also *J. W. Longworth*, *ibid.* *59*, 829 (1968); d) *R. O. Rahn* and *J. L. Hosszu*, Photochem. and Photobiol. *8*, 53 (1968); *7*, 637 (1968); e) *R. B. Setlow*, *ibid.* *7*, 643 (1968).

[133] It has been found, for example, that dimerization accounts for 90% of the UV damage with low doses, but only about 50% with high doses.

[134] See *E. M. Witkin*, Radiat. Res. Suppl. *6*, 30 (1966).

[135] The polymerization of nucleotides by ionizing radiation to form polynucleotides has been observed by various authors, *e.g.*, *S. Fischer* and *A. Ohlbaum*, Inter-Amer. Symp. Peaceful Appl. Nucl. Energy *5*, 19 (1965); Chem. Abstr. *63*, 11967 (1965); *A. Aguilera*, *E. Colombara*, *R. Jiménez*, and *J. Toha*, Biochim. biophysica Acta *95*, 569 (1965); *A. Aguilera*, *Z. Gampel*, *M. Pieber*, and *J. Tohá*, Photochem. and Photobiol. *7*, 711 (1968).

described in Section 3, the results of unpublished experiments[80], and knowledge of the results of UV irradiation suggest the following possibilities[136]:

i) A "direct hit" by the radiation can lead to irreparable breakdown of the nucleic acid molecule.

ii) The breakdown of one strand of the DNA double strand can in certain circumstances (depending on the nature of the break) be repaired by a mechanism corresponding to enzymatic reactivation.

iii) The addition of water (*via* H and HO radicals) to the cytosine portion of the DNA leads to a change in the base pairing during the reduplication of the DNA; this could lead *inter alia* to the mutations resulting from ionizing radiation.

iv) The biological importance of other products [peroxides, dihydrothymine, dihydrouracil, thymine glycols, *etc.* (see Schemes 3 and 4)] formed on irradiation is largely unknown. It is necessary to consider both blockage of the reduplication of the DNA at the modified base and the modification of the genetic code[137]. It is not known whether and how the cell is able to recognize and eliminate bases that have been "modified" in this way.

I am grateful to Dr. G. Dörhöfer, Dr. G. Fürst, Dr. H. Gattner, Dr. R. Kleber, B. Lösche, R. Pastille, H. Popp, P. Richter, Dr. W. Rohlfing, G. Roos, Dr. B. Sojka, H. Wieser, Frau B. Leitermeier, and Fräulein E. Boebinger for their collaboration in our investigations.

We are indebted to Professor M. Scheer, Physikalisches Institut der Universität Würzburg, who made it possible for us to carry out the irradiations with ionizing radiation. We also thank Dr. T. Nowak and Dr. W. Järisch for carrying out the irradiations and Dozent Dr. D. Harder and Dr. A. Przybylski for their advice. Special thanks are due to Professor G. Hartmann, Institut für Biochemie der Universität Würzburg, for his advice and suggestions. We are grateful to the Deutsche Forschungsgemeinschaft and to the Verband der Chemischen Industrie (Fonds der Chemischen Industrie) for their generous support of these investigations.

Received: March 27, 1969 [A 715 IE]
German version: Angew. Chem. *81*, 581 (1969)
Translated by Express Translation Service, London.

[136] See *W. C. Summers* and *W. Szybalski*, J. molecular Biol. *26*, 227 (1967); *A. Rafi, J. J. Weiss*, and *C. M. Wheeler*, Biochim. biophysica Acta *169*, 230 (1968); *M. Ullrich* and *U. Hagen*, Z. Naturforsch. *23b*, 1176 (1968), as well as [16].

[137] Cf. [122a].

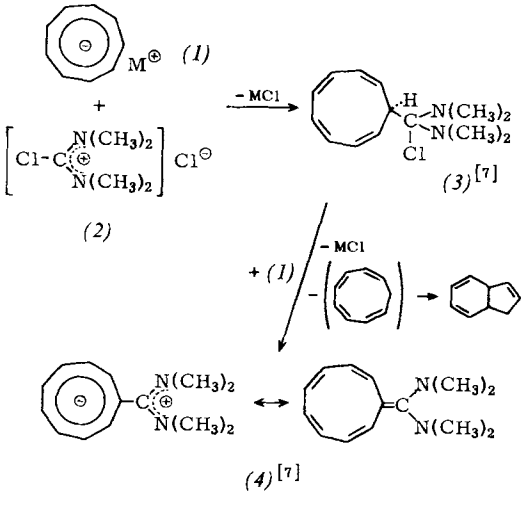
COMMUNICATIONS

10,10-Bis(dimethylamino)nonafulvene[**]

By *K. Hafner* and *H. Tappe*[*]

Dedicated to Professor Cl. Schöpf on the occasion of his 70th birthday

Li-, K- and $[(CH_3)_4N]$ cyclononatetraenides *(1)*[1] are the only monocyclic derivatives of the hypothetical cyclononatetraene that have been isolated so far[2]. Nonafulvenes, being cross-conjugated 10 π electron systems and homologs of the fulvenes, are of particular interest. Like the fulvene and isobenzofulvene systems[3], nonafulvenes should also be stabilized by electron-donating substituents on the exocyclic C-atom. The successful synthesis of 10,10-bis(dimethylamino)-nonafulvene *(4)* confirms this presumption.



Compound *(1)*, M = Li, reacts with *N,N,N',N'*-tetramethylchloroformamidinium chloride *(2)*[4] at −70 °C in tetrahydrofuran to give the so far non-isolable cyclononatetraene derivative *(3)*, which, in the presence of an excess of *(1)*, is rapidly converted into the nonafulvene *(4)* as yellow crystals that are sensitive to light and air [yield 7%; m.p. 109–110 °C (from ethanol)][5]. In addition, 3a,7a-dihydroindene[6] is formed as a result of protonation of *(1)* and subsequent valence isomerization of the cyclononatetraene thus formed. Elemental analysis and molecular weight determination confirm the constitution of *(4)*; its configuration, however, has not yet been elucidated[7]. During quantitative microhydrogenation, compound *(4)* takes up H_2 in amounts calculated for five double bonds. The mass spectrum of *(4)* shows several, but uncharacteristic, fragmentation peaks in addition to the molecular peak *m/e* = 216.

UV and NMR spectra of *(4)* indicate the presence of a temperature- and solvent-dependent conformational equilibrium. In *n*-hexane at room temperature, compound *(4)* absorbs at 330 nm (log ε = 4.34), whereas in methylene chloride it absorbs at 403 (3.90), 340 (4.05), 298 (4.05), and 244 (4.28) nm (log ε), and in tetrahydrofuran at 334 (4.19) and at 240 (4.15) nm (log ε). Although the UV spectrum of *(4)* in *n*-hexane remains unchanged at low temperatures, in methylene chloride the extinction of the bands at 403, 296, and 244 increases whereas the absorption maximum of the band at 340 decreases; at −80 °C that at 340 disappears. [λ_{max} at 0 °C: 403 (3.9), 340 (4.0), 296 (4.1), 244 (4.3); at −35 °C: 403 (3.9), 296 (4.2), 244 (4.4); at −80 °C[7a]: 403 (4.1), 294 (4.4), 244 (4.7) nm (log ε)]. In tetrahydrofuran at temperatures below 0 °C, two additional maxima appear at 404 and 296 nm whose intensities increase on lowering the temperature [λ_{max} at −35 °C[7a]: 404 (3.8), 335 (4.1), 296 (4.1), 244 (4.4); at −80 °C: 404 (4.1), 335 (4.0), 296 (4.3), 244 (4.6) nm (log ε)].

The NMR spectrum of *(4)* (in CD_2Cl_2) (Fig. 1) at 35 °C shows a sharp singlet at τ = 7.22 for the twelve methyl

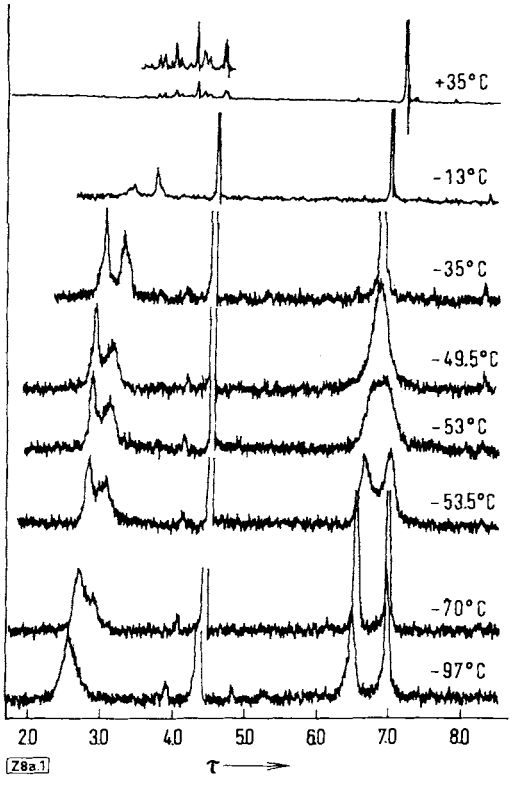
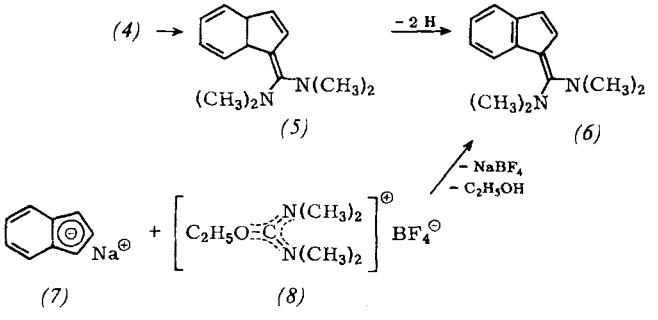


Fig. 1. NMR spectra of 10,10-bis(dimethylamino)nonafulvene *(4)* at various temperatures in CD_2Cl_2 (60MHz; tetramethylsilane as internal standard).

protons, in addition to a complicated multiplet between τ = 3.63 and 4.67 for the eight ring protons. At lower temperatures the multiplet of the ring protons is shifted to lower field with diminution of the fine structure, while the singlet of the methyl protons is split into a doublet (coalescence point: *ca.* −53 °C). This may be ascribed to either restricted rotation of the C—N bonds or formation of an unsymmetrical conformation of the nine-membered ring relative to the dimethylamino groups at low temperatures[8]. The temperature-dependent changes in the NMR and UV spectra of *(4)* are reversible.



As a derivative of the hypothetical cyclononatetraene, compound *(4)* undergoes an irreversible thermal valence isomerization in benzene, slowly at room temperature but rapidly at 60 °C, to give the 3a,7a-dihydroindene derivative *(5)* [yield 50%; yellow oil, sensitive to oxygen; b.p. 80 °C/0.003 torr; UV spectrum (in *n*-hexane): 302 (4.17), 270 (4.12), 260 (4.06) nm (log ε); NMR spectrum (in $CDCl_3$); doublet centered at τ = 7.34 ($4CH_3$), multiplets centered at τ = 6.17 (H-3a, H-7a), at 4.55 (H-2, H-3, H-4, H-5, H-6), and at 3.65 (H-7)]. The NMR spectrum of *(5)* does not provide sufficient data for a differentiation between the *cis* and *trans* isomer. Oxidation of *(5)* with active lead dioxide[9] leads to the formation of 6,6-bis(dimethylamino)benzo[*b*]fulvene[1-(tetramethyldiaminomethylene)indene] *(6)*, which can also be prepared from sodium indenide *(7)* and bis(dimethylamino)ethoxycarbonium fluoroborate *(8)*[10] [yellow crystals, sensitive to light, m.p. 55 °C; UV spectrum (in *n*-hexane): 375 (4.36), 279 (4.08), 255 (3.96) nm (log ε); NMR spectrum (in $CDCl_3$): singlet at τ = 6.99 ($4CH_3$), AB system at τ = 3.32 and 3.42 (2H) (J_{AB} = 5 Hz), multiplet centered at τ = 2.75 (4 benzenoid H)].

Received: June 6, 1969 [Z 8a IE]
German version: Angew. Chem. *81*, 564 (1969)

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61 Darmstadt, Schlossgartenstr. 2 (Germany)

[**] We are grateful to Badische Anilin- & Soda-Fabrik AG for kindly supplying the cyclooctatetraene.

[1] *T. J. Katz* and *P. J. Garrat*, J. Amer. chem. Soc. *86*, 5194 (1964); *E. A. LaLancette* and *R. E. Benson*, *ibid. 87*, 1941 (1965); *H. E. Simmons*, *D. B. Chesnut*, and *E. A. LaLancette*, *ibid. 87*, 982 (1965).

[2] *D. Lloyd* and *N. W. Preston*, Chem. and Ind. *1966*, 1039, reported on the synthesis of diazocyclononatetraene but the product could not be obtained in an analytically pure state; proof of structure was based on IR spectroscopic findings alone. The structure of the cyclononatetraene-$M(CO)_3$ complexes (M = Mo, W, Cr) prepared by *R. B. King* and *F. G. Stone*, J. Amer. chem. Soc. *82*, 4557 (1960), was, as far as we know, not unequivocally proved.

[3] *K. Hafner*, *K. H. Häfner*, *C. König*, *M. Kreuder*, *G. Ploss*, *G. Schulz*, *E. Sturm*, and *K. H. Vöpel*, Angew. Chem. *75*, 35 (1963); Angew. Chem. internat. Edit. *2*, 123 (1963); *K. Hafner*, *K. H. Vöpel*, *G. Ploss*, and *C. König*, Liebigs Ann. Chem. *661*, 52 (1963); *K. Hafner*, *G. Schulz*, and *K. Wagner*, *ibid. 678*, 39 (1964); *K. Hafner* and *W. Bauer*, Angew. Chem. *80*, 312 (1968); Angew. Chem. internat. Edit. *7*, 297 (1968).

[4] *H. Eilingsfeld*, *G. Neubauer*, *M. Seefelder*, and *H. Weidinger*, Chem. Ber. *97*, 1232 (1964).

[5] Correct analytical results were obtained for all the products described.

[6] *St. W. Staley* and *T. J. Henry*, J. Amer. chem. Soc. *91*, 1239 (1969); *P. Radlick* and *W. Fenical*, *ibid. 91*, 1560 (1969); further literature cited therein.

[7] The all *cis*-configuration given in the scheme for *(3)* and *(4)* is arbitrary.

[7a] The average error of the extinction coefficients in the low-temperature spectra is about ±5–10%.

[8] We thank Dr. *D. Jung* for recording and discussing the NMR spectra.

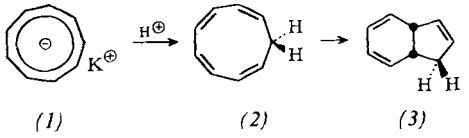
[9] *R. Kuhn* and *J. Hammer*, Chem. Ber. *83*, 413 (1950).

[10] *H. Meerwein*, *W. Florian*, *N. Schön*, and *G. Stopp*, Liebigs Ann. Chem. *641*, 1 (1961).

cis,cis,cis,cis-1,3,5,7-Cyclononatetraene

By *G. Boche*, *H. Böhme*, and *D. Martens*[*]

Cyclononatetraenes possibly occur as intermediates in the thermal and in the photochemical valence isomerization of *cis*-bicyclo[6.1.0]nona-2,4,6-triene or various 9- and 9,9'-substituted *cis*-bicyclo[6.1.0]nona-2,4,6-trienes into *cis*- and *trans*-bicyclo[4.3.0]nona-2,4,7-trienes (*cis*- and *trans*-dihydroindenes)[1]. Furthermore, *cis,cis,cis,cis*-1,3,5,7-cyclononatetraene[1g] *(2)* and 9-methyl-*cis,cis,cis,cis*-1,3,5,7-cyclononatetraene[1k] are assumed to occur as non-isolable primary products in the protonation and methylation of the cyclononatetraenyl anion *(1)*. *King* and *Stone*[2] have reported that the tricarbonylmetal complexes obtained in small yield by reaction of dihydroindene with $Cr(CO)_6$, $Mo(CO)_6$, and $W(CO)_6$ probably contain *cis,trans,cis,trans*-1,3,5,7-cyclononatetraene as olefinic ligand.



We have found that the light-yellow *cis,cis,cis,cis*-1,3,5,7-cyclononatetraene *(2)* is formed in good yield when the potassium salt *(1)* is protonated with 0.1 N acetic acid at 0 °C.

Compound *(2)* always contains about 2—4% *cis*-dihydroindene *(3)*, which presumably is formed during the working up and distillation at 0 °C. The method of preparation and the catalytic hydrogenation at 0 °C that leads to formation of cyclononane, as well as the practically quantitative valence isomerization to *(3)* [3], afford chemical proof of the structure of *(2)*. The half-life of the first-order rearrangement *(2)*→*(3)* is 16 min at 35 °C; the activation parameters, determined at temperatures between 18 °C and 35 °C, have the following values: $\Delta H^{\neq} = 19.8 \pm 1$ kcal/mole, $\Delta S^{\neq} = -10.4$ e.u. On the basis of orbital symmetry considerations [4,5], simple disrotatory ring closure of the type $6\pi \rightarrow 4\pi + 2\sigma$ to *(3)* is to be expected in the case of the strained compound *(2)*. Moreover, *(2)* regenerates *(1)* on treatment with potassium *tert*-butoxide in tetrahydrofuran at temperatures below 0 °C.

Spectroscopic findings confirm the structure of *(2)*. The NMR spectrum of *(2)* (in CCl_4) contains the expected absorption bands of the eight olefinic protons (multiplet with intense signal at $\tau = 4.28$) and of the two CH_2 protons (broadened triplet at $\tau = 6.95$, apparent coupling constant $J = 5.5$ Hz). The low-intensity, broadened absorption band of the C=C stetching vibration occurs in the IR spectrum (in CCl_4) at 1632 cm^{-1}; the out-of-plane deformation vibrations of the *cis* double bonds give rise to a band at 700 cm^{-1}. Essentially no absorption takes place in the region of the C—H deformation vibrations of the *trans* double bond. The UV spectrum of *(2)* (in ether) is unusual for a tetraene having four alternating double bonds but is, however, similar to that of cyclooctatetraene [6,7]: up to 2100 Å it shows only increase of the extinction towards shorter wave lengths with a shoulder at 2450 Å ($\varepsilon_0 = 2600$). An absorption maximum does not occur. The spectrum is consistent with *(2)* having a relatively rigid boat configuration in which the neighboring double bonds are not conjugated.

Reaction of *(2)* with silver nitrate in water leads to the formation of a 1:2 complex, m.p. 86—88 °C. That *(2)* occurs in the complex as a ligand was confirmed by displacement of the cycloolefin by aqueous ammonia at 0 °C; pure *(2)* is recovered. The NMR spectrum of the complex (recorded in D_2O at 0 °C) also proves the presence of *(2)* as ligand. In contrast to the spectrum of free *(2)* it shows the shifted signals of the eight olefin protons (multiplet, centered at $\tau = 3.6$) and the two methylene protons (multiplet centered at $\tau = 6.64$).

The thermal rearrangement of *cis*-bicyclo[6.1.0]nona-2,4,6-triene affords *cis*- and *trans*-dihydroindene in the ratio 9:1 [1a,1c,1h]. Synchronous ring opening and ring closure should convert the highly strained *cis,cis,cis,trans*-1,3,5,7-cyclononatetraene into *trans*-dihydroindene [4,5]. The questions (i) whether *(2)* also occurs as intermediate and rapidly isomerizes to *(3)* and (ii) how *(2)* is actually formed have yet to be answered.

Received: June 10, 1969 [Z 8b IE]
German version: Angew. Chem. *81*, 565 (1969)

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Crystal Structure of Uridine 2′,3′-*O*,*O*-Cyclophosphorothioate

By *W. Saenger* and *F. Eckstein* [*]

We have recently accomplished the synthesis of uridine 2′,3′-*O*,*O*-cyclophosphorothioate [1] and successfully isolated one of the two diastereomers by crystallization [2]. This isomer *(1)* is a substrate for pancreatic ribonuclease with the same K_m value as uridine 2′,3′-cyclophosphate [2]. In the presence of methanol, the enzyme converts the substrate into uridine 3′-*O*-(*O*-methyl)phosphorothioate, which we have also been able to obtain in crystalline form. Knowledge of the absolute configurations of these two compounds would deepen our understanding of the course of enzymatic methanolysis and hydrolysis.

The triethylammonium salt of *(1)* crystallizes from ethanol in the form of prisms in the orthorhombic space group $P2_12_12_1$, the unit cell having the dimensions $a = 12.495$, $b = 7.079$, $c = 22.574$ Å. About 1200 reflection intensities were measured on a four-circle diffractometer and the data were corrected for geometric factors but not for absorption. The

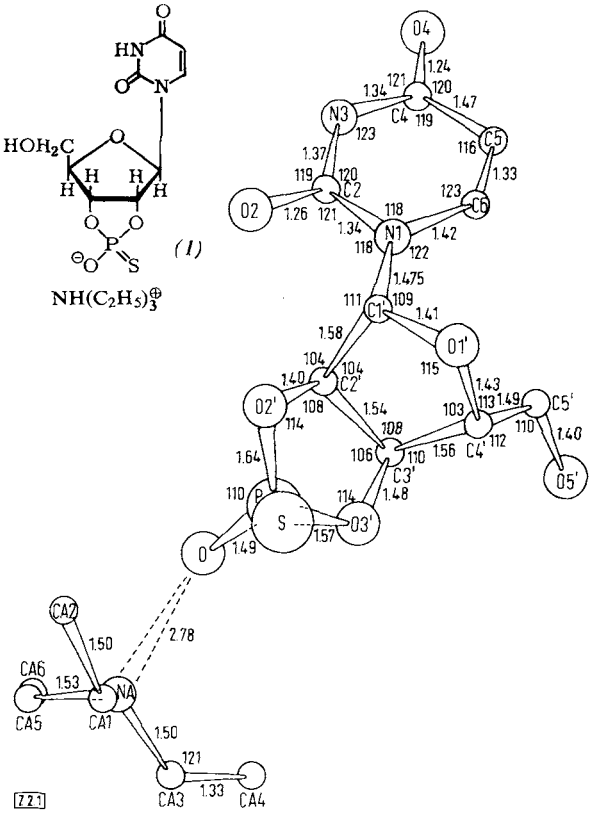


Fig. 1. Crystal structure of triethylammonium uridine 2′,3′-*O*,*O*-cyclophosphorothioate *(1)*. Projection on 001. Standard deviations for bond lengths and angles are ±0.01 Å and ±0.7 ° for bonds involving phosphorus, otherwise ±0.02 Å and ±1.0 °. The bond lengths (Å) and angles (°) not given in the Figure are:

P—S	= 1.96	CA3—NA—CA1	= 105
NA—CA1	= 1.53	CA3—NA—CA5	= 111
CA5—CA6	= 1.37	NA—CA1—CA2	= 109
O2′—P—S	= 112	CA1—NA—CA5	= 106
O2′—P—O3′	= 96	NA—CA5—CA6	= 115
O3′—P—S	= 110	C2′—C1′—O1′	= 106
O3′—P—O	= 109		
S—P—O	= 117		

structure of the molecule was determined by the "heavy-atom" method. Two cycles of isotropic and three cycles of anisotropic full-matrix refinement by the method of least squares led to an R factor of 0.094 for the 986 strongest reflections. A projection of the molecule on the 001 plane is shown in Fig. 1.

The heterocyclic ring has a not uncommon geometry. The structural data found agree well with those obtained for 1-methyluracil[3] and uridine 5'-phosphate[4]. The ring atoms and all the substituents except C-1' lie in a planar arrangement, the maximum deviation from the "best" plane being 0.08 Å.

A considerable puckering of the ribose unit has been found in all the nucleosides investigated previously, one atom jutting out of the plane described by the other four atoms by about 0.6 Å[5,6]. In the case of *(1)*, however, C-3' is displaced from the "best plane" through C-4', O-1', C-1', and C-2' by only 0.15 Å; thus the ribose ring is almost planar and the substituents on C-1', C-2', C-3', and O-4' are staggered. Compared to nucleosides without 2',3'-cyclization[6], the bond lengths C-1'–C-2', C-2'–C-3', and C-3'–C-4' in *(1)*, but not C-4'–O-1' and O-1'–C-1', are therefore lengthened by about 0.06, 0.01, and 0.04 Å, respectively, whereas the bond angles in the ribose part of the molecule are changed only slightly. The bond length O-1'–C-1' is somewhat shorter than C-4'–O-1', as has always been found previously.

The bond lengths and angles found in the cyclophosphorothioate ring are similar to those found in methyl ethylene 1,2-cyclophosphate[7]. The configurations of the two molecules also show a close resemblance: the four atoms O-3', C-3', C-2', and O-2' are in a planar arrangement and the phosphorus atom is situated 0.23 Å from the plane on the same side as the oxygen atom O which is oriented away from the ribose, whereas the sulfur atom is found under the ribose in the *endo* position.

The P–S bond has predominantly double-bond character[8]; the P–O bond length is characteristic for $P-O^{\ominus}$[9]. This charge distribution is also indicated by the facts that the cation is unequivocally positioned opposite the oxygen atom O and that the O–N distance of 2.78 Å corresponds to a hydrogen bond.

The position of the heterocycle relative to the ribose corresponds to the *anti*-conformation. The angle of twist about the glycosidic bond, φ_{CN}, which was defined[10] as the dihedral angle C-6–N-1–C-1'–C-2', is 128.8 °.

The triethylammonium ion possesses almost trigonal symmetry. The interatomic distances C-A5–C-A6 and C-A3–C-A4 (and likewise C-5'–O-5' in the ribose group) are shortened[11] because the atoms C-A6, C-A4, and O-5' undergo considerable thermal vibrations.

Received: May 19, 1969 [Z 2 IE]
German version: Angew. Chem. *81*, 566 (1969)

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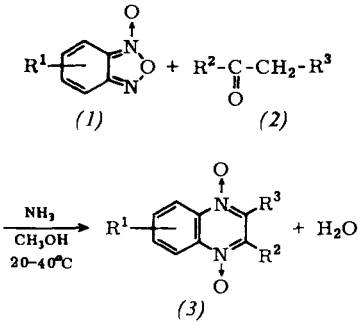
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New Syntheses of Quinoxaline and Phenazine Di-*N*-oxides

By *K. Ley*, *F. Seng*, *U. Eholzer*, *R. Nast*, and *R. Schubart*[*]

The benzofuroxanes *(1)*[1], which are readily accessible by dehydrogenation of *o*-nitroanilines with sodium hypochlorite, react with ketimines or aldimines or with ketones or aldehydes and primary amines or ammonia[2] to give quinoxaline di-*N*-oxides *(3)*. The reaction is of a general nature and is widely modifiable with respect to the carbonyl component.



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

R^1 = H, alkyl, CH_3O, C_2H_5O, halogen, COOR

R^2 = CH_3, H

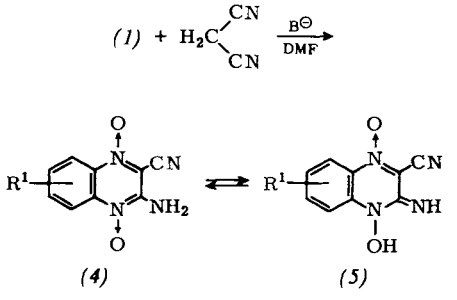
R^3 = *e.g.* alkyl, aryl; CH_3CO, XO–CO, X–NH–CO, X_2N–CO, XO–CO–CH_2, X–NH–CO–CH_2, X_2N–CO–CH_2, XC(=NOH);

R^2 and R^3 can also be coupled cyclically;

X = alkyl or aryl

Reaction of oxaloacetate [*(2)*, R^2 = R^3 = $COOC_2H_5$] and *(1)* (NH_3/CH_3OH, 20–40 °C) leads to the formation of *(3)* in which R^2 = R^3 = $CONH_2$. On reaction with potassium hydroxide, methylisoxazole is converted into the potassium salt of 1-cyanoacetone, which affords compound *(3)*, R^2 = CN, R^3 = CH_3, when reacted with *(1)* in the presence of NH_3/NH_4Cl[3]. Reaction of *(1)* and chloroacetaldehyde with primary amines leads to the formation of monoalkyl aminoquinoxaline di-*N*-oxides *(3)*, R^2 = H, R^3 = NH-alkyl or NH-cycloalkyl[4].

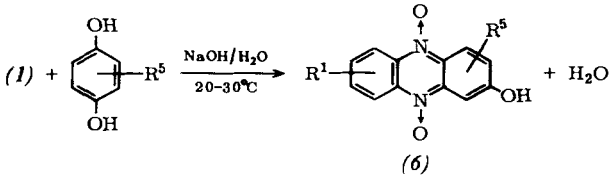
A further variant of the method is the reaction of *(1)* with ynamines $C_2H_5(R^4)N-C\equiv C-C_2H_5$ (THF, 10–30 °C) to give *(3)*, R^2 = C_2H_5, R^3 = $N(R^4)C_2H_5$ with R^4 = CH_3 or C_6H_5.



(4) *(5)*

(1) adds on malonodinitrile in the presence of amines or ammonia to give 2-amino-3-cyanoquinoxaline di-*N*-oxides[5].

The deep-red compounds *(4)* occur in tautomeric equilibrium with *(5)*.

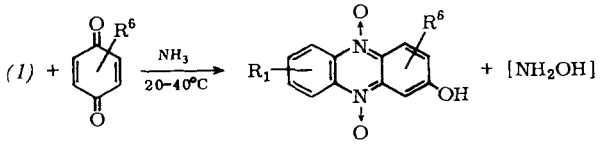


(6)

R^5 = H, alkyl, aryl, halogen, C_6H_5–SO_2, NO_2, –COOH, –SO_2-alkyl, CH_2–CO–NR_2

In aqueous alkaline suspension at temperatures between 20—30 °C, the benzofuroxanes *(1)* undergo a coupling reaction with hydroquinones, naphthohydroquinones, β-naphthols, and with α-naphthols (or phenols, 60 °C) with simultaneous cyclization to give good, in some cases quantitative, yields of phenazine *(6)* or benzophenazine di-*N*-oxides[6,9].

Compounds *(6)* can also be obtained by reaction of *(1)* with benzoquinone or 1,4-naphthoquinone in alcohol or carbon tetrachloride in the presence of ammonia at 20—40 °C[7] (yield 90%).



(7)

R^6 = H, aryl, substituted aryl, halogen, C_6H_5—SO_2

2,3-Dimethylquinoxaline di-N-oxide (3), $R^1 = H$, $R^2 = R^3 = CH_3$

Benzofuroxane (204 g, 1.5 moles) and methyl ethyl ketone (118 g, 1.64 moles) are dissolved in methanol (700 ml) and ammonia is fed into the resulting solution for 8 hours. During reaction the mixture is kept at a temperature of 50 to 55 °C by some suitable form of cooling; finally, the reaction mixture is cooled to 5 °C and the precipitate is separated off by suction. 260 g (91%) 2,3-dimethylquinoxaline di-*N*-oxide is obtained in the form of yellow crystals, which, after recrystallization from ethanol, melt with decomposition at 189 °C.

2-Hydroxyphenazine di-N-oxide (6), $R^1 = R^5 = H$

Hydroquinone (110 g, 1 mole) and sodium hydroxide (2 g, 0.05 mole) are added to a suspension of benzofuroxane (136 g, 1 mole) in water (2 l) and the whole is stirred for 10 hours at room temperature. The mixture is then acidified and filtered with suction. 222 g (97%) 2-hydroxyphenazine di-*N*-oxide is obtained as red crystals which, after recrystallization from dimethylformamide, melt with decomposition at 255 to 260 °C[8]. If stoichiometric amounts of sodium hydroxide are used an exothermic reaction takes place within a few minutes resulting in the formation of the intense blue-violet salt solution of 2-hydroxyphenazine di-*N*-oxide, from which the free compound can be obtained by acidification.

2-Amino-3-cyanoquinoxaline di-N-oxide (4), $R^1 = H$

Triethylamine (50 g, 0.5 mole) is added over a period of 30 minutes to a mixture of benzofuroxane (326 g, 2.4 moles) and malonodinitrile (132 g, 2 moles) in dimethylformamide (750 ml). During the ensuing strongly exothermic reaction, the mixture is kept at a temperature between 20 and 30 °C by some suitable form of cooling. When reaction dies down the mixture is stirred for a further 90 minutes, cooled with ice, and filtered by suction. After washing with methanol, 335 g (83%) of analytically pure 2-amino-3-cyanoquinoxaline di-*N*-oxide (decomp. 232 °C) is obtained.

Received: March 10, 1969; revised: May 7, 1969 [Z 17 IE]
German version: Angew. Chem. *81*, 569 (1969)

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The Structure of Perchloro-[4]radialene

By *F. P. van Remoortere* and *F. P. Boer*[*]

The synthesis of perchloro-[4]radialene by thermal dimerization of perchlorobutatriene has recently been reported by *Heinrich* and *Roedig*[1]. Radialenes are of considerable spectroscopic and theoretical interest: their ultraviolet spectra show unusual low energy transitions which, for radialenes with an even number (*n*) of carbons in the central ring, have been attributed to reduction of molecular symmetry from planar D_{nh} to $D_{\frac{n}{2}d}$ *via* either permanent deformation or strong bending modes[2]. We present below direct confirmation of the structure of perchloro-[4]radialene by a single crystal X-ray diffraction study.

The compound crystallizes[3] in space group Pbcn with lattice parameters $a = 14.719 \pm 0.007$, $b = 9.156 \pm 0.003$, and $c = 9.923 \pm 0.005$ Å and four molecules per unit cell. The intensities of 1528 independent reflections were measured on a Picker automatic diffractometer by the $\theta/2\theta$ scan technique using MoK_α radiation. The structure was solved by reiterative application of *Sayre*'s equation[4] and refined by full-matrix least-squares to an *R*-factor of 4.2% for the 1034 reflections above background.

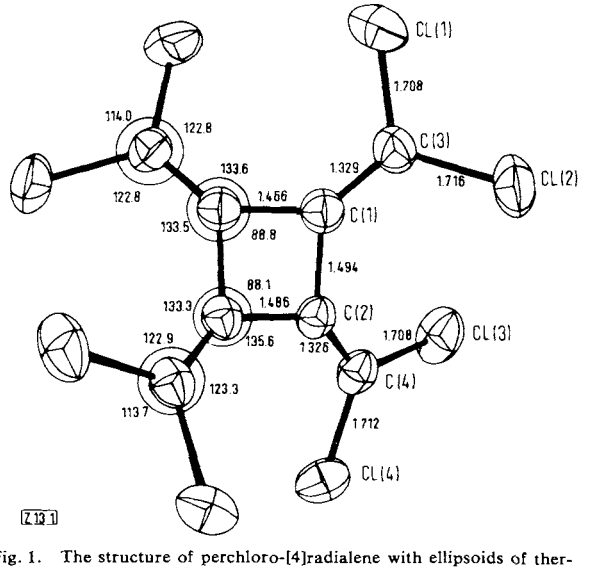


Fig. 1. The structure of perchloro-[4]radialene with ellipsoids of thermal motion, bond lengths, and bond angles. The calculated standard deviations are all less than 0.007 Å for the distances and less than 0.3° for the angles.

The molecule is found to be highly nonplanar and to conform very closely to molecular D_{2d} symmetry, although only a single twofold axis is required by the space group. This result is consistent with the theoretical interpretation of the UV spectrum proposed by *Heilbronner*[2]. Deformation of the molecule from a planar geometry is achieved largely by bending the four-membered ring to a dihedral angle of 153.5 ± 0.6°, a value characteristic of puckered cyclobut-

anes[5]. As a result the intramolecular Cl...Cl contacts are increased to values ranging from 3.308 to 3.338 Å, and the planes of the four chlorines above, and the four chlorines below the central ring are separated by 2.454 Å.

The bond distances give no evidence for conjugation. The distances in the ring are normal for single bonds between sp^2 hybridized carbons, and the C=C and C–Cl bonds compare closely to their respective values (1.324 and 1.710 Å) in 1,1-dichloroethylene[6].

Received: April 29, 1969 [Z 13 IE]
German version: Angew. Chem. *81*, 567 (1969)

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The Bis(chlorosulfur)nitrogen Cation in $[NS_2Cl_2]^+[BCl_4]^-$

By *O. Glemser, B. Krebs, J. Wegener*, and *E. Kindler*[*]

If boron trifluoride (p = 450 torr) is allowed to react with sulfur nitride trifluoride (p = 300 torr) for a few days in a 2-l glass flask, 3–4 g of a yellow crystalline substance is formed which has the composition BNS_2Cl_6 and which proved to be the ionic compound $[NS_2Cl_2]^+[BCl_4]^-$.

$$2\,NSF_3 + 3\,BCl_3 \rightarrow [NS_2Cl_2]^+[BCl_4]^- + {}^1/_2\,N_2 + {}^3/_2\,Cl_2 + 2\,BF_3$$

The gaseous products of this reaction are N_2, Cl_2, BF_3, and BF_2Cl. The new compound is also formed in the reaction of trithiazyl chloride, $N_3S_3Cl_3$, with Cl_2 and BCl_3 or SCl_2 and BCl_3.

Bis(chlorosulfur)nitrogen tetrachloroborate, $[NS_2Cl_3]^+[BCl_4]^-$ *(1)* is very hygroscopic and rapidly decomposes with incomplete evolution of BCl_3; the stoichiometric amounts of N_2, S_2Cl_2, SCl_2, and BCl_3 corresponding to the empirical formula are liberated on heating in a bomb tube at 80 °C. d_4^{20} = 1.98 g/cm³. Mass spectrum (rel. intensities): SN^+ (100), SCl^+ (79), BCl_2^+ (33), $NSCl^+$ (33), Cl^+ (33), S^+ (25), SCl_2^+(10), BCl_3^+ (3). Infrared spectrum (cm^{-1}): 1380 (s), 1340 (s), 1325 (s), 1265 (m), 705 (w), 525 (s), 423 (s), 408 (s). Raman spectrum (cm^{-1}): 720 (s), 706 (w), 652 (w), 516 (s), 499 (m), 452 (s), 408 (m), 200 (s), 132 (s), 83 (s), 38 (m), 21 (m). The molecular weight was determined cryoscopically in benzene as 156.6 (calc. 301.7), thus indicating dissociation of the compound into two parts.

Compound *(1)* crystallizes monoclinically in the space group C_{2h}^5 $P2_1/C$ with a = 6.441 ± 0.005, b = 16.008 ± 0.010, c = 9.864 ± 0.007 Å, β = 103.30 ± 0.05 °. Z = 4; $d_{X\text{-}xay}$ = 2.024 gm/cm³. The composition and structure of the compound was determined by X-ray structural analysis. The structure could be determined directly by iterative use of the Sayre equation. For this purpose about 1800 independent reflections were determined on a single crystal diffractometer ($Mo_{K\alpha}$ radiation, scintillation counter). After refinement by the method of least squares, a discrepancy factor R = 5.9% was obtained. The structures and structural parameters of the cation and anion are as shown in Figures 1a and 1b. Two doubly degenerate resonance structures are possible for the $[NS_2Cl_2]^+$ ion.

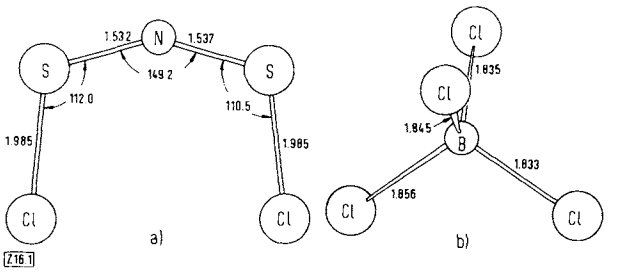


Fig. 1. Bond lengths (Å) and bond angles (°) (a) in the $[NS_2Cl_2]^+$ ion and (b) in the $[BCl_4]^-$ ion.

The experimentally determined dimensions are in good agreement with such a type of bonding: a previously derived empirical relation[1] gave a bond order of about 1.7–1.8 for the observed N–S bond length; the S–Cl bond length corresponds to that of an ideal single bond. The $[NS_2Cl_2]^+$ ion is, within the limits of error, planar and has *cis* configuration with approximate C_{2v} symmetry. On the basis of the electron pair repulsion model, the bond angles are plausible if one assumes an approximately equal participation of the resonance structures *(2)* and *(3)*. The structure of the remarkably stable tetrahedral $[BCl_4]^-$ ion in compound *(1)* has not as yet been investigated; in this compound there is virtually no distortion of the tetrahedron, the bond angles varying between 109.0 and 109.9 °.

Received: May 14, 1969 [Z 16 IE]
German version: Angew. Chem. *81*, 568 (1969)

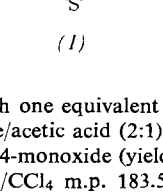
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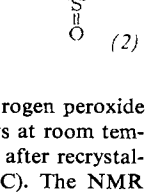
Dithieno[3,4-*b*,3′,4′-*e*]-[1,4]-dithiine

By *M. J. Janssen* and *J. Bos*[*]

Woronkow and *Pereferkowitsch*[1] have recently reported on the preparation of dithieno[2,3-*b*,3′,2′-*e*]-[1,4]-dithiine. We have now prepared the isomeric compound dithieno[3,4-*b*,3′,-4′-*e*]-[1,4]-dithiine *(1)*[2] by heating 3-bromo-4-thiophenethiol (15.6 g, 0.08 mole)[3] with 4.5 g KOH (0.08 mole) and 5.7 g Cu_2O (0.04 mole) in 300 ml dimethylformamide for 20 h at 130 °C (yield 3.7 g = 40%, after recrystallization from cyclohexane m.p. 145–146 °C). NMR: δ = 7.40 ppm (s); UV: λ_{max} (ethanol) = 270 nm (ε = 9100).



(1)



(2)

Oxidation of *(1)* with one equivalent of hydrogen peroxide in methylene chloride/acetic acid (2:1) (6 days at room temperature) affords the 4-monoxide (yield 66%, after recrystallization from $CHCl_3/CCl_4$ m.p. 183.5–184 °C). The NMR spectrum shows two doublets at δ = 8.04 and 7.36 ppm (J = 3 Hz). This spectrum is consistent with the given structure only, since the coupling constant of 3 Hz is characteristic of 2,5-hydrogen atoms in thiophene[4]. UV: λ_{max} (ethanol) = 244 nm (ε = 15400). The 4,8-dioxide *(2)* is formed when *(1)* is boiled under reflux for 24 h with two equivalents (or the 4-oxide with one equivalent) of H_2O_2 in acetic acid/methylene chloride. The yield of *(2)*, after recrystallization from acetic acid, amounts to 40% [from *(1)*]; m.p. 230 °C, λ_{max} (ethanol) = 250 nm (shoulder) (ε = *ca.* 8600).

The NMR-spectrum of *(2)* (in [D_6]-DMSO) shows two sharp signals of unequal height at $\delta = 8.50$ and 8.60 ppm. At 120 °C the signals broaden, at 180 °C there is only one sharp absorption ($\delta = 8.55$). Compound *(2)* obviously gives rise to two isomers in which the SO groups are either *cis* or *trans*[5] and which are interconverted rapidly at higher temperatures. The original signals are observed in the same intensity ratio when the solution is cooled. Prolonged heating at 200 °C does not alter the ratio of the components.

Received: May 27, 1969 [Z 19 IE]
German version: Angew. Chem. *81*, 570 (1969)

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2,2'-Bipyridine Adducts of Disilanes

By *D. Kummer*, *H. Köster*, and *M. Speck*[*]

During studies of the chemistry of polysilanes we succeeded in the first synthesis of amine complexes of disilanes, namely, tetrachlorodimethyldisilane-bipyridine *(1)* and hexachlorodisilane-bipyridine *(2)*. Previous attempts to isolate such substances failed because of base-catalyzed rearrangement of the disilanes[1,2]. Compounds *(1)* and *(2)* provide examples of a class of compound that is important for, *inter alia*, the study of the nature of donor-acceptor complexes and of the rearrangements of di- and poly-silanes.

The 1:1 bipyridine (= bipy) addition compound of *(1)* is formed smoothly from the components in apolar organic solvents at room temperature, separating as a lemon-yellow crystalline powder.

$$Cl_2CH_3SiSiCH_3Cl_2 + x\ \text{bipy} \xrightarrow{\text{Pentane}} Cl_2CH_3SiSiCH_3Cl_2 \cdot \text{bipy} + (x-1)\ \text{bipy}$$

(1)

Analysis and ^{1}H-NMR spectra confirm the 1:1 composition; it was not possible to obtain an addition compound containing more bipyridine (*e.g.*, 1:2) even when using a large excess of bipy.

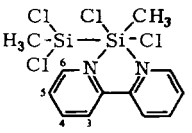
The complex *(1)* dissolves easily in benzene and tetrahydrofuran with a pale yellow color, but according to the cryoscopically determined molecular weight (found, 177 in benzene) and the NMR spectra it is widely dissociated therein into the starting materials (see Table). The UV spectrum of the colorless THF solution (10^{-3} mole/l) shows only the two unchanged bands of bipy (235, 281 nm); in the solid state spectrum (Nujol suspension) there appears also a broad, weaker absorption band without a definite maximum, stretching to 600 nm. The yellow color is ascribed to charge-transfer transitions. Measurements of conductivity of *(1)* in acetonitrile at 25 °C show no change from that of the pure solvent.

Compound *(1)* sublimes in a vacuum at 40–50 °C, being thereby completely dissociated also in the vapor state, according to the mass spectrum. The dissociation equilibrium in solution:

$$(Cl_2CH_3Si)_2 + \text{bipy} \rightleftarrows (Cl_2CH_3Si)_2 \cdot \text{bipy}$$

can be shifted at lower temperatures largely towards the complex. In THF solution the simple $SiCH_3$ proton resonance signal splits at −85 °C into two lines of equal intensity, and the signals for bipy correspond to bipy bound as complex [cf. $(C_2H_5)_2Ni \cdot$ bipy[3]].

These results accord with the proposed structure *(1a)*, in agreement with binding of the bipy to only one Si atom of a molecular adduct (non-equivalence of the two Si-methyl groups!).



(1a)

No further indication can yet be given about the arrangement of the bipy in this structure (*cis-cis* or *cis-trans* to the neighboring Si atom). A single-crystal X-ray structure determination is in progress[4]. Although the solid compound remains unchanged for months at room temperature, solutions of *(1)* in THF or dioxane are not stable at 25 °C; they change within a few weeks to deep reddish-brown solutions from which a new bipyridine-silicon complex can be isolated; this is amorphous (X-rays) and, according to ^{1}H-NMR studies, is of stoichiometric composition. This intermediate also decomposes above 150 °C giving CH_3SiCl_3 and unidentified higher methylchlorosilicon compounds. Chlorosilane catalyzes the solution reaction.

Like $(Cl_2CH_3Si)_2$, Si_2Cl_6 reacts with bipy in pentane giving exclusively the yellowish-white 1:1 adduct *(2)*, whose existence is secured by analyses, X-ray powder diagrams (individual diagram, no bipy, $SiCl_4 \cdot$ bipy, bipy · HCl), and thermal sensitivity (formation of a dark green color above 80 °C). In tetrahydrofuran another reaction takes place at 25 °C, formation of a dark green color and decomposition occurring within a few minutes; but the solid complex *(2)* is completely stable at 25 °C.

^{1}H-NMR data (ν in Hz at 60MHz; TMS = 0 Hz) of *(1)* and its components (*ca.* 10% in THF).

	T(°C)	$SiCH_3$	bipy-H^3	-H^4	-H^5	-H^6
$(Cl_2CH_3Si)_2$	32	61.0	—	—	—	—
bipy	32	—	509.3	465.1	433.5	516.0
(1)	32	60.0	508.2	466.4	435.3	517.9
$(Cl_2CH_3Si)_2$	−85	65.2	—	—	—	—
bipy	−85	—	530.5	488.0	455.3	536.0
(1)	−85	50.5; 47.5	552.5	531.3	499.6	619.2

Tetrachlorodimethylsilane-2,2'-bipyridine (1)

$(Cl_2CH_3Si)_2$ (3.19 g, 15.0 mmoles) is condensed under reduced pressure onto bipy (2.87 g, 18.4 mmoles) in pure pentane. The mixture is allowed to warm slowly to room temperature with stirring. A yellow precipitate is formed which two hours later is filtered off in absence of air and washed several times with dry pentane. Recrystallization from acetonitrile affords *(1)* as large, yellow, transparent crystals, m.p. 102 °C (decomp.) (3.7 g, 70%). If there is even a slight excess of the chlorosilane component, the precipitate, which is yellow at first, becomes dark green within an hour, giving, *inter alia*, CH_3SiCl_3.

Hexachlorodisilane-2,2'-bipyridine (2)

The preparation is analogous to that above, with condensation of less than an equivalent amount of $(Cl_3Si)_2$ onto a bipy solution in pentane. The yield is almost quantitative. It was not possible to find a solvent for the complex. Decomp. pt. 108 °C (green color).

X-ray powder diagram (Cu–K_α): 5.9 vs, 6.6 vs, 7.6 vw, 8.8 m, 9.65 vw, 10.6 w, 11.75 vs, 13.4 m, 14.25 m, 14.75 m, 15.85 s,

20.5 w, 22.65 vw, 24.75 vw, 26.65 vw, 28.25 vw, 30.05 vw, 31.5 vw.

Received: May 22; revised: June 19, 1969 [Z 21 IE]
German version: Angew. Chem. *81*, 574 (1969)

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Application of the Mössbauer Effect to Investigation of the Solid State Reaction of Iron(II) Sulfate with Potassium Cyanide[1]

By *P. Gütlich* and *K. M. Hasselbach* [*]

The Mössbauer effect[2] has been used to study the reaction of iron(II) sulfate with potassium cyanide in the solid state as a function of reaction time, temperature, and content of water of crystallization of the iron(II) sulfate.

The reactants were mixed in the molar ratio $FeSO_4 \cdot 7H_2O$: KCN = 1 : 6 (particle size of both components = 0.2—0.3 mm) and pressed to tablets. The course of the reaction was followed at 5 °C and at 20 °C [Mössbauer spectra measured at −96 °C (temperature of the absorber); radiation source: ^{57}Co in platinum (room temperature)].

Depending on the reaction time, the Mössbauer spectra contained up to five, partially overlapping resonance lines. The iron compounds assigned to the experimentally observed data are shown in the Table.

Complex	Chemical isomer shift δ (mm/s)	Quadrupole splitting ΔE_Q (mm/s)
$FeSO_4 \cdot 7H_2O$	+0.98 ± 0.02	3.41 ± 0.02
$K_4[Fe(CN)_6] \cdot 3H_2O$	−0.34 ± 0.02	0
$K_3[Fe(CN)_5H_2O]$	−0.21 ± 0.02	0.75 ± 0.03

The values of the chemical isomer shifts and quadrupole splittings agree very well with those reported in the literature[3].

During the reaction the water molecules in the coordination sphere of the magnetically normal ("high spin") complex $[Fe(H_2O)_6]^{2+}$ are replaced by cyanide ions. Under the experimental conditions used the sole intermediate visible in the Mössbauer spectrum is the magnetically abnormal ("low spin") complex $[Fe(CN)_5H_2O]^{3-}$, which is unstable and reacts with further cyanide ions to give the stable complex $[Fe(CN)_6]^{4-}$.

After suitable standardization of the Mössbauer spectra the three complexes $[Fe(H_2O)_6]^{2+}$, $[Fe(CN)_6]^{4-}$, and $[Fe(CN)_5H_2O]^{3-}$ can be determined quantitatively (mean error $< \pm 3\%$) in the presence of each other as a function of various reaction conditions.

Surprisingly, the reaction between $FeSO_4 \cdot 7H_2O$ and KCN in the solid state is relatively fast at 5 °C: the iron(II) sulfate has reacted almost quantitatively after about 30 h. Two partial steps were observed for the consumption of iron(II) sulfate, the rate constants being $k(I)_5 = (3.75 \pm 0.20) \times 10^{-2}$ min^{-1} and $k(II)_5 = (1.5 \pm 0.1) \times 10^{-3}$ min^{-1}. The two steps are ascribed to diffusion of cyanide ions and $[Fe(H_2O)_6]^{2+}$ ions, respectively, through a zone that is softened by water liberated on substitution by cyanide ions in the coordination sphere of the iron; the activation energies for the two diffusion steps are $\Delta E_A(I) = 12.5 \pm 2.0$ and $\Delta E_A(II) = 17.5 \pm 2.5$ kcal mole^{-1}.

The water content of the iron(II) sulfate plays a very important part in the reaction. This was shown by experiments with $FeSO_4 \cdot 2.5H_2O$ instead of $FeSO_4 \cdot 7H_2O$; in these experiments no change was observed even after 30 days at 5 °C. Use of the Mössbauer effect for the investigation of solid state reactions of the kind described here has the particular advantage that the samples remain in closed containers and can be analyzed without destruction.

Received: June 25, 1969 [Z 24 IE]
German version: Angew. Chem. *81*, 627 (1969)

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Potassium Hexacyanopalladate(IV)

By *H. Siebert* and *A. Siebert* [*]

Hexacyanoplatinates(IV) were first described several years ago[1]. $K_2[Pt(CN)_6]$ *(1)* is formed on reaction of $K_2[PtI_6]$ and KCN in the solid state and is very stable. This made it seem possible that hexacyanopalladates(IV) might also exist although Pd^{IV} compounds are in general much less stable than their Pt^{IV} analogs.

An attempted synthesis analogous to that of *(1)* failed. $K_2[PdI_6]$ is unknown; $K_2[PdCl_6]$ and $K_2[PdBr_6]$ react with KCN in the solid state and in aqueous solution with complete reduction of the Pd^{IV}, partly to tetracyanopalladate(II) and partly to metallic palladium. However, $[Pd(CN)_6]^{2-}$ can be synthesized in aqueous solution if the reduction is prevented by addition of potassium peroxodisulfate.

$$K_2[PdCl_6] + 6\,KCN \xrightarrow{K_2S_2O_8} K_2[Pd(CN)_6] + 6\,KCl \qquad (2)$$

On fractional crystallization of the reaction mixture, $K_2S_2O_8$ separates first, then *(2)*, and finally $K_2[Pd(CN)_4]$ and K_2SO_4. The presence of *(2)* in individual fractions can be determined through the characteristic IR band at 2185 cm^{-1}. The yield averages 19%; use of $K_2[PdBr_6]$ as starting material gives lower yields.

Crystals of *(2)* are colorless, six-sided, domed prisms. The salt is moderately soluble in water, very slightly soluble in ethanol, and insoluble in ether. Above 160 °C it decomposes slowly; it is stable at room temperature to water, dilute acids, concentrated nitric acid, and bromine water. Concentrated sulfuric or hydrochloric acid at room temperature and boiling water decompose it slowly, with reduction to tetracyanopalladate(II) and palladium(II) cyanide. The CN stretching vibration appears in the IR spectrum of *(2)* at 2185 cm^{-1}, which is appreciably higher than that for $[Pd(CN)_4]^{2-}$ (2136 cm^{-1}). The relations are similar to those for the corresponding platinum compounds[2].

Potassium hexacyanopalladate(IV) (2)

A solution of KCN (29.3 g, 0.45 mole) and $K_2S_2O_8$ (12.2 g, 0.045 mole) in water (2.3 l) is added slowly and with stirring to a suspension of K_2PdCl_6 (20.0 g, 0.05 mole) in a solution of $K_2S_2O_8$ (1.35 g, 5 mmoles) in water (250 ml). The prod-

ucts crystallize fractionally on evaporation of the clear, yellow solution in a vacuum below 40 °C. The fractions that contain $K_2[Pd(CN)_6]$ (IR band at 2185 cm^{-1}) are united and recrystallized from hot water.

Received: June 12, 1969 [Z 23 IE]
German version: Angew. Chem. *81*, 575 (1969)

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Simple Preparation of Cyanogen Fluoride

By *E. Mayer* [*]

Pure cyanogen fluoride was prepared for the first time in 1960, by pyrolysis of cyanuric trifluoride at 1300 °C [1,2]. This synthesis requires special, rather complicated equipment for the decomposition and for fractionation of the mixed products. Because of these experimental difficulties FCN is one of the least investigated of the three-atomic molecules.

Tetracyanomethane reacts with alkali-metal chlorides or bromides to yield tricyanomethyl-alkali metal and cyanogen chloride or bromide [3], so that it was appropriate to investigate the reaction with fluorides.

$C(CN)_4$ reacts with CsF with formation of tricyanomethyl-cesium and pure cyanogen fluoride:

$$C(CN)_4 + CsF \rightarrow CsC(CN)_3 + FCN$$

Finely powdered $C(CN)_4$ is mixed as thoroughly as possible with an excess of CsF in a shaking apparatus at room temperature, the FCN formed in the reaction being pumped off and condensed at the temperature of liquid nitrogen. Yields are up to 95 %.

The way in which the reactants are mixed has a pronounced effect on the rate of formation of FCN: to obtain *ca.* 1 mmole of FCN we had to carry out the reaction for 5 hours in the shaker, but about 30 hours were required when magnetic stirring was used. IR and mass spectra of the FCN produced in this way agree with spectra recorded in the literature [2,4] and show minor amounts of CO_2 as the only impurity.

$C(CN)_4$ also reacts quantitatively with KF at room temperature, with formation of tricyanomethylpotassium, but the FCN formed at the same time largely polymerizes and the yield thereof is only about 5 %. (Since the polymerization of FCN is catalyzed by Lewis acids [2], the polymerization may be caused by HF present in the KF as impurity.)

No reaction occurs when $C(CN)_4$ is mixed with NaF at room temperature.

From the various behaviors of the alkali-metal fluorides it can be concluded that formation of a tricyanomethyl-alkali metal is energetically favored by a large cation such as K^+ or Cs^+.

Received: June 18, 1969 [Z 26 IE]
German version: Angew. Chem. *81*, 627 (1969)

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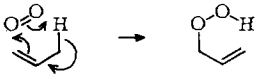
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Catalytic Oxidation of Olefins *via* an Allyl Radical [**]

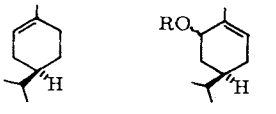
By *J. E. Baldwin* and *J. C. Swallow* [*]

We have recently commented on the similarity between the oxygenation patterns found in the reactions of singlet oxygen with olefins and those observed in many natural product series [1], and have suggested the possibility that some singlet oxygen-like species is operative in certain oxidase mechanisms [2]. Since most oxidases are metalloenzymes [2], the observation that a number of transition metal complexes catalyze allylic oxidation and epoxidation caused us to examine these reports [3] in order to compare the product oxygen patterns with that expected from the well-known "ene" addition pathway of singlet oxygen, that is, *(1)* to *(2)* [4].



(1) *(2)*

Thus (+)-carvomenthene *(3)* is converted in part by photosensitized oxidation to isomeric carvotanacetols *(4)* by way of the corresponding hydroperoxide *(5)* [5].



(4), R = H
(5), R = OH

(3)

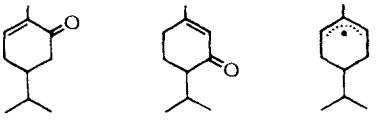
Consequently, an "ene" addition of oxygen by the rhodium catalyst, chlorotris(triphenylphosphine)rhodium(I), would be expected to follow the same course. An alternative process could be the specific insertion of oxygen into the allyl methylene group yielding in this case the enantiomorph of *(5)*. In either case, α-elimination of the hydroperoxide [6] would yield optically active carvotanacetone *(6)*. We have observed that the oxygenation of *(3)* catalyzed by chlorotris(triphenylphosphine)rhodium(I) (10^{-2} M) in benzene at 60 °C (monitored by gas-liquid chromatography), gives a mixture of carvotanacetone *(6)*, piperitone *(7)*, and several of the derived alcohols.

Careful separation (preparative gas-liquid chromatography) of the mechanistically significant enone *(6)* was followed by characterization as the 2,4-dinitrophenylhydrazone (m.p. 196 °C), identical in spectral properties with that prepared from authentic (—)-carvotanacetone [m.p. 194—196 °C, $[\alpha]_D^{25}$ −104, (*c* = 0.64, chloroform)]. The carvotanacetone obtained from this oxidation was completely racemized.

In order to exclude the possibility of prior racemization in the olefin by a rapid valence tautomerism of a reversibly formed π-allyl rhodium complex [7], which could conceivably have been an intermediate in the oxygenation, a reaction taken to 50 % conversion was stopped and unchanged carvomenthene reisolated (preparative gas-liquid chromatography). It retained its full optical rotation.

Since the hydroperoxide *(5)* is optically stable under these mild conditions [5] we conclude that the mechanism of this oxygenation involves a symmetrized intermediate, which is most probably the radical *(8)*.

Other workers [8] have noted that the product distribution in these reactions is similar to that observed in classical autoxi-



(6) *(7)* *(8)*

dation chains and have also observed phenolic inhibition and polymerization initiation. The latter observations, however, raise the question of catalyst inactivation.

We have here reported direct evidence for an allyl radical intermediate in an unperturbed system, and concur with the previous conclusions that a Haber-Weiss oxidation chain process[9] is in operation in these reactions, as opposed to insertions or concerted additions.

Received: May 28, 1969 [Z 27 IE]
German version: Angew. Chem. *81*, 571 (1969)

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[**] This work was generously supported by Eli Lilly and Company.

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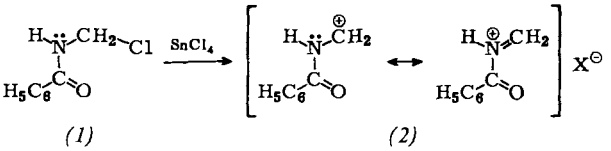
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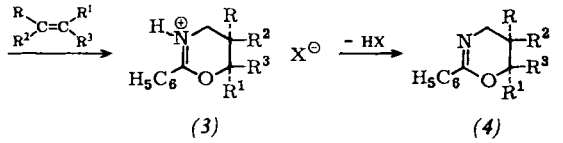
Stereospecific Synthesis of 5,6-Dihydro-4*H*-1,3-oxazines *via* Polar 1,4-Cycloaddition[1] [**]

By *R. R. Schmidt* [*]

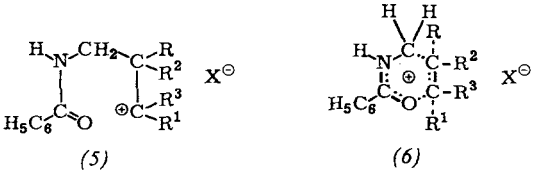
Polar 1,4-cycloaddition[2] can formally be assigned a place intermediate between the concerted Diels-Alder reaction and two-step 1,4-dipolar cycloaddition[3].



(1) *(2)*



(3) *(4)*



(5) *(6)*

$X^{\ominus} = {}^1/_2\ SnCl_6^{2\ominus}$

Polar 1,4-cycloaddition of the benzamidomethylium ion *(2)* to olefins[4] leads to an unexpected result of mechanistic importance[2e]: If *(2)* is produced from *N*-(hydroxymethyl)-benzamide by proton catalysis in glacial acetic acid[4] or *in situ* by treatment of *N*-(chloromethyl)benzamide *(1)* with tin(IV) chloride in glacial acetic acid, carbon tetrachloride, or chloroform[2c], regiospecific[5] and stereospecific reaction ensues to form 5,6-dihydro-4*H*-1,3-oxazinium salts *(3)*, which are isolated in the form of the free bases *(4)*. The latter method gives almost quantitative yields. Specific formation of the 5,6-dihydro-4*H*-1,3-oxazines *(4a)–(4f)* was deduced from NMR studies. The experimental coupling constants correspond to the values estimated from structural models of *(4a)–(4f)* with the aid of the Karplus equation[6].

The stereospecificity of the reaction casts doubt on a two-step mechanism with *(5)* as intermediate[4]. Rather, the above observations suggest concerted formation of the two new σ bonds[7], although not necessarily at the same rate, with *(6)* as intermediate.

Table 1. 5,6-Dihydro-4*H*-1,3-oxazines *(4)* synthesized from *(1)*, olefins, and $SnCl_4$.

(4)	R	R^1	R^2	R^3	B.p. (°C/torr)	Yield (%)	$J_{a,b}$	$J_{a,c}$
(a)	H	H	$-(CH_2)_4-$		110/0.01 [4]	85		
(b)	H_b	H_a	H_b	OAc	102/0.001 [4]	81	3.2(t)	
(c)	H_b	H_a	H_c	C_6H_5	143/0.002 [4]	82	4.1	8.9
(d)	CH_3	H_a	H_c	C_6H_5	144/0.001 [a]	95		9.1
(e)	CH_3	H_a	H_c	CH_3	70/0.005 [b]	93		9.1
(f)	H_b	H_a	CH_3	CH_3	77/0.005 [c]	89	3.5	

[a] M.p. 84 °C; [b] m.p. 44 °C; [c] $n_D^{20} = 1.5420$.

5,6-Dihydro-4H-1,3-oxazines (4)

A solution of $SnCl_4$ (0.01 mole) in anhydrous chloroform (10 ml) was added over a period of 5 min to a solution of *(1)* (0.01 mole) and the relevant olefin (0.011 mole) in anhydrous chloroform (30 ml) at 0 °C. After 2 h the reaction mixture was stirred into 2 N sodium hydroxide solution (50 ml) at 0 °C, the chloroform phase separated off, dried over K_2CO_3, and distilled to give *(4)*.

Received: June 6, 1969 [Z 28 IE]
German version: Angew. Chem. *81*, 576 (1969)

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

[1] Part 6 of Polar 1,4-Cycloaddition. – Part 5: Ref. [2e].

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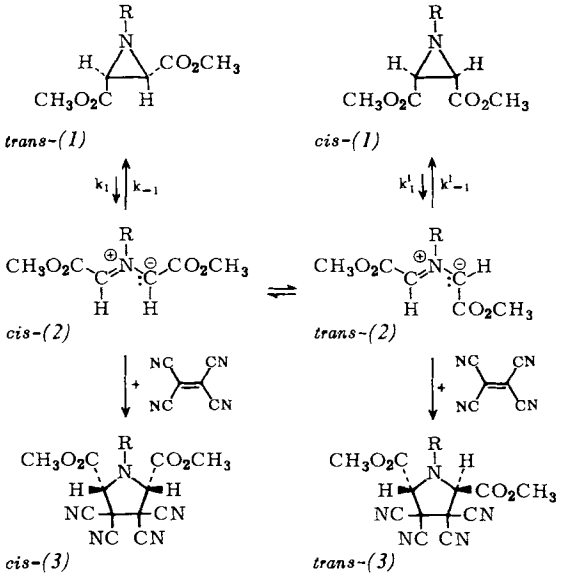
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Azomethine Ylides from Aziridinedicarboxylic Esters: Kinetics of the *cis-trans* Isomerization and of the Ring Opening

By *R. Huisgen, W. Scheer,* and *H. Mäder* [*]

Although the epimeric dimethyl 1-(4-methoxyphenyl)aziridine-2,3-dicarboxylates, *cis-(1)* and *trans-(1)*, are stable at room temperature, they equilibrate at 100 °C. The fact that

this *cis-trans* isomerization proceeds *via* a novel aziridine ring opening at the C–C bond to give the geometrically isomeric azomethine ylide dicarboxylic esters, *trans-(2)* and *cis-(2)*, is proved by 1,3-dipolar cycloadditions of *(2)* with dipolarophiles a–b [1,2]. Active dipolarophiles suppress the stereoisomerization *trans-(2)* ⇆ *cis-(2)*; the stereospecific formation of adducts with dimethyl acetylenedicarboxylate establishes the *conrotatory* opening of the aziridine ring [2]. Conrotation was predicted by *Woodward* and *Hoffmann* [3] for the ring opening of the isoelectronic cyclopropyl anion to give the allyl anion.



R = *p*-CH_3O-C_6H_4

Kinetics of the ring opening: Dilatometric studies of the formation of *cis-(3)* and *trans-(3)* from *trans-(1)* and *cis-(1)*, respectively, with an excess of tetracyanoethylene in ethyl acetate gave first order rate constants, which, surprisingly, are independent of the concentration of tetracyanoethylene (Table 1). Thus, the rate-determining step is not the bimolecular combination with the dipolarophile, but a preceding first order reaction. Tetracyanoethylene is such an effective trapping agent for the azomethine ylides that not only the isomerization *cis-(2)* ⇄ *trans-(2)* but also the electrocyclic

Table 1. Kinetics of ring opening of *(1)* in ethyl acetate; measurement of adduct formation with tetracyanoethylene (TCNE).

trans-(1), 30.6 mmole/l; $\Delta H^{\ddagger}$ = 29.5 kcal/mole, $\Delta S^{\ddagger}$ = +0.5 (e.u.)

TCNE (mol. equiv.)	10	20	30
$k_d \times 10^5$ (s^{-1}) at 100.2 °C	5.13	5.16	5.15
$k_d \times 10^5$ (s^{-1}) at 110.0 °C	15.1	15.0	14.8
$k_d \times 10^5$ (s^{-1}) at 119.7 °C	39.0	39.1	39.1

cis-(1), 40 mmole/l; $\Delta H^{\ddagger}$ = 28.6 kcal/mole, $\Delta S^{\ddagger}$ = −1.7 (e.u.)

TCNE (mol. equiv.)	7.5	15
$k_d \times 10^5$ (s^{-1}) at 100.0 °C	6.24	6.12
$k_d \times 10^5$ (s^{-1}) at 110.0 °C	17.5	17.5
$k_d \times 10^5$ (s^{-1}) at 120.0 °C	46.2	46.1

regeneration of *trans-(1)* and *cis-(1)* is completely suppressed. The dilatometric rate constants k_d are thus the ring-opening constants k_1 and k_1', respectively. The Eyring parameters (Table 1) are similar for the *cis* and *trans* forms; the low entropy of activation is indicative of the conversion of one rigid molecule into a new rigid molecule. The structures of the adducts *(3)* were confirmed by NMR spectra and elemental analyses.

Aziridine equilibration and rate of *cis-trans* isomerization: The course of the isomerization can be followed NMR spectroscopically by means of the singlet due to the ring protons of *trans-(1)* and *cis-(1)*. The rate constant for the equilibration,

$$trans\text{-}(1) \underset{k_{-I}}{\overset{k_I}{\rightleftharpoons}} cis\text{-}(1)$$

$k_I + k_{-I}$, is measured from both sides of the equation (Table 2). The difference in the free enthalpies of activation

Table 2. Kinetics of *cis-trans* isomerization of *(1)* in ethyl acetate.

T (°C)	$10^5 (k_I + k_{-I})$ (s^{-1})	$10^5 k_I$ (s^{-1})	$10^5 k_{-I}$ (s^{-1})
100	2.44	0.71	1.73
110	6.55	1.93	4.62
120	17.04	5.01	12.03

	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (e.u.)	$\Delta G^{\ddagger}$ (kcal/mole)
trans-(1) → *cis-(1)*	28.6	−6.1	30.9 (100 °C)
cis-(1) → *trans-(1)*	28.1	−5.6	30.2 (100 °C)

agrees with the value of ΔG = 0.65 kcal/mole determined from the equilibrium constant, K = 0.42.

The content of *cis-(1)* in the equilibrium mixture increases with increasing polarity of the solvent (Table 3). The calculated free energy changes show a linear correlation with the polarity parameter E_T [4]. A similar solvent effect leading to an even stronger preference of the *cis* isomer was observed with 1-benzyl-2,3-dibenzoylaziridine [5]. Slow dimerization of *trans-(1)* and *cis-(1)* to diastereomeric *N,N'*-bis(*p*-methoxyphenyl)piperazinetetracarboxylic esters occurs as an interfering reaction [1].

Table 3. Percentage of *cis-(1)* in *cis-trans* equilibrium mixture at 120 °C.

Solvent	*cis-(1)* (%)	E_T
Carbon tetrachloride	22	32.5
Ether	26	34.6
Dioxane	29	36.0
Ethyl acetate	30	38.1
Deuteriochloroform	32	39.1
Methylene chloride	32	41.1
Acetone	36	42.2
1,3-Dioxolan-2-one	47	46.6

Energy profile: By combination of the kinetic data obtained, it is possible to construct a free energy profile for ring opening and isomerization (Fig. 1). Only one of eight molecules of *trans-(1)* that reach the energy dip corresponding to the intermediate *cis-(2)* surmounts the next barrier leading to the second intermediate, *trans-(2)*; the remainder revert to *trans-(1)*. In the case of the intermediate *trans-(2)*, cyclization to *cis-(1)* is four times as fast as conversion into *cis-(2)*. The depths of the troughs corresponding to the azomethine ylide intermediates, *cis-(2)* and *trans-(2)*, are unknown.

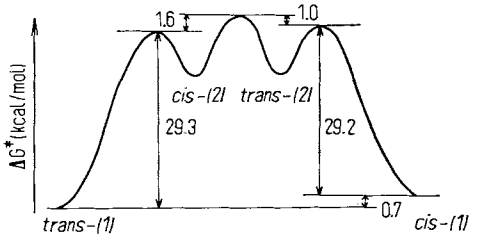
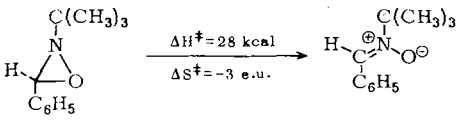


Figure 1. Energy profile for the conversions *trans-(1)* ⇌ *cis-(2)* ⇌ *trans-(2)* ⇌ *cis-(1)* at 100 °C.

In azomethine oxides (nitrones) the oxygen stabilizes the negative charge better than the carbon of the carbanion in



[6]

azomethine ylides. This is responsible for the conversion of oxaziranes into the open-chain nitrones.

Received: June 4, 1969 [Z 29a IE]
German version: Angew. Chem. *81*, 619 (1969)

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[1] *R. Huisgen, W. Scheer, G. Szeimies,* and *H. Huber,* Tetrahedron Letters *1966*, 397.

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Differing 1,3-Dipolar Activity of *cis-trans* Isomeric Azomethine Ylide Dicarboxylic Esters[**]

By *R. Huisgen, W. Scheer, H. Mäder,* and *E. Brunn*[*]

The stereoisomeric dimethyl azomethine ylide dicarboxylates, *cis-(2)* and *trans-(2)*, which arise from the dimethyl aziridinedicarboxylates *trans-(1)* and *cis-(1)*, combine stereospecifically with highly active dipolarophiles such as acetylenedicarboxylic ester[1] or tetracyanoethylene[2]. If the dipolarophilic activity of the multiple bond system a=b is reduced, *cis-trans* isomerization of the azomethine ylides competes with cycloaddition to a=b.

A characteristic difference between *trans-(2)* and *cis-(2)* becomes apparent under the above conditions. Cycloadditions of *trans-(2)* remain stereospecific, even with "poor" dipolarophiles (Table 1); *trans-(3)* is the sole product detectable by NMR spectroscopy. With *cis-(2)*, on the other hand, the lower the activity of the dipolarophile the greater the amount of the sterically "wrong" adduct *trans-(3)*. With norbornene nearly half of the *cis-(2)* isomerizes to *trans-(2)* before it enters into cycloaddition with a=b; the cyclohexene adduct has 83% *trans* configuration with respect to the carboxylate groups. Finally, with phenanthrene the sequence *trans-(1)* → *cis-(2)* → *trans-(2)* leads to the adduct-2,5-*trans*-diester, *trans-(3)*. No subsequent stereoisomerization of the adducts *(3)* could be detected under the reaction conditions or during the work-up procedure.

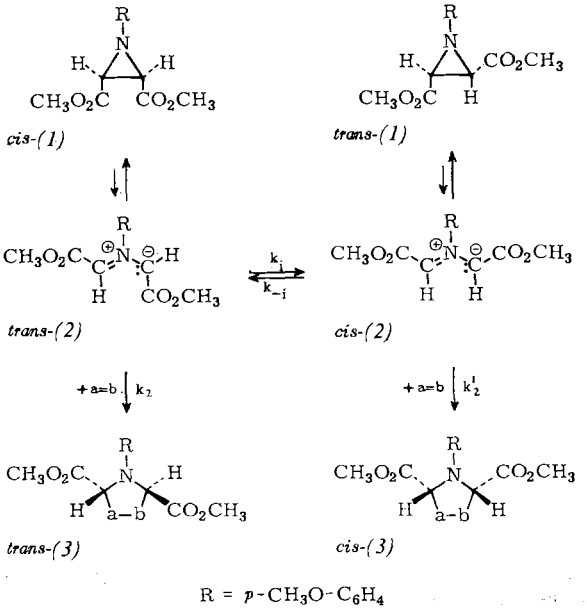


Table 1. Steric course of some reactions of *cis-(1)* [*via trans-(2)*] and *trans-(1)* [*via cis-(2)*] with dipolarophiles at 100–140 °C [a].

Dipolarophile a = b	From *cis-(1)* [b] *(3)*, yield (%)	From *trans-(1)* *(3)*, yield (%)	*trans-(3)*:*cis(3)*
Tetracyanoethylene	88	100	0:100
Dimethyl acetylenedicarboxylate	98	78	0:100
Diethyl azodicarboxylate	96	78	6: 94
Diethyl mesoxalate	94	75	7: 93
Dimethyl fumarate	100	93	9: 91
Tetraethyl ethylene-tetracarboxylate	99	90	25: 75
Norbornene	86	98	45: 55
Cyclohexene	78	71	83: 17
Phenanthrene		36	100: 0

[a] Most of the adducts *(3)* listed in the Table are new and gave correct analyses.

[b] The ratio of *trans-(3)* to *cis-(3)* was 100:0 in all these cases.

What is the cause of this striking phenomenon? Initially we suspected that the azomethine ylide equilibrium lies largely on the side of *trans-(2)*, *i.e.* that $k_{-i} \gg k_i$. However, the energy profile of the ring opening and isomerization[2] does not lead one to expect such an energy difference between *trans-(2)* and *cis-(2)*; differing rate constants for the cycloaddition, namely $k_2 > k_2'$, must therefore be responsible. A molecular model shows that strong van der Waals repulsion and restriction of rotation of the *cis* ester groups in *cis-(3)* can occur. It is also possible that the transition state of the cycloaddition – here the carbon atoms of *(2)* are intermediate between sp^2 and sp^3 hybridization – is affected by such an overlapping of the substituent radii as well. It is only with extremely active dipolarophiles that k_2' remains large enough to preclude competition from k_{-i}.

Received: June 4, 1969 [Z 29b IE]
German version: Angew. Chem. *81*, 621 (1969)

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

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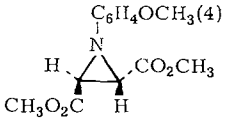
[2] *R. Huisgen, W. Scheer,* and *H. Mäder,* Angew. Chem. *81*, 619 (1969); Angew. Chem. internat. Edit. *8*, 602 (1969).

Configuration of a *cis*-Disubstituted Azomethine Ylide

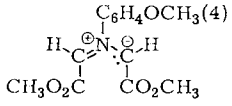
By *R. Huisgen* and *H. Mäder*[*]

The *conrotatory* ring opening of dimethyl 1-(4-methoxyphenyl)aziridine-*cis*-2,3-dicarboxylate[1] to give the azomethine ylide *trans*-dicarboxylate is structurally unambiguous. In contrast, the conrotation of the *trans*-isomer *(1)* can give the azomethine ylide dicarboxylate in the horse-shoe form *(2)* or in the W form *(3)*; in the latter form the van der

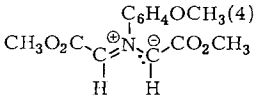
Waals strain is lower if no stipulations are made regarding coplanarity of the methoxyphenyl group with the planar azomethine ylide system.



(1)

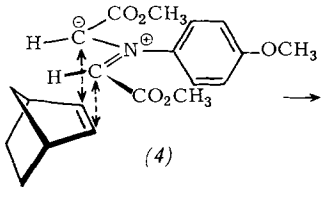


(2)

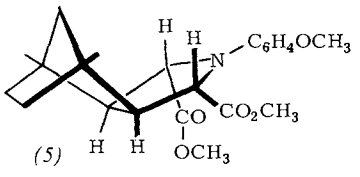


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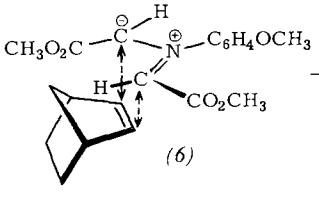
The reaction of *(1)* with norbornene at 100 °C afforded 98% of a mixture of the *exo*-adducts *(5)* and *(7)* in the ratio 55:45; the configurations of the adducts were determined from the NMR spectra[2]. The main component is the *cis* diester *(5)*, whose ester groups are directed "downwards". Formation of the *trans*-diester *(7)* was preceded by an isomerization of the azomethine ylide *cis*-dicarboxylate to the *trans*-dicarboxylate[3].



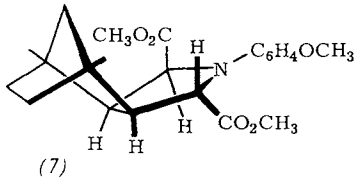
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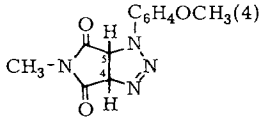


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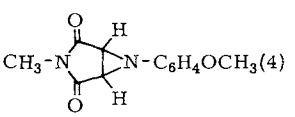
Two biplanar orientation complexes[4,5] of the 1,3-dipolar cycloaddition to norbornene that lead to *exo*-adducts can be predicted for the horse-shoe form *(2)* and for the W form *(3)*.

Examination of models shows that the arrangement *(4)* is the sterically most favorable. In confirmation, *(5)* was the only *cis*-diester adduct.

Both of the orientation complexes derived from the horse-shoe form *(2)* should be about equally unfavorable. A study of the cycloaddition of the model compound *(10)*, which is fixed in the horse-shoe form, confirmed this prediction. The cycloaddition of 4-methoxyphenyl azide to *N*-methylmaleimide at 120 °C gave 79% of the triazoline *(8)* having m.p. 131–132 °C (decomp.)[6]; NMR ($CDCl_3$): τ = 4.37 (4-H, d) and 5.29 (5-H, d) with J_{45} = 11.0 Hz, τ = 6.22 (OCH_3, s), τ = 7.02 (NCH_3, s). A solution of *(8)* in toluene at 100 °C liberated one mol. equiv. of nitrogen over a period of five hours.

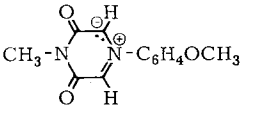


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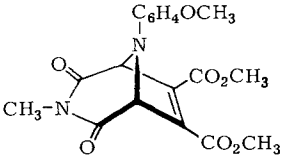


(9)

We isolated a 97% yield of the bicyclic aziridine *(9)* having m.p. 98 °C; IR (KBr): C=O 1698 (st) and 1776 cm^{-1} (w); NMR ($CDCl_3$): τ = 6.40 (2 tertiary protons, s), τ = 6.25 (OCH_3, s), τ = 7.35 (NCH_3, s). In earlier experiments on the thermolysis of maleimide-azide adducts[7,8] it was not determined whether enamines or aziridines are formed; however, *Awad et al.*[9] isolated a mixture of both compounds.



(10)

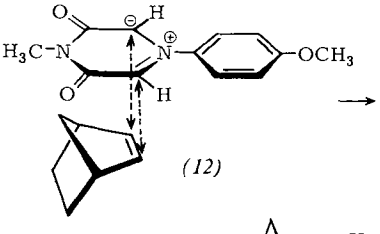


(11)

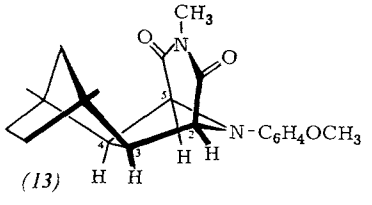
The geometry of the bicyclic ring system *(9)* permits only *disrotatory* ring opening. Since thermally only conrotation is the allowed concerted process[10], it is hardly surprising that cycloaddition of *(9)* to norbornene could not be accomplished even at 180 °C. *Disrotatory* photolysis of aziridines to azomethine ylides was established in our laboratory[1]. The photochemical ring opening of *(9)* to give *(10)* occurred readily (high-pressure mercury arc, quartz vessel); reaction in the presence of dimethyl acetylenedicarboxylate in dioxane afforded 70% of *(11)* having m.p. 202–203 °C; NMR ($CDCl_3$): τ = 4.82 (2 tertiary protons, s), τ = 6.14 (2 ester CH_3, s), τ = 6.27 (ether CH_3, s), τ = 7.08 (NCH_3, s). *Oida* and *Ohki*[11] recently reported on the photolysis of a similar bicyclic aziridine which was found to give 4% of a dimethyl acetylenedicarboxylate adduct analogous to *(11)*, along with 36% of an isomeric photoadduct.

We irradiated *(9)* in the presence of 20 mol. equiv. of norbornene in dioxane at 9 °C and obtained 33% of a mixture of the *exo*-adducts *(13)* and *(14)* in the ratio 46:54; they were separated by thick-layer chromatography.

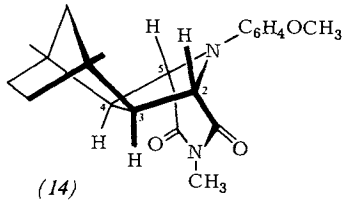
Isomer *(13)*: m.p. 170 °C; NMR ($CDCl_3$): the tertiary protons at C-2 and C-5 show τ = 5.38 and couple with 3-H and 4-H (τ = 7.34) to give an AA'MM' spectrum without any



(12)



(13)



(14)

coupling of 3-H and 4-H with the norbornane bridgehead protons, τ = 6.28 (OCH_3, s), τ = 7.17 (NCH_3, s).

Isomer *(14)*: m.p. 142–143 °C, NMR ($CDCl_3$): The somewhat broadened singlet due to 2-H and 5-H (τ = 5.58), *i.e.* the absence of any significant coupling with 3-H and 4-H, indicates a *trans* relationship, τ = 6.27 (OCH_3, s), τ = 7.17 (NCH_3, s).

The cycloaddition of *(10)* to norbornene therefore proceeds to almost equal extents *via (12)* and the corresponding orientation complex that leads to *(14)*. Consideration of

models shows that the van der Waals repulsions to be overcome in each case are comparable.

Received: June 4, 1969 [Z 29c IE]
German version: Angew. Chem. *81*, 621 (1969)

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[1] *R. Huisgen, W. Scheer,* and *H. Huber,* J. Amer. chem. Soc. *89*, 1753 (1967).

[2] *R. Huisgen, W. Scheer, G. Szeimies,* and *H. Huber,* Tetrahedron Letters *1966*, 397.

[3] *R. Huisgen, W. Scheer, H. Mäder,* and *E. Brunn,* Angew. Chem. *81*, 621 (1969); Angew. Chem. internat. Edit. *8*, 604 (1969).

[4] *R. Huisgen,* Angew. Chem. *75*, 742, 754 (1963); Angew. Chem. internat. Edit. *2*, 633, 645 (1963); J. org. Chemistry *33*, 2291 (1968).

[5] *R. Huisgen* and *G. Gotthardt,* Chem. Ber. *101*, 1059 (1968).

[6] All new compounds gave correct elemental analyses.

[7] *A. Mustafa, S. M. A. D. Zayed,* and *S. Khattab,* J. Amer. chem. Soc. *78*, 145 (1956).

[8] *S. J. Davis* and *C. S. Rondestvedt jr.*, Chem. and Ind. *1956*, 845.

[9] *W. J. Awad, S. M. A. R. Omran,* and *F. Nagieb,* Tetrahedron *19*, 1591 (1963).

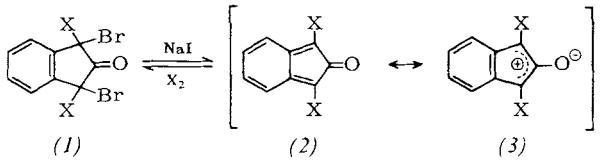
[10] For the ring opening of the cyclopropyl anion see *R. B. Woodward* and *R. Hoffmann,* J. Amer. chem. Soc. *87*, 395 (1965).

[11] *S. Oida* and *E. Ohki,* Chem. pharmac. Bull. (Tokyo) *16*, 764 (1968).

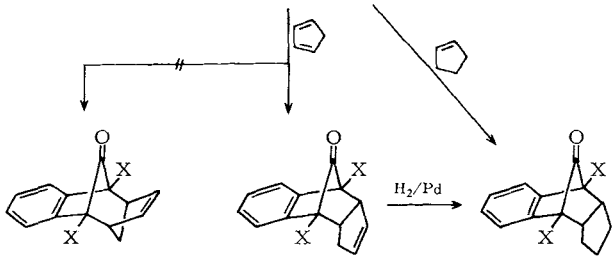
Reactivity of 1,3-Dihalogenoisoindenones

By *K. Blatt* and *R. W. Hoffmann*[*]

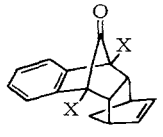
Isoindenones *(2)* are cross-conjugated 10π electron systems whose reactivity can be determined by an "oxyallyl" resonance structure *(3)* [1]. Treatment of *(1a)* with NaI in acetone



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



(4) *(5)* *(6)*



(7)

(a), X = Br
(b), X = Br or I

liberates isoindenones *(2)* [2] which can be trapped *in situ* by cycloaddition to olefins [3]. Lower yields of adduct are obtained on dehalogenation of *(1a)* with Zn in DMF.

Addition to cyclopentadiene provides us with information regarding the reactivity of *(2)*: If *(2)* were to react as a diene, compound *(5)* would result; if *(2)* reacted as an oxyallyl, compound *(4)* would be obtained [4]. The adduct obtained is actually *(5)*, as is shown by its hydrogenation to *(6)*. It therefore follows – insofar as the cycloaddition is irreversible – that compound *(2)* behaves as a cyclopentadienone rather than as an oxyallyl derivative.

During the liberation of *(2)* from *(1a)* with NaI, competing iodine/bromine exchange gives rise to iodine-containing cycloadducts. Since the adducts are stable toward iodide, exchange of iodine for bromine could take place, *e.g.* by addition of iodine or of iodine bromide to *(2)* with formation of *(1b)* [5]. The iodine/bromine exchange should proceed at a constant rate under standard conditions. The extent of the observed incorporation of iodine into the adducts depends on the relative rate of the competing irreversible Diels-Alder reaction. It therefore follows from the iodine contents of the adducts that the rate of addition of *(2)* to olefins decreases in the order: norbornadiene > cyclopentadiene > cyclopentene > norbornene > 2,3-dihydropyran (see Table). The yield of adduct also decreases correspondingly.

Adduct with		Yield (%)	M.p. (°C)	IR (cm^{-1})	Remarks	Halogen content (%) 2 Br	BrI	2 I
Norbornadiene	*(7)*	55	130–131	1810	One-proton signal at τ = 10.7 [a, b]	100	—	—
Cyclopentadiene	*(5)*	67	137–139	1805		95	5	—
Cyclopentene	*(6)*	63	101–102	1800	One-proton signal at τ = 9.4–9.9	80	20	—
Norbornene		19	174–176	1810	One-proton signal at τ = 10.6 [a]	32	65	3
2,3-Dihydropyran		8	140–141	1810	*exo/endo* mixture	—	< 1	>99

[a] Position of this signal is not shifted after reduction of the carbonyl group with $NaBH_4$.
[b] Pyrolysis at 220 °C gives 1,4-dibromonaphthalene in 60% yield.

Received: June 16, 1969 [Z 32 IE]
German version: Angew. Chem. *81*, 623 (1969)

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[1] *R. Hoffmann,* J. Amer. chem. Soc. *90*, 1475 (1968).

[2] *J. M. Holland* and *D. W. Jones,* Chem. Commun. *1969*, 587, have also generated isoindenones in this way and by other methods.

[3] 1,3-Diphenylisoindenone can also be liberated in the same manner and added to norbornadiene in 67% yield.

[4] *A. W. Fort,* J. Amer. chem. Soc. *84*, 4979 (1962); *H. G. Richey, J. M. Richey,* and *D. C. Clagett, ibid. 86*, 3907 (1964); *R. C. Cookson, M. J. Nye,* and *G. Subrahmanyam,* J. chem. Soc. (London) *C 1967*, 473, and further literature cited there.

[5] For a discussion of alternate mechanisms having the same implications see *K. Blatt,* Dissertation, Universität Heidelberg, February 1969, p. 48.

N-Chlorochloroformimidoyl Chloride[**] from Cyanogen Chloride and Chlorine

By *H. Hagemann, D. Arlt,* and *I. Ugi*[*]

Cyanogen chloride adds on chlorine with formation of *N*-chlorochloroformimidoyl chloride *(1)* [1].

$$Cl-C\equiv N + Cl_2 \rightarrow Cl_2C=N-Cl \quad (1)$$

If chlorine and cyanogen chloride in the molar ratio 3:2 are heated in the presence of *ca.* 1% active charcoal in a bomb tube or in a nickel autoclave at 60 °C for 18 hours a 77% conversion (based on cyanogen chloride) occurs with formation of 95% *(1)* and less than 5% cyanuric chloride.

Previously, this chlorination could not be achieved because in most systems cyanogen chloride is rapidly trimerized to

cyanuric chloride. Conditions which accelerate the trimerization of the cyanogen chloride, such as presence of Lewis acids, HCl, H_2O, and a ratio of $Cl_2 : ClCN < 1:1$, should therefore be avoided. Compound *(1)*, which is a colorless liquid having b.p. 87 °C, can be distilled under normal pressure. *(1)* is comparable with sulfuryl chloride regarding its tendency to lose chlorine. It is a strong chlorinating agent but, like other *N*-halogen compounds, also adds on olefins. The corresponding fluorine compound [2] boils at −60 °C and explodes on warming.

The characteristic intense IR bands at 1560, 945, and 730 cm^{-1}, the molecular weights determined by mass spectrometry, and the result of elemental analyses confirm the given structure of *(1)*.

Received: May 30, 1969 [Z 33 IE]
German version: Angew. Chem. *81*, 572 (1969)

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[**] Departing from IUPAC rules on nomenclature, also called *N*-chloroisocyanide dichloride

[1] *H. Hagemann, D. Arlt*, and *I. Ugi*, German Pat.-Appl. F 52233 IVa/12 (April 24, 1967), Farbenfabriken Bayer AG.

[2] *V. A. Ginsberg* and *K. N. Smirnov*, Ž. obšč. Chim. *37*, 1413 (1967).

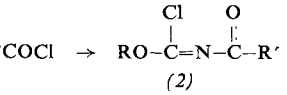
Addition of Acyl Chlorides to the C≡N Bond of Cyanates

By *E. Grigat* [*]

Because of the pronounced electrophilic character of their N≡C–O group, cyanates *(1)* show only a slight tendency to add electrophilic agents at the nitrogen atom [1]. Attempts to carry out *N*-acylations of cyanates usually fail since the cyanates are trimerized by small amounts of liberated acid [2] or by added catalysts [3] and are thus not available for reaction.

The only successful reaction with an acid chloride was afforded by reaction of benzoyl chloride with 2 moles of *(1)* in the presence of $SbCl_5$ which, in two special cases, leads to formation of 4,6-bis(aryloxy)-3,5-diazapyrylium hexachloroantimonate [3]; a 1:1-addition product could not be isolated. Previously, addition of an acyl chloride to the nitrile group of the cyanate was possible only with halide salts of *N,N*-dialkylated imido chlorides [4,5].

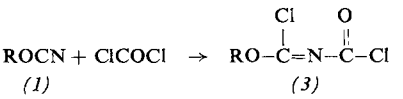
We have now found that the new *N*-acyliminocarbonic ester halides *(2)* are formed in yields of 45 to 90% [6] along with small amounts of the trimerizate of *(1)* when pure acyl chlorides are heated with cyanates in inert solvents (aliphatic acyl chlorides: 20–120 °C; aromatic acyl chlorides: up to 220 °C, also without solvent). The compounts *(2)* are surprisingly



(1) *(2)*

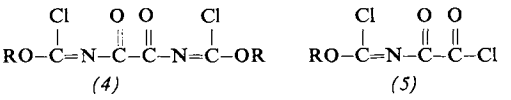
stable, the majority even being distillable. Their halogen atom is readily replaced by nucleophiles:

At temperatures as low as 0–20 °C, phosgene adds smoothly to *(1)* to give *N*-chloroformyliminocarbonic halides *(3)* [7].



(1) *(3)*

The halogen atom on the formyl groups is the more reactive; the chlorine atoms can be successively replaced by nucleophiles. Reaction of *(1)* with half-molar amounts of oxalyl chloride affords homogeneously *N,N*-bis[alkoxy-(or aroxy-)-chloromethylene]oxamide *(4)* while on reaction with an excess of oxalyl chloride only compound *(5)* is obtained [8,9].



(4) *(5)*

The halogen atoms in *(4)* and *(5)* and in *(2)* and *(3)* are of similar reactivity.

The same type of reactions take place with cyanamides in place of cyanates and oxalic acid esters (acid thioester, acid amide)-halides, (thio-)carbonic esters halides, trichloromethylsulfenyl chloride and chlorocarbonylsulfenyl chloride instead of acyl chlorides.

Experimental:

Phenyl cyanate (23.8 g, 0.2 mole) is added dropwise and slowly to a solution of dichloroacetyl chloride (29.4 g, 0.2 mole) in toluene (100 ml). Reaction is complete after one hour's stirring at the reflux temperature (116 °C). A small amount of trisphenyl cyanurate precipitates out; this is filtered off and the filtrate is concentrated by evaporation under vacuum (water-pump). Distillation of the crude product (50 g) yields 38 g (72% yield) of compound *(2)* with R = C_6H_5 and R′ = $CHCl_2$; b.p. 99 °C/0.2 torr.

Received: June 16, 1969 [Z 34 IE]
German version: Angew. Chem. *81*, 623 (1969)

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[1] a) For reviews see *E. Grigat* and *R. Pütter*, Angew. Chem. *79*, 219 (1967); Angew. Chem. internat. Edit. *6*, 206 (1967); b) *D. Martin*, Z. Chem. *7*, 123 (1967).

[2] *E. Grigat* and *R. Pütter*, Chem. Ber. *98*, 1359 (1965).

[3] *D. Martin* and *A. Weise*, Chem. Ber. *100*, 3736 (1967).

[4] See [1a] p. 231 and p. 218.

[5] *J. Zirner, E. Grigat*, and *R. Pütter*, German Pat. 1293753 (Feb. 18, 1966), Farbenfabriken Bayer AG.

[6] *E. Grigat* and *R. Pütter*, German Pat.-Appl. P 1768678.1, (June 15, 1968), Farbenfabriken Bayer AG.

[7] *E. Grigat* and *R. Pütter*, German Pat.-Appl. P 1668108.6, (March 9, 1968), Farbenfabriken Bayer AG.

[8] *E. Grigat* and *R. Pütter*, German Pat.-Appl. P 1905562.0, (Feb. 5, 1969), Farbenfabriken Bayer AG.

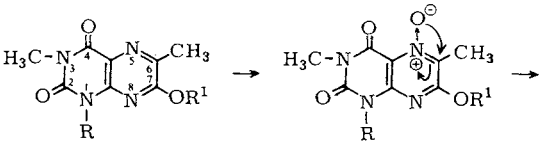
[9] *E. Grigat* and *R. Pütter*, German Pat.-Appl. P 1928130.2, (June 3, 1969), Farbenfabriken Bayer AG.

		(2)		*(3)*	*(4)*	*(5)*
R	R′	B.p. (°C/torr)	M.p. (°C)	B.p. (°C/torr)	M.p. (°C)	M.p. (°C)
C_6H_5	CH_3	71/0.15		66/0.18	103–104	96–99
CCl_3–CH_2	CH_2Cl	97/0.3		76–78/0.5		
p-Cl–C_6H_4	$CHCl_2$		47	104/0.7	136–137	44–46
C_6H_5	CCl_3	108/0.4				
C_6H_5	C_6H_5	138/0.3	74–76			
p-CH_3–C_6H_4	2,5-Cl_2–C_6H_3	169/0.3	68–69	81–82/0.18		
α-Naphthyl					145–146 (dec.)	66–68

A New Pteridine → Purine Transformation

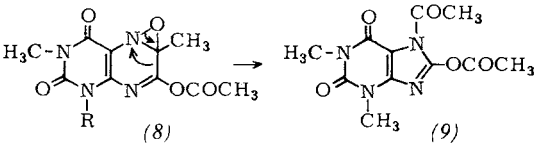
By *W. Hutzenlaub, G. B. Barlin,* and *W. Pfleiderer* [*]

Whereas the conversion of purines into pteridines by chemical methods [1,2] has already been described on a number of occasions and a ring expansion of this kind plays a decisive role in the biosynthesis of pteridines [3], the reverse reaction, *i.e.* the ring contraction of the pyrazine to the imidazole nucleus, has hitherto only been observed in an enzymatic reaction that proceeds in the presence of the organism *Alcaligenes faecalis* [4,5]. We have now found that the 5-oxides *(4)* and *(5)*, formed by H_2O_2 oxidation of 7-hydroxy-1,3,6-trimethyl-2,4-dioxotetrahydropteridine *(1)* and the 3,6-dimethyl-1-phenyl derivative *(2)*, respectively, do not undergo Boekelheide rearrangement to give the 6-acetoxymethyl derivatives when boiled with acetic anhydride but instead undergo ring contraction to give 1,3-dimethyluric acid *(10)* and 1-methyl-3-phenyluric acid *(11)*, respectively.

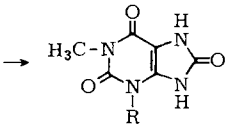


	R	R^1
(1)	CH_3	H
(2)	C_6H_5	H
(3)	CH_3	CH_3

	R	R^1
(4)	CH_3	H
(5)	C_6H_5	H
(6)	CH_3	CH_3
(7)	CH_3	$COCH_3$



(8) *(9)*



	R
(10)	CH_3
(11)	C_6H_5

In order to elucidate the course of this ring contraction we first attempted to bring about reaction of 1,3,6-trimethyl-7-methoxy-2,4-dioxotetrahydropteridine 5-oxide *(6)* with acetic anhydride in the same way; however, deoxygenation to the starting material *(3)* was the only reaction that took place. Experiments with isotopes showed that radioactive 1,3-dimethyluric acid is obtained only when position 7 of compound *(4)* is labeled with [^{14}C], whereas neither the [6-^{14}C] derivative of *(4)* nor reaction with [1-^{14}C]-acetic anhydride lead to activity in the purine derivative. It may be concluded from these findings that *(4)* is first acetylated to 7-acetoxy-1,3,6-trimethyl-2,4-dioxotetrahydropteridine 5-oxide *(7)* by the acetic anhydride, thus facilitating nucleophilic attack of the *N*-oxide oxygen on the neighboring C-6 atom to give *(8)*. Stabilization of *(8)* by valence isomerization then takes place to give 8-acetoxy-7-acetyl-1,3-dimethylxanthine *(9)*, which has, however, not yet been isolated as the pure substance but only in the form of its hydrolysis product 1,3-dimethyluric acid *(10)*.

This novel rearrangement appears to be of a general nature since ring contraction of quinoxalones to benzimidazol-2-ones [6] has also been observed recently.

7-Hydroxy-1,3,6-trimethyl-2,4-dioxotetrahydropteridine *(4)* (0.5 g) is refluxed for 20 min in acetic anhydride (5 ml). The mixture is then evaporated to dryness, and the residue is taken up in water and reprecipitated from dilute ammonia/HCl. Recrystallization from a large volume of water gives 0.32 g (84%) of colorless, crystalline 1,3-dimethyluric acid *(10)*, m.p. $>360\,^{\circ}C$ (literature value [7]: $>360\,^{\circ}C$), which proves to be identical with authentic material on chromatography.

Received: June 19, 1969 [Z 35 IE]
German version: Angew. Chem. *81*, 624 (1969)

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[1] *A. Albert*, Biochem. J. *65*, 124 (1957).
[2] *W. Pfleiderer*, Chem. Ber. *92*, 2468 (1959).
[3] *F. Weygand, H. Simon, G. Dahms, M. Waldschmidt, H. J. Schliep,* and *H. Wacker*, Angew. Chem. *73*, 402 (1961).
[4] *W. S. McNutt*, J. biol. Chemistry *238*, 1116 (1963).
[5] *W. S. McNutt* and *S. P. Damle*, J. biol. Chemistry *239*, 4272 (1964).
[6] *Y. Ahmad, M. S. Habib, A. Mohammady, B. Bakhtiari,* and *S. A. Shamsi*, J. org. Chemistry *33*, 201 (1968).
[7] *E. Fischer* and *H. Clemm*, Ber. dtsch. chem. Ges. *30*, 3094 (1897); *H. Biltz* and *M. Heyn*, Liebigs Ann. Chem. *423*, 185 (1921).

Reactions in Chiral Crystals: An Absolute Asymmetric Synthesis

By *K. Penzien* and *G. M. J. Schmidt* [*]

An absolute optical synthesis has been carried out in a chemical system composed of optically inactive molecules, *i.e.* molecules which are either achiral or whose chiral conformations interconvert so rapidly that optical rotation cannot be measured in the disperse phases; as the required chiral influence we have successfully used the enantiomorphic crystal structure of one of the reactants [1].

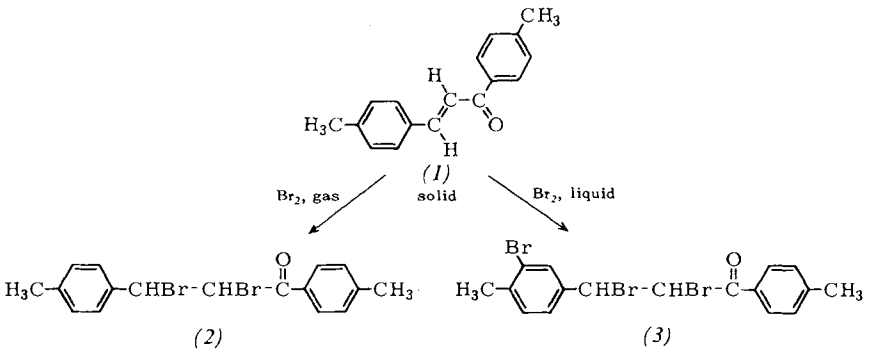
The underlying thesis that the crystal lattice maintains control over the configuration and conformation of the reacting components, at least until the formation of a transition state of defined geometry, has been developed in the topochemical studies conducted in this Laboratory [2].

Three lines of work have merged in the design of appropriate experiments: first, in our study of molecular packing modes [3] we have observed that α,β-unsaturated ketones frequently crystallize in non-centrosymmetric and occasionally in enantiomorphic space groups [4]. Secondly, molecular conformation of this group of compounds has been shown to be a function of packing arrangement [4]. Thirdly, a study of gas/solid reactions has shown that reaction of bromine in the vapor phase with solid 1,2-disubstituted *trans*-ethylenes yields the *meso*- or *erythro*-dibromides in suitable crystal structures [5]. Following these leads we have carried out the gas/solid and liquid/solid brominations of individual monocrystals (space group $P2_12_12_1$; D_2^4) of 4,4'-dimethylchalcone *(1)*; the reactions afford, in chemical yields $>90\%$, one of the diastereoisomers of *(2)* or *(3)*, with one enantiomer in excess.

Rotations approximately (±10%) proportional to the weight of the crystals (6–60 mg) of $\alpha_D = 0.06$ to 0.6° and having either sign were observed consistently.

The specific rotation $[\alpha]_D^{28} = 9.8$ of the product of the gas/solid reaction, and the specific rotation of optically pure *(2)*, $[\alpha]_D^{28} = 167$, indicate an average optical yield of 6%.

The following control experiments have been carried out: a single crystal (~200 mg) of *(1)* was cut, and one half bro-



minated in chloroform solution: zero rotation. The other half was directly exposed to bromine gas and gave optically active dibromide. Bromination of a mixture made up of crystals grown in separate vessels (to eliminate observed inoculation effects) gave a product having zero rotation.

Because of the absence of well defined { *hkl* } forms and our inability to measure optical rotation of the crystals, correlation between the sign of rotation of the initial matrix and of the reaction product could not be achieved.

We believe that experiments of the kind described are relevant, apart from their synthetic implications, to the analysis of solid-state and enzymatic reaction mechanisms.

Experimental:

Adequately homogeneous crystals of 4,4′-dimethylchalcone, m.p. 132 °C, were grown from slowly cooled solutions (60 to 20 °C in 10 days) in ethyl acetate. Crystallographic constants [6]: $a = 15.26$, $b = 5.91$, $c = 14.65$ Å. Space group $P2_12_12_1$. D_X ($Z = 4$): 1.19 g/cm³.

The gas/solid reaction has been carried out in a flask containing a powdered single crystal of *(1)*; bromine (10% excess) was admitted as vapor and the material agitated at room temperature with a magnetic stirrer. After the reaction had been completed (2–3 h) the product was chromatographed (hexane : benzene) over a Kieselgel column to remove traces of *(1)* or *(3)*. Alternately, the crushed crystal in a round-bottom flask was covered with cold liquid bromine (excess) and the whole shaken for 5 min at 0 °C. Excess bromine was partially removed in a stream of nitrogen. The remaining brown oil was dissolved in chloroform, and the solvent, some bromine and HBr evaporated with nitrogen; three such operations produced crystalline material which, if still slightly yellow, was passed through a short Kieselgel column.

Rotation of the colorless chloroform solutions of the so purified compounds ($c = 1.2$–12 g/100 ml) was measured in a polarimeter [Perkin-Elmer 141; 1 ml cuvette, $l = 10$ cm]. Rotation was constant over weeks, even after addition of acid or of small amounts of bromine. An optically pure enantiomer of *(2)* ($[\alpha]_D^{28} = 167$) was obtained from the reaction product after nine recrystallizations (constant specific rotation) from benzene : hexane (1:1) in the temperature range 60–10 °C.

The structure of *(2)* (m.p. 175–179 °C, decomp., from benzene : hexane) is based on elemental analysis and its NMR spectrum. *(3)* (m.p. 153–154 °C, from hexane : chloroform) has been prepared independently from 3-bromo-4,4′-dimethylchalcone (m.p. 140 °C, from benzene) by bromine addition; elemental analysis and its NMR spectrum afford proof of structure.

Received: July 16, 1969 [Z 40 IE]
German version: Angew. Chem. *81*, 628 (1969)

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[**] K.P. acknowledges the award of a Stiftung Volkswagenwerk Stipend.

[1] Cf. *F. Wudl, D. A. Lightner*, and *D. J. Cram*, J. Amer. chem. Soc. *89*, 4099 (1967).

[2] *G. M. J. Schmidt*, Photochemistry of the Solid State, in Reactivity of the Photoexcited Organic Molecule. J. Wiley, New York 1967, p. 227.

[3] *e.g. L. Leiserowitz* and *G. M. J. Schmidt*, J. chem. Soc. (London) A, in press.

[4] *D. Rabinovich, G. M. J. Schmidt*, and *Z. Shaked*, J. chem. Soc. (London) B, in press.

[5] *E. Hadjoudis, E. Kariv*, and *G. M. J. Schmidt*, unpublished.

[6] *D. Rabinovich*, unpublished.

Nucleophilic Substitutions with Pyrimidine Nucleoside N³ Sodium Salts

By *H. Seliger* and *F. Cramer* [*]

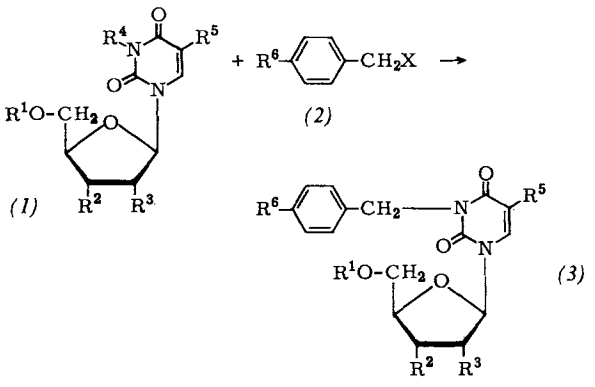
As can be deduced from the pH dependence of the ultraviolet spectrum of pyrimidine nucleosides [1], the nucleobases are deprotonated at N³ in alkaline media. The resulting pyrimidine nucleoside N³-anions can act as nucleophiles in addition and in substitution reactions [2]. We have prepared the N³ sodium salts of derivatives of uridine and thymidine in non-aqueous medium and studied their reactions with aralkyl halides.

2′,3′-*O*,*O*-(2,4-Dimethoxybenzylidene)uridine *(1a)* [3], dissolved in 1,2-dichloroethane, is treated with the stoichiometric amount of sodium ethoxide in ethanol. After removal of the solvent, the sodium salt *(1b)* is precipitated by addition of light petroleum. 3′,5′-*O*,*O*-Ditritylthymidine *(1c)* is converted into the sodium salt *(1d)* in a similar manner. The uridine N³ sodium salt *(1e)* precipitates from an ethanolic solution of uridine on addition of sodium ethoxide. The UV spectra of the sodium salts, recorded in absolute CH_2Cl_2 or $C_2H_4Cl_2$, agree with the spectra of the corresponding nucleosides and nucleoside derivatives in aqueous-alcoholic KOH (pH > 12): *(1b)*, $\lambda_{max} = 261$ nm, $\lambda_{min} = 246$ nm; *(1d)*, $\lambda_{max} = 264$ nm, $\lambda_{min} = 250$ nm; *(1e)*, $\lambda_{max} = 261$ nm, $\lambda_{min} = 242$ nm.

The reaction of pyrimidine nucleoside sodium salts with aralkyl halides *(2)* in inert, anhydrous solvents yields N³-aralkylated derivatives *(3)*, whose UV spectra no longer change on going from neutral to alkaline media. Substitution of the sugar alcohol group or removal of the protective groups does not occur under the above conditions. The reaction conditions and yields are given in the Table. As expected, the reaction is facilitated by electron-attracting *p*-substituents on the benzyl halide; the reactivity, and also the tendency to undergo side reactions, increases on going from chloride to iodide.

The sugar protective group is removed by treatment with 80% acetic acid. After 60–100 min at room temperature, *(3ba)*, *(3bb)*, *(3bc)*, and *(3bd)* give quantitative yields of the N³-aralkylated uridines. Removal of the trityl groups from *(3dc)* and *(3dd)* (two hours at 100 °C) gave 93% of *p*-nitrobenzylthymidine and 80% of *p*-bromobenzylthymidine respectively.

In contrast to techniques used previously for the aralkylation of pyrimidine nucleosides [4,5], in which predominantly or ex-



(1) (2) (3)

clusively the sugar component is substituted, the present method permits the preparation, in high yield, of pyrimidine nucleosides that are aralkylated at the base only.

Compound *(1b)* also reacts with chloromethylated polystyrene and thus makes possible the linkage of nucleotides and oligonucleotides with "Merrifield polymers"[6] *via* dimethoxybenzylideneuridine as phosphate-protecting group[7]. Studies on the use of this possible mode of linkage in the synthesis of oligonucleotides on carriers[8] are in progress.

Received: June 9, 1969 [Z 30 IE]
German version: Angew. Chem. *81*, 576 (1969)

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[1] See, *e.g. J. Sugar* and *J. J. Fox*, Biochim. biophysica Acta *9*, 269 (1952).

[2] *R. W. Chambers*, Biochemistry *4*, 219 (1965).

[3] *F. Cramer, W. Saenger, K. H. Scheit*, and *J. Tennigkeit*, Liebigs Ann. Chem. *679*, 159 (1964); see also ref. [7].

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[8] Cf., *inter alia, F. Cramer, R. Helbig, H. Hettler, K. H. Scheit*, and *H. Seliger*, Angew. Chem. *78*, 640 (1966); Angew. Chem. internat. Edit. *5*, 601 (1966); *F. Cramer* and *H. Köster*, Angew. Chem. *80*, 488 (1968); Angew. Chem. internat. Edit. *7*, 473 (1968).

The Absolute Configuration of Bacteriochlorophyll-*a*[1] [**]

By *H. Brockmann jr.* and *Ingrid Kleber*[*]

We recently derived the absolute configuration (3*R*, 4*R*, 7*S*, 8*S*) for bacteriochlorophyll-*a*[2] and thus also for bacteriomethylpheophorbide-*a* *(1)*[1b]. In order to confirm unequivocally this configurational assignment two experiments remained to be carried out:

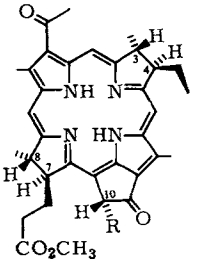
1. Direct comparison of the bis(*p*-bromophenacyl) 3-ethyl-2′ methylsuccinate *(4)* obtained by oxidative degradation of bacteriochlorophyll-*a* derivatives with an authentic sample[1b] of known absolute configuration[3].

	(1) R¹	R²	R³	R⁴	R⁵	(2)	R⁶	X	Solvent	Time (h)	*T* (°C)	Product [a]	Yield (%)[b]
(a)	H	*O,O*-(2,4-dimethoxybenzylidene)		H	H								
(b)	H	*O,O*-(2,4-dimethoxybenzylidene)		Na	H	*(a)*	H	Cl	CH_2Cl_2	72	90	*(3ba)*	52
									acetonitrile	48	90	*(3ba)*	80
						(a′)	H	Br	CH_2Cl_2	48	90	*(3ba)*	73
						(a″)	H	I	CH_2Cl_2	72	80	*(3ba)*	15
						(b)	Cl	Cl	acetonitrile	48	90	*(3bb)*	58
						(c)	NO_2	Br	acetonitrile	132	20	*(3bc)*	78
						(d)	Br	Br	acetonitrile	60	20	*(3bd)*	91
									then	60	40		
(c)	$(C_6H_5)_3C$	$(C_6H_5)_3CO$	H	H	CH_3								
(d)	$(C_6H_5)_3C$	$(C_6H_5)_3CO$	H	Na	CH_3	*(c)*	NO_2	Br	dichloroethane	20	reflux	*(3dc)*	90
						(d)	Br	Br	dichloroethane	8	reflux	*(3dd)*	89
(e)	H	OH	OH	Na	H								

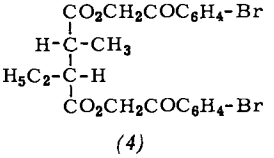
[a] R^1—R^6 as for *(1)* and *(2)*. [b] Products obtained analytically pure by preparative thin-layer chromatography and crystallization

2. Confirmation of the (7*S*, 8*S*) configuration of bacteriochlorophyll-*a*.

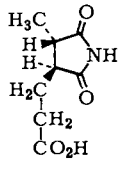
The latter follows from the identity of 3,4-dehydrobacteriochlorophyll-*a* derivatives[4–6] with compounds that are accessible from chlorophyll-*a*[7,8] whose (7*S*, 8*S*) configuration has been proved[9,10]. The proofs of identity used



(1), R = CO_2CH_3
(2), R = H
(3), R = H, double bond between C-3 and C-4



(4)



(5)

hitherto were based mainly on agreement of melting points, basicity, crystalline form, absorption spectra, and Debye-Scherrer photographs, whereas the values obtained for optical rotation agreed only qualitatively[5]. Moreover, the acidic, levorotatory oil obtained on oxidative degradation of bacteriochlorophyll-*a* could only be insufficiently characterized as (—)-*threo*-dihydrohematinimide *(5)*[5,6].

We have isolated bacteriochlorophyll-*a* from *Rhodospirillum rubrum* and thence prepared bacteriomethylpheophorbide-*a* *(1)*[11]. Oxidative degradation of *(1)* with CrO_3 in 25% H_2SO_4 (3 h at —10 °C[12]) and subsequent chromatography on silica gel with light petroleum (40—60 °C), ethyl acetate, isopropanol (44:5:1) afforded *threo*-3-ethyl-2-methylsuccin-

imide as a colorless oil ($[\alpha]_D^{20} = +57°$, $c = 1.2$ in chloroform) which yielded the ester *(4)* (m.p. 114–115 °C, $[\alpha]_D^{20} = -35 \pm 3°$, $c = 0.9$ in chloroform) on hydrolysis (3 hours' boiling with 5 N HCl) and subsequent esterification with *p*-bromophenacyl bromide. No depression of melting point was observed with a mixture of *(4)* with an authentic sample[1b], but such a depression was found with a mixture of *(4)* with *rac-(4)*. Optical rotation, chromatographic behavior, and IR spectrum (KBr)[13] of *(4)* were as for the authentic material.

Treatment of bacteriomethylpheophorbide-*a* *(1)* with tetrachloro-*o*-benzoquinone in benzene at 25 °C led to 3,4-dehydro compounds (absorption spectrum); the reaction is, however, accompanied by oxidation at C-10[14]. In order to avoid such oxidation we removed the methoxycarbonyl group from *(1)* by boiling it for 48 h in pyridine. The resulting bacteriopyromethylpheophorbide-*a* *(2)* reacted smoothly with tetrachloro-*o*-benzoquinone in benzene to give 2-acetyl-2-devinylpyromethylpheophorbide-*a* *(3)* whose physical properties (m.p., absorption spectrum, IR, NMR, mass spectrum), and particularly the ORD spectrum[15], all agreed with those of a sample prepared from chlorophyll-*a*[16].

Received: June 19, 1969 [Z 36 IE]
German version: Angew. Chem. *81*, 626 (1969)

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

[1] Part 3 of Absolute Configuration of Chlorophylls. – Parts 1 and 2 are a) *H. Brockmann jr.*, Angew. Chem. *80*, 233 (1968); Angew. Chem. internat. Edit. *7*, 221 (1968); b) *H. Brockmann jr.*, Angew. Chem. *80*, 234 (1968); Angew. Chem. internat. Edit. *7*, 222 (1968).

[2] According to a suggestion by *K. E. Eimhjellen*, *O. Aasmundrud*, and *A. Jensen*, Biochem. biophysic. Res. Commun. *10*, 232 (1963); Biochem. biophysica Acta *88*, 466 (1964), bacteriochlorophyll should in future be designated bacteriochlorophyll-*a* in order to distinguish it from other bacteriochlorophylls.

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[4] *H. Fischer*, *R. Lambrecht*, and *H. Mittenzwei*, Hoppe-Seylers Z. physiol. Chem. *253*, 38 (1938).

[5] *H. Mittenzwei*, Hoppe-Seylers Z. physiol. Chem. *275*, 93 (1942).

[6] *J. H. Golden*, *R. P. Linstead*, and *G. H. Whitham*, J. chem. Soc. (London) *1958*, 1725

[7] *H. Fischer*, *W. Lautsch*, and *K.-H. Lin*, Liebigs Ann. Chem. *534*, 1 (1938).

[8] *H. Fischer*, *H. Mittenzwei*, and *D. B. Hevèr*, Liebigs Ann. Chem. *545*, 145 (1940).

[9] *H. Brockmann jr.*, Angew. Chem. *80*, 233 (1968); Angew. Chem. internat. Edit. *7*, 221 (1968).

[10] *I. Fleming*, Nature (London) *216*, 151 (1967); J. chem. Soc. (London) *C 1968*, 2765.

[11] We are grateful to Professor *N. Pfennig*, Göttingen, for the *Rhodospirillum rubrum* strain No. 9960 and for valuable advice concerning its cultivation.

[12] *R. K. Ellsworth* and *S. Aronoff*, Arch. Biochem. Biophysics *124*, 358 (1968).

[13] Racemic *(4)* and optically active *(4)* give different IR spectra in KBr, compare ref. [6].

[14] *H. Wolf*, *H. Brockmann jr.*, *H. Biere*, and *H. H. Inhoffen*, Liebigs Ann. Chem. *704*, 208 (1967).

[15] We wish to thank Doz. Dr. *H. Wolf*, Braunschweig, for recording the ORD spectra.

[16] *H. H. Inhoffen*, *P. Jäger*, *R. Mählhop*, and *C.-D. Mengler*, Liebigs Ann. Chem. *704*, 188 (1967).

Preparation of the Compounds $R_3El-Hg-ElR_3$ (El = C, Si, Ge, Sn) and their Synthetic Applications[1]

By *W. P. Neumann* and *U. Blaukat*[*]

The wide variety of reactions possible with R_3Si-Hg and R_3Ge-Hg bonds, *e.g.* additions[2,3], prompted an inquiry into the behavior of the analogous R_3C-Hg group.

The simplest bis(*tert*-alkyl)mercury compound $[(CH_3)_3C]_2Hg$[4] *(1)* is formed in a Grignard reaction at 0 °C in tetrahydrofuran and is obtained in 60% yield as colorless crystals [m.p. 56–58 °C, b.p. 80 °C/10^{-4} torr after purification by chromatography (neutral Al_2O_3; ether)]. It was characterized by elemental analysis as well as by its ^{1}H-NMR spectrum (τ 8.8, $J(^{199}Hg-CH_3) = 103.6$ Hz), and is homogeneous on gas chromatography, sensitive to air, and decomposes under argon at temperatures above 120 °C.

The reactivity of the C–Hg bonds in *(1)* is extremely high, exceeding that of such bonds in $(C_2H_5)_2Hg$[**]. We have investigated additions to, *e.g.*, $-N=N-$ or $-C\equiv C-$ groups (see Table 1): The mercury-containing adducts were identified, either immediately or after hydrolysis, by elemental analysis and by their IR and ^{1}H-NMR spectra; the *cis* or *trans* structures given were deduced from the NMR spectra.

Reaction of *(1)* and the hydrides R_3ElH (El = Si, Ge, Sn) in the absence of a solvent proceeds smoothly[6] to give the corresponding compounds $(R_3El)_2Hg$ (see Table 2).

$$[(CH_3)_3C]_2Hg + 2\ R_3ElH \rightarrow (R_3El)_2Hg + 2\ \text{iso-}C_4H_{10} \qquad (1)$$
(1)

Tin-mercury compounds containing aliphatic groups were previously inaccessible[7]; they generate stannyl radicals even at low temperatures and are therefore of significance for studies on radical reaction mechanisms[8].

Table 1. Addition of $[(CH_3)_3C]_2Hg$ to $-N=N-$ and $-C\equiv C-$ bonds.

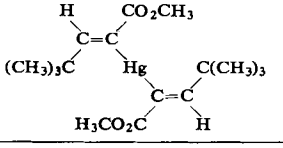
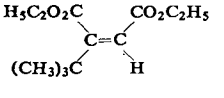
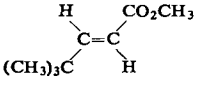
Reaction partners	$H_5C_2O_2C-N=N-CO_2C_2H_5$	$H_5C_2O_2C-C\equiv C-CO_2C_2H_5$	$H-C\equiv C-CO_2CH_3$
Reaction conditions (°C/h)	−20/0.17	0/4	25/330
Product	a) $(CH_3)_3C\ C(CH_3)_3$ $H_5C_2O_2C-N-N-CO_2C_2H_5$ b) $(CH_3)_3C-Hg\ Hg-C(CH_3)_3$ $H_5C_2O_2C-N-N-CO_2C_2H_5$	not isolated	
Properties	a) colorless oil; impure b) colorless crystals; m.p. 193 °C	pale yellow oil	colorless crystals, m.p. 95 °C
After hydrolysis	a) $(CH_3)_3C\ C(CH_3)_3$ $H_5C_2O_2C-N-N-CO_2C_2H_5$ b) $H\ H$ $H_5C_2O_2C-N-N-CO_2C_2H_5$		

Table 2. Compounds $(R_3El)_2Hg$ (El = Si, Ge, Sn) prepared according to eq. (1).

Product	Reaction conditions (°C/h)	Properties	Yield (%)
$[(C_2H_5)_3Si]_2Hg$	90—100/72	yellow liquid; b.p. 100 °C/0.3 torr [3]	50
$[(CH_3)_3Ge]_2Hg$	25/30 in benzene	yellow crystals; m.p. 120 °C [3]	90—95 [5]
$[(C_2H_5)_3Ge]_2Hg$	25/18	deep yellow liquid; b.p. 110 °C/ 0.05 torr [2, 3]	98
$[(CH_3)_3Sn]_2Hg$	—25/2	deep red crystals; decomp. pt. —10 °C	75
$[(C_2H_5)_3Sn]_2Hg$	—25/8	yellow liquid; decomp. pt. —10 °C	73
$[(C_4H_9)_3Sn]_2Hg$	—25/24	yellow liquid; decomp. pt. —10 °C	50—70

Received: June 16, 1969 [Z 37 IE]
German version: Angew. Chem. *81*, 625 (1969)

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[**] For example, $(C_2H_5)_2Hg$ reacts with diethyl azodicarboxylate (8 h at 20 °C) to give the corresponding adduct (see Table 1).

[1] Part of the Diploma Thesis by *U. Blaukat*, Universität Giessen 1968.

[2] *K. Kühlein*, Diploma Thesis, Universität Giessen 1963; *K. Kühlein, W. P. Neumann*, and *H. P. Becker*, Angew. Chem. *79*, 870 (1967); Angew. Chem. internat. Edit. *6*, 876 (1967).

[3] Cf. *N. S. Vyazankin, G. A. Razuvaev*, and *O. A. Kruglaya*, Organometallic Chem. Rev. *A 3*, 323 (1968).

[4] Has only been described on one occasion previously, and then as an oil and without accurate characterization: *S. Marvel* and *H. O. Calvery*, J. Amer. chem. Soc. *45*, 820 (1923).

[5] *T. N. Mitchell*, unpublished.

[6] $(C_2H_5)_2Hg$ reacts in a manner analogous to that shown in eq. (1), M = Si, only at temperatures above 140 °C and then giving a very low yield [3]; when El = Sn, only decomposition occurs (experiment by *K. Kühlein*).

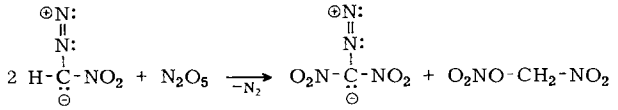
[7] The corresponding phenyl compound was recently prepared by another route: *C. Eaborn, A. R. Thompson*, and *D. R. M. Walton*, Chem. Commun. *1968*, 1051.

[8] *K. Rübsamen, W. P. Neumann, Ra. Sommer*, and *U. Frommer*, Chem. Ber. *102*, 1290 (1969); and further literature cited there.

Preparation of Dinitrodiazomethane by Nitration of Nitrodiazomethane

By *U. Schöllkopf* and *P. Markusch* [*]

During our studies on heterocarbenes our interest was attracted to dinitrocarbene because theory predicts that this species should be the most electrophilic of all carbenes [1]. Since photolysis and thermolysis are generally recognized as being the most reliable routes to carbenes we synthesized the unusual compound dinitrodiazomethane *(2)* by nitration of nitrodiazomethane *(1)* [2] with dinitrogen pentoxide [3].



(1) *(2)*

The colorless compound *(2)*, m.p. 65 °C (decomp.), explodes on impact, when heated rapidly, and on treatment with concentrated sulfuric acid [4]. Its characteristic IR bands (KBr) are observed at 2120 [5] (νN_2) and 1475 and 1315 cm^{-1} (ν_s and $\nu_{as}NO_2$, respectively).

Procedure:

9 ml (9.7 mmoles) of a 1.08 M solution of dinitrogen pentoxide in methylene chloride is added dropwise at −30 °C to a solution of 1.6 g (19 mmoles) of nitrodiazomethane [2] in 120 ml of methylene chloride over a period of 30 min. After four hours' stirring the solution is evaporated down to a volume of about 30 ml at room temperature in a vacuum. Dinitrodiazomethane crystallizes from the concentrated solution on standing for a few hours at −15 °C; yield 480 mg (42%).

Received: July 4, 1969 [Z 38 IE]
German version: Angew. Chem. *81*, 577 (1969)

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[1] For the electrophilicity and electronic state of nitrocarbene see *R. Gleiter* and *R. Hoffmann*, J. Amer. chem. Soc. *90*, 5457 (1968); *R. Hoffmann, G. D. Zeiss*, and *G. W. Van Dine*, J. Amer. chem. Soc. *90*, 1485 (1968).

[2] *U. Schöllkopf* and *P. Markusch*, Tetrahedron Letters *1966*, 6199.

[3] For the mechanism of the nitration of diazo compounds with dinitrogen pentoxide see *U. Schöllkopf, P. Tonne, H. Schäfer*, and *P. Markusch*, Liebigs Ann. Chem. *722*, 45 (1969).

[4] Dicyanodiazomethane behaves similarly; see *E. Ciganek*, J. org. Chemistry *30*, 4198 (1965).

[5] In methylene chloride at 2150 cm^{-1}.

Stereochemical Course of Grignard Reactions at Asymmetric Sulfur [***]

By *H. Hope, U. de la Camp, G. D. Homer, A. W. Messing*, and *L. H. Sommer* [*]

Nucleophilic displacement of the alkoxy group from sulfur in a sulfinate provides a general route to sulfoxides *via* reaction with a Grignard reagent, and (−)-menthyl (−)-*p*-toluenesulfinate *(−1)* is an easily prepared diastereomeric precursor that gives optically active sulfoxides, $p\text{-}CH_3C_6H_4S^*OR$ [1, 2].

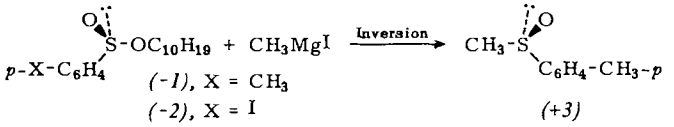
The most direct and rigorous solution of the problem of whether this Grignard synthesis proceeds with retention or inversion at asymmetric sulfur would be X-ray determinations of absolute configuration at sulfur in *(−1)* and in a derived, optically active sulfoxide. The first part of this task has already been substantially completed by an X-ray determination of absolute configuration at sulfur in (−)-menthyl (−)-*p*-iodobenzenesulfinate *(−2)*, which has the same configuration as *(−1)* [2, 3]. Considering, for nomenclature purposes, that the S—O bonds in *(−1)* and *(−2)* are single bonds, the configuration at sulfur was found to be (*S*) in both molecules.

We now wish to report the X-ray determination of the absolute configuration at sulfur in (+)-methyl *p*-tolyl sulfoxide *(+3)*, $[\alpha]_D = +145°$ (*c* = 1.1, acetone), derived from reaction of *(−1)*, $[\alpha]_D = -196°$ (*c* = 1.3, acetone), with CH_3MgBr.

Crystals of *(+3)* are orthorhombic, space group $P2_12_12_1$, with four molecules in the unit cell of dimensions a = 5.826 (6), b = 8.621 (8), and c = 16.433 (3) Å. Three-dimensional intensity data for one octant were collected with $Cu_{K\alpha}$ radiation with a Picker automatic diffractometer. The structure was solved by use of the sulfur as a heavy atom. The positional parameters for all atoms, together with anisotropic temperature parameters for the nonhydrogen atoms and isotropic ones for hydrogen, were refined by full-matrix least-squares methods. When anomalous scattering terms were included in the scattering factor of sulfur ($\Delta f_S' = 0.3$, $\Delta f_S'' = 0.6$) [4], and after correction for secondary extinction effects [5], the (*R*) configuration could be refined to a final *R* index of 3.4% whereas the lowest value of *R* for the (*S*) configuration was 4.4%. Application of *Hamilton*'s "R index test" [6] to these results indicates that the absolute configuration of *(+3)* is (*R*) to a significance level of better than 99.99% [7]. *Mislow* and co-workers have previously adduced

evidence based on ORD and CD data for *(−1)* and a variety of sulfoxides, including *(+3)*, which is in complete accord with our present finding of an (*R*) configuration for *(+3)*.

Thus, the evidence is now complete for rigorous formulation of the Grignard synthesis of optically active sulfoxides as proceeding with *inversion of configuration* at asymmetric sulfur.



On the basis of ORD and CD evidence for (+)-phenyl *p*-tolyl sulfoxide *(+4)*, *Mislow et al.*[2] have assigned the (*R*) configuration to this substance as derived from *(−1)* by an inversion path in the Grignard synthesis. We have extended this synthesis of *(+4)* to include organometallic reagents other than the Grignard (Table 1). It is of considerable interest that rather drastic changes in the nature of the organometallic reagent leave both the stereochemical path and the stereospecificity unchanged. In the case of methylmethoxy-α-naphthylphenylsilane, sensitivity of stereochemistry to the nature of the organometallic reagent has been demonstrated for nucleophilic displacement of methoxy.

Table 1. Phenyl *p*-tolyl sulfoxide from (−)-menthyl (−)-(*S*)-*p*-toluenesulfinate *(−1)* [a].

Reagent [b]	Sulfoxide, configuration	$[\alpha]_D$ in acetone (°)	M.p. (°C)	Yield (%)
C_6H_5MgBr	(*R*) − (+)	+21.2	90–92	73
$(C_6H_5)_2Zn$ [c]	(*R*) − (+)	+21.6	90–92	70
$(C_6H_5)_2Cd$ [c]	(*R*) − (+)	+21.6	90–92	68

[a] $[\alpha]_D = -198°$ (in acetone).
[b] C_6H_5Li metalates the benzylic protons in *(−1)*.
[c] The reactions were run in refluxing benzene for 16 hours.

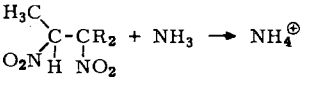
Simple alkyl or aryl organometallic reagents (Grignards and RLi reagents) give *retention* of configuration, whereas charge-delocalized reagents such as $C_6H_5CH_2Li$ give *inversion* of configuration[8]. In the organosilicon stereochemistry of monofunctional R_3Si^*-systems, inversion and an S_N2–Si mechanism appear to be the most common, but many examples of retention reactions involving poor leaving groups are also known[9]. In organosulfur stereochemistry, nucleophilic displacement reactions at the asymmetric sulfur center appear, thus far, to involve only inversion of configuration[10].

Received: May 27, 1967 [Z 39 IE]
German version: Angew. Chem. *81*, 619 (1969)

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[***] We thank the National Science Foundation for support of this work.

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(1a)

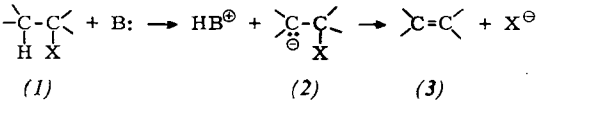
R = $C(CH_3)_3$

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[9] *L. H. Sommer*: Stereochemistry, Mechanism and Silicon. McGraw-Hill, New York 1965.
[10] See, for example, *C. R. Johnson* and *D. McCants, Jr.*, J. Amer. chem. Soc. *87*, 5404 (1965) and earlier references cited therein; *A. Nudelman* and *D. J. Cram*, J. Amer. chem. Soc. *90*, 3869 (1968).

Isolation and Decomposition of the Intermediate of an ElcB Elimination

By *A. Berndt* [*]

ElcB reactions are two-step 1,2-eliminations; in the first step the conjugate base *(2)* is formed from the substrate *(1)*; in the second step *(2)* decomposes by way of a first order reaction to give the elimination product *(3)* and $X^{\ominus}$[1].

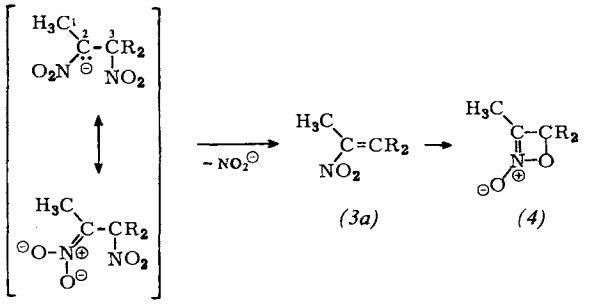


(1) *(2)* *(3)*

In all previous investigations, *(2)* occurred in such low concentration that its intermediary character could be detected only indirectly[2]. We have now been able to isolate the conjugate base of a 1,2-elimination in substance and investigate the kinetics of its decomposition in solution.

If a solution of *(1a)*[3] in ether is added with stirring to an ice-cooled saturated solution of NH_3 in ether, a yellowish-white precipitate separates after 5–10 minutes which is also insoluble in other aprotic organic solvents and in water. The substance can be recrystallized from methanol at temperatures below 0 °C. It melts at 85–90 °C. C, H, N analyses and the other experimental data support the structure of the ammonium salt of the conjugate base *(2a)* (ammonium 3-*tert*-butyl-4,4-dimethyl-2,3-dinitro-2-pentanide), which is obtained in almost quantitative yield. In methanol, the NH_4 salt of *(2a)* decomposes within a few minutes at 30 °C to give nitrite and the olefin *(3a)*, which cyclizes to 4,4-di-*tert*-butyl-3-methyl-4*H*-1,2-oxazete *N*-oxide *(4)*[4]. In the solid state the NH_4 salt of *(2a)* is transformed into *(4)* within a few weeks.

On shaking a suspension of the salt in chloroform with dilute mineral acid, products are obtained in which only the nitro group at C-3 is still present in the molecule[5]; this nitro group cleaves off as nitrite during the elimination. It is thus shown that *(2a)* still contains both nitro groups.



(2a) *(3a)* *(4)*

This finding is confirmed by the IR spectrum of the salt of *(2a)* (in Nujol) which shows, beside the band of the $NH_4^{\oplus}$ ion, two bands at 1510 and 1550 cm^{-1} in the region of the assymetric vibrations of nitro groups. The NMR spectrum (in CD_3OD at 10 °C) shows two singlets at δ = 2.18 and 1.37 ppm in the ratio 1:6.

The kinetics of decomposition of *(2a)* was studied by NMR spectroscopy (in CD_3OD between 20 and 33 °C). In all the cases investigated the results pointed to reactions of first order, the half-lives being between *ca.* 10 minutes at 20 °C and *ca.* 2 minutes at 30 °C. The activation energy of the decomposition proved to be 22 ± 5 kcal/mole.

The unusual stability of the ammonium salt of *(2a)* must be due to steric hindrance; no intermediate can be isolated in the case of 2-*tert*-butyl-3,3-dimethyl-1,2-dinitrobutane, which contains only one methyl group less than *(1a)*.

Received: May 19, 1969 [Z 7 IE]
German version: Angew. Chem. *81*, 567 (1969)

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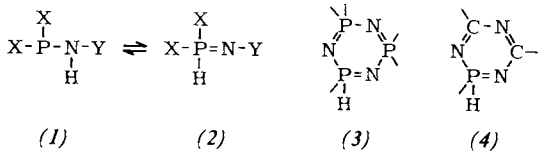
[4] *A. Berndt*, Angew. Chem. *80*, 666 (1968); Angew. Chem. internat. Edit. *7*, 637 (1968).

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The Prototropic System Aminophosphine/Iminophosphorane[1]

By *A. Schmidpeter* and *H. Rossknecht* [*]

Although hydroxyphosphines as such are, with very few exceptions, unstable and rearrange to phosphine oxides with transference of the proton onto the phosphorus, quite the reverse is the rule in the case of aminophosphines (phosphazanes) *(1)*. Phosphazanes are always present as such and no proton migration from nitrogen to phosphorus takes place — not even in the sense of an equilibrium[2]: Accordingly (P)H-iminophosphoranes (phosphazenes) also could not be prepared; they rearrange spontaneously to the tautomeric (N)H-aminophosphines *(1)* [3,4,5].

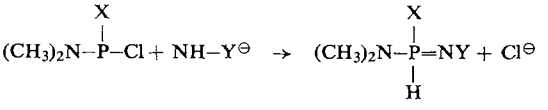


(1) *(2)* *(3)* *(4)*

Previously, the sole exception to this rule were compounds in which the phosphazene grouping *(2)* is part of a cyclotriphosphazene ring *(3)* or triazaphosphorine ring *(4)* [6].

Is the (P)H form possible only as a part of such a ring system or may it not be achieved even in simple, open-chain compounds by suitable substituent effects? Substituents X capable of increasing the basicity at the P atom and substituents Y capable of increasing the acidity at the N atom should favor the bonding of the proton to the phosphorus *i.e.* favor structure *(2)*; on the other hand, however, they should also weaken the phosphazene bond and the stability of *(2)*.

A compound in which X = NR_2 and Y = SO_2R would represent a typical case in this connection. Such a compound can be prepared from the aminochlorophosphine *(5)*, X = $N(CH_3)_2$, and the sodium salt of *p*-toluenesulfonamide *(6)*, Y = $SO_2C_6H_4CH_3$. Adverse secondary reactions can be avoided by keeping the concentration of *(5)* very low. The product is a colorless, viscous liquid that does not react with sulfur in boiling benzene as would be expected for an aminophosphine *(1)*. The IR spectrum shows the characteristic absorptions of the P—H- and P=N-vibrations (Table) and thus substantiates the phosphazene structure *(2)*. The most convincing evidence for structure *(7)*, however, is provided by the large doublet splitting of the NMR signals of the single proton and of the phosphorus.



(5) *(6)* *(7)*

A similar result is obtained in the reaction of *(5)* with the potassium salt of diphenylthiophosphoric, diphenylphosphinic, or diphenylthiophosphinic acid amide *(6)*, Y = $PS(OC_6H_5)_2$, $PO(C_6H_5)_2$, $PS(C_6H_5)_2$, if it is carried out at −70 °C, thus avoiding side-reactions. The (P)H-iminophosphorane *(7)* is formed in each case. The values νPH and J_{PH} for the compounds *(7b–d)* obtained from the above mentioned series of amides change proportionally [7] and decrease both with decreasing acidity of the amide.

	(7a)	*(7b)*	*(7c)*	*(7d)*	*(7e)*
Y	$SO_2C_6H_4CH_3$	$PS(OC_6H_5)_2$	$PO(C_6H_5)_2$	$PS(C_6H_5)_2$	$SO_2C_6H_4CH_3$
X	$N(CH_3)_2$	$N(CH_3)_2$	$N(CH_3)_2$	$N(CH_3)_2$	CH_3
IR Bands (cm^{-1})					
νP—H	2460 m, 2400 sh	2450 w, 2370 w	2410 m, 2350 sh	2400 sh, 2340 w	2400 m, 2350 sh
νP=N	1140 vs	1200 vs	1220 vs	1190 vs	1140 vs
Chemical shifts [a] (ppm)					
$\delta^{31}P$ [e] (PH)	−21.5; double tredecalet	−23.3; doublet [b]	−22.4; doublet [b]	−24.4; doublet [b]	+1.4; doublet [b]
(Z)		−52.7; doublet	−12.0 [b]	−42.5 [b]	
$\delta^{1}H$ (PH)	−6.82; doublet	−6.90 [c]; double doublet	−6.86; double doublet	−7.12; double doublet	−7.07; doublet [c]
(NCH_3)	−2.52; doublet	−2.48; doublet	−2.48; doublet	−2.50; doublet	−2.53; doublet
(PCH_3)					−1.66; doublet
Spin-spin coupling (Hz)					
J_{PH}	587	583	575	564	508
J_{PNP}		51	[d]	[d]	
J_{PNPH}		3.5	3.2	4.0	
J_{PCH}					14.0
J_{PNCH}	11.6	11.7	12.2	11.7	12.4

[a] Measured in CH_2Cl_2 against 85% phosphoric acid (external) or TMS (internal); shifts to lower field strengths negative.
[b] Signal or signal components broadened by splitting, multiplet structure not (clearly) recognizable.
[c] Indirect, not measurable directly because of superposition.
[d] Not measurable because of superposition.
[e] We are grateful to Dipl.-Chem. *K. Schumann* for recording the ^{31}P—NMR spectra.

The reaction is more sensitive to variation of X than to variation of Y: with dimethylaminomethylchlorophosphine *(5)*, X = CH_3, iminophosphorane *(7e)* is still the only product formed; with dimethylchlorophosphine, the (P)H-iminophosphorane can also be detected spectroscopically in the reaction product; however, it is not stable enough to avoid entering into secondary reactions. Finally, the corresponding diphenyl compounds (with Y = $SO_2C_6H_4CH_3$[8] and $PO(C_6H_5)_2$[4]) are described only as aminophosphines *(1)*. In the equilibrium *(1)* ⇌ *(2)* the tendency to form *(2)* increases in the series X = C_6H_5, CH_3, $N(CH_3)_2$.

Experimental:

A solution of chlorophosphine *(5)* (10 mmoles) in methylene chloride or ether (100 ml) is added dropwise over a period of one hour at −70 °C and with vigorous stirring to a suspension of the sodium or potassium acid amide *(6)* (10 mmoles) in the same solvent (100 ml). The reaction mixture is then filtered under nitrogen at room temperature to remove precipitated alkali metal chloride and the solvent is subsequently removed from the filtrate by evaporation under vacuum at 20 °C.

Received: May 20, 1969 [Z 20a IE]
German version: Angew. Chem. *81*, 572 (1969)

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[1] Part 31 of Phosphazenes. This work was supported by the Deutsche Forschungsgemeinschaft. – Part 30: *A. Schmidpeter, C. Weingand*, and *E. Hafner-Roll*, Z. Naturforsch. *24b*, 799 (1969).

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Two New Products of Ammonolysis of Phosphorus Pentachloride $[P(NH_2)_4]Cl$ and $[P(NPCl_3)_4]Cl$[1]

By *A. Schmidpeter* and *C. Weingand*[*]

It has recently been reported[3] that triaminophosphoranylideneaminotriaminophosphonium chloride *(2)*, X = Cl, was obtained from the much investigated reaction of PCl_5 with NH_3[2].

$$PCl_5 + 8\ NH_3 \rightarrow \left[H_2N\text{-}P(NH_2)_2\text{-}NH_2 \right]^+ Cl^- + 4\ NH_4Cl$$

(1)

This represents the lowest condensation product so far obtained from PCl_5 and NH_3; the expected and long sought for uncondensed substitution product *(1)* was not isolable. We have been able to prepare the tetraaminophosphonium iodide *(1)*, I instead of Cl, $\delta^{31}P$ (H_2O) = −31.6 ppm (H_3PO_4), by an indirect route[4] and have found that it is remarkably stable towards heat but readily condenses in the presence of bases.

On re-examination of the reaction of PCl_5 with liquid NH_3 it has now been shown that actually only *(1)*, $\delta^{31}P$ (H_2O) = 28.4 ppm[10], is formed first and condenses during working up with diethylamine/chloroform, according to the method

$$2\left[H_2N\text{-}P(NH_2)_2\text{-}NH_2 \right]^+ X^- + B \rightarrow$$

$$\left[H_2N\text{-}P(NH_2)=N\text{-}P(NH_2)_2\text{-}NH_2 \right]^+ X^- + NH_3 + BHX$$

(2)

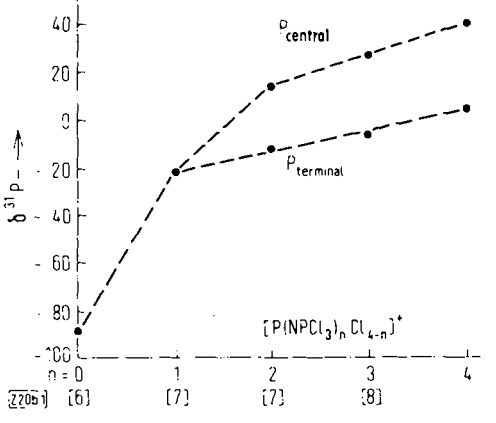
of *Klement* and *Koch*[5], to give *(2)*, X = Cl, $\delta^{31}P$ (H_2O) = −15.5 ppm (ref.[3] (CH_3OH or NH_3): −15.6 ppm). If, however, NH_4Cl is removed from the reaction product by sublimation in vacuum at 150 °C and the residue is extracted with methanol, pure *(1)* can be obtained.

If carried out in one stage, the ammonolysis of PCl_5 affords linear or cyclic phosphazenes, each phosphorus atom contributing only one or two of its four coordination sites bonds; the phosphazenes thus formed are consequently unbranched. Furthermore, branching condensation is avoided at lower NH_3/PCl_5 ratios by deficiency of PNH_2 functions and at higher NH_3/PCl_5 ratios by shortage of PCl functions[2]. On the other hand, chain branching should be achieved by successive reactions with NH_3 and PCl_5 in excess. Thus, the first doubly branched open-chain phosphazene *(3)* was obtained from *(1)* by reaction with PCl_5.

$$(1) + 4\ PCl_5 \rightarrow \left[Cl_2P(NPCl_2)_2NPCl_3 \right]^+ Cl^- + 8\ HCl$$

(3)

With this cation, which we call neo-$[P_5N_4Cl_{12}]^+$ in order to differentiate it from its isomers by analogy with neopentane, one can also prepare the hexachloroantimonate, from *(3)* and $SbCl_5$, the dichloroiodate [$\delta^{31}P$ (C_2Cl_4) = +3.4 ppm (doublet), +38.5 ppm (quintet); J_{PNP} = 29.9 Hz], from tetraaminophosphonium iodide and phosphorus pentachloride, as well as the triiodomercurate [$\delta^{31}P$ ($C_6H_5NO_2$) = +4.1 ppm (doublet), +39.3 ppm (quintet); J_{PNP} = 28.7 Hz]. Its ^{31}P-NMR spectrum[**] shows the characteristic set of peaks (as such, not previously observed) of an AB_4 spin system (J/ν_0 = 0.02) and thus affords evidence for the symmetrical structure. The large shifts correspond to the considerable increase with n of all $\delta^{31}P$ values of the cations $[P(NPCl_3)_n\ Cl_{4-n}]^+$; *(3)* completes this series with n = 4. $\delta^{31}P$ (terminal) reveals the additive dependence of the substituents on the neighboring phosphorus atoms in PNP systems[9].



Tetraaminophosphonium chloride (1)

PCl_5 is added portionwise with vigorous stirring to liquid NH_3 at −70 °C. An almost clear solution is obtained which yields a white powder when the NH_3 is evaporated off. The weight of the final precipitate reveals that 8 moles of NH_3 have been taken up for each mole of PCl_5. The product is kept at 150—155 °C and at 5×10^{-3} torr for 30 hours whence 4 moles NH_4Cl/mole PCl_5 sublimes off. The residue is taken up in anhydrous methanol and the resulting solution is filtered off and treated with an equal volume of ether. *(1)* precipitates as fine crystals, which are immediately separated off and dried. About 3 g of *(1)* dissolves in 100 ml CH_3OH. Yield 46%. *(1)* decomposes without melting at 200 °C.

Tetrakis(trichlorophosphazo)phosphonium-chloride (3) and -dichloroiodate

A suspension of *(1)* and PCl_5 (molar ratio 1:4) in $CHCl_3$ is prepared and heated under reflux. Liberation of HCl is complete after 3 hours. *(3)* can be reprecipitated from C_2Cl_4 with CCl_4. The salt having ICl_2^- in place of Cl^- can be obtained as large pale yellow crystals from $[P(NH_2)_4]I$ and PCl_5 (molar ratio 1:5); it is much more readily soluble than *(3)*.

Received: June 10, 1969 [Z 20b IE]
German version: Angew. Chem. *81*, 573 (1969)

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[**] We thank *K. Schumann* for the recording of the ^{31}P-NMR-spectra.

[1] Part 33 of Phosphazenes. – Part 32: *J. Ebeling, N. Schindler,* and *A. Schmidpeter*, Chem. Ber., in press; Part 31: *A. Schmidpeter* and *H. Rossknecht*, Angew. Chem. *81*, 572 (1969); Angew. Chem. internat. Edit. *8*, 614 (1969).

[2] *A. Schmidpeter, C. Weingand,* and *E. Hafner-Roll*, Z. Naturforsch. *24b*, 799 (1969).

[3] *M. Becke-Goehring* and *B. Scharf*, Z. anorg. allg. Chem. *353*, 320 (1967).

[4] *A. Schmidpeter* and *C. Weingand*, Angew. Chem. *80*, 234 (1968); Angew. Chem. internat. Edit. *7*, 210 (1968).

[5] *R. Klement* and *O. Koch*, Chem. Ber. *87*, 333 (1954).

[6] *A. Schmidpeter* and *H. Brecht*, Angew. Chem. *79*, 535 (1967); Angew. Chem. internat. Edit. *6*, 564 (1967).

[7] *E. Fluck*, Z. anorg. allg. Chem. *315*, 181 (1962).

[8] *H. P. Latscha, W. Haubold,* and *M. Becke-Goehring*, Z. anorg. allg. Chem. *339*, 82 (1965).

[9] *A. Schmidpeter, H. Brecht,* and *J. Ebeling*, Chem. Ber. *101*, 3902 (1968).

[10] *R. Appel* and *G. Köhnlein* previously obtained *(1)* on reaction of triphenyl phosphite with a mixture of NH_2Cl and NH_3 (personal communication; Dissertation, *G. Köhnlein*, Universität Heidelberg 1963).

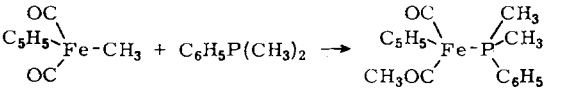
Magnetic Non-equivalence of Methylene Protons and *gem*-Methyl Groups in Asymmetric Iron Complexes

By *H. Brunner* and *E. Schmidt* [*]

After separation of diastereoisomeric compounds containing an asymmetric Mn atom [1] we have been able to demonstrate asymmetric metallic centers also by ^1H-NMR spectroscopy.

The protons of methylene or *gem*-methyl groups in compounds of the "ethane type" are magnetically non-equivalent if these groups are attached to an optically active center [2]. The non-equivalence arises because the H atoms or CH_3 groups are in different surroundings, no matter what the conformation, because of the symmetry at the neighboring atom. Further, the magnetic non-equivalence is not destroyed by rapid rotation.

In the reaction of dicarbonylcyclopentadienylmethyliron(II) with dimethyl(phenyl)phosphine in boiling THF the methyl

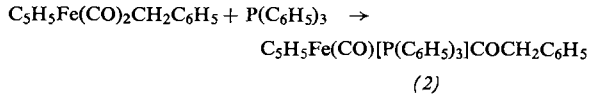


(1)

group migrates from the Fe atom to one of the carbonyl ligands [3] so that a compound of the "ethane type" is formed with two *gem*-methyl groups on P and an asymmetric center at the Fe atom.

The orange-yellow crystals of *(1)* give a solution of monomer in benzene. In the KBr spectrum the band of the metal-CO group occurs at 1894 cm^{-1} and that of the acetyl-CO group at 1597 cm^{-1}. In the ^1H-NMR spectrum (see Figure and Table) the signals of the phenyl protons of the phosphine, of the cyclopentadienyl protons, and the protons of the acetyl group are accompanied by four signals that are to be assigned to the two non-equivalent methyl groups. If the spectrum is recorded at 100 MHz instead of at 60 MHz the inner and the outer pairs of signals become further apart from each other, this fact being of decisive importance in the assignment. At higher temperatures the separation of the two doublets decreases, and at lower temperatures increases. These shifts are to be ascribed to differing population of the three staggered conformations, which are energetically different; thus increasing temperature should decrease the differences in population. At −100 °C the methyl signals become broader; separation into the signals of the three different conformations is thus to be expected at a still lower temperature.

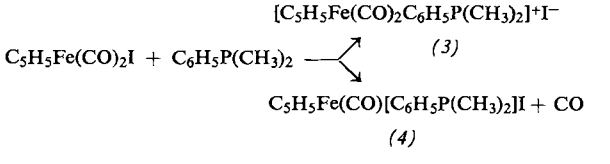
An orange-yellow complex *(2)* prepared as follows:



(2)

has in its KBr spectrum the metal-CO vibration at 1912 cm^{-1}, the CO vibration of the phenylacetyl group at 1603 cm^{-1}. In *(2)* the methylene group is separated from the asymmetry center on the Fe atom by a CO group; in spite of this a clearly split AB system is observed for the two non-equivalent methylene protons H^1 and H^2 (cf. Table).

$C_6H_5P(CH_3)_2$ reacts with $C_5H_5Fe(CO)_2I$ thus:



(3) *(4)*

with formation of an ionic compound *(3)* and a neutral complex *(4)* [4].

In its IR spectrum the yellow salt *(3)* shows two CO bands at 2110 and 1996 cm^{-1}. Since the complex cation has a symmetry plane the two *gem*-methyl groups on the P atom are magnetically equivalent, so that only a doublet is observed in the ^1H-NMR spectrum (cf. Table). However, in the green complex *(4)* (ν_{CO} = 1946 cm^{-1}) the Fe atom is attached to four different ligands, wherefore the ^1H-NMR spectrum contains two doublets for the pair of non-equivalent methyl groups (see Table). The intensity ratios of the signals in all the ^1H-NMR spectra are in accord with the formulas given here.

Table: ^{1}H-NMR spectra of the complexes *(1)*—*(4)*; chemical shifts in τ (TMS as internal standard), and coupling constants J in Hz; *(1)*, *(2)*, and *(4)* in CS_2, *(3)* in CD_3COCD_3 solution.

	$\tau Me_{1(2)}$ ($J_{P-CH_3^1(2)}$)	$\tau H_{1(2)}$ ($J_{H^1-H^2}$)	τC_5H_5 ($J_{P-C_5H_5}$)	τC_6H_5 ($J_{P-C_6H_5}$)	τCOMe
(1)	8.60 (9.3) 8.24 (10)		5.78 (1.5)	2.68 (3)	7.63
(2)		6.51 5.98 (13.5)	5.86 (1.5)	2.99 [$CH_2C_6H_5$] 2.69 [$P(C_6H_5)_3$]	
(3)	7.68 (11.5)		4.31 (1.5)	2.40 (3)	
(4)	8.27 (9.3) 7.86 (10)		5.74 (1.5)	2.66	

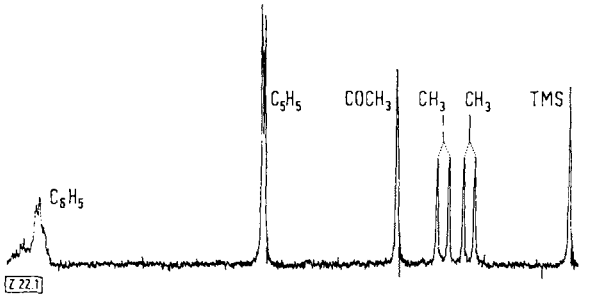


Figure: ^{1}H-NMR spectrum of $C_5H_5Fe(CO)(COCH_3)C_6H_5P(CH_3)_2$ in CS_2-solution.

Magnetic non-equivalence of methylene protons or of *gem*-methyl groups attached to asymmetric centers has been often demonstrated for organic compounds and for compounds of elements of the main groups [2]; among transition metals this effect was used to explain the complex ^{19}F-NMR spectrum of $C_5H_5Co(CO)(C_2F_5)_2I$ [5]. Further, magnetic non-equivalence has been demonstrated during determination of the configuration of multi-substituted octahedral complexes [6,7].

Received: May 23, 1969 [Z 22 IE]
German version: Angew. Chem. *81*, 570 (1969)

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[1] *H. Brunner*, Angew. Chem. *81*, 395 (1969); Angew. Chem. internat. Edit. *8*, 382 (1969).

[2] *M. van Gorkom* and *G. E. Hall*, Quart. Rev. (chem. Soc., London) *22*, 14 (1968).

[3] *J. P. Bibler* and *A. Wojcicki*, Inorg. Chem. *5*, 889 (1966).

[4] *P. M. Treichel, R. L. Shubkin, K. W. Barnett*, and *D. Reichard*, Inorg. Chem. *5*, 1177 (1966).

[5] *J. A. McCleverty* and *G. Wilkinson*, J. chem. Soc. (London) *1964*, 4200.

[6] *B. L. Shaw* and *A. C. Smithies*, J. chem. Soc. (London) *1968*, 2784, and earlier papers.

[7] *Note added in proof* (July 12, 1969): *J. W. Faller* and *A. S. Anderson*, J. Amer. chem. Soc. *91*, 1550 (1969), have shown independently that $C_5H_5Fe(CO)(CH_2C_6H_5)P(C_6H_5)_3$ gives an ABX spectrum for the magnetically non-equivalent methylene protons.

Errata

The title of the communication by *H. U. Sieveking* and *W. Lüttke*, Volume 8, June 1969, p. 458, should read "Preparation of Enamino Nitriles and Pyridines by Reduction of Geminal Dinitriles with $LiAlH_4$".

In the communication "Preparation of Cyclic Amidines by Reduction of Dinitriles with $LiAlH_4$" by *H. U. Sieveking* and *W. Lüttke*, Volume 8, June 1969, p. 457 (Angew. Chem. *81*, 431 (1969)) the following correction should be made:

The numbers *(2b)* and *(2d)* in Scheme 1 should read *(1b)* and *(1d)*.

CONFERENCE REPORTS

Oligomeric and Polymeric Nitrogen-Phosphorus Compounds: New Aspects of Plant Nutrition

By *W. Waněk*

The trend in the development of industrial fertilizers has been toward higher nutrient contents. This trend has resulted from technical developments and leads *e.g.* in the case of phosphate fertilizers from decomposition of the crude phosphate with sulfuric acid, *via* decomposition with nitric acid, to decomposition with phosphoric acid as well as to the preparation of phosphates and polyphosphates (nutrient content: product of H_2SO_4 decomposition *ca.* 17% P_2O_5; product of HNO_3 decomposition 33—40% P_2O_5N; ammonium phosphate and ammonium polyphosphate *ca.* 80% P_2O_5N). Criteria for "ideal fertilizers" were worked out as a basis for research work on future fertilizers: highest nutrition coefficient: no complex formation with soil micelles (retrogradation, particularly of phosphates); adequate sorption in soil (elutriation *e.g.* of nitrate ions); ready assimilation by plants; little or no ion formation in the soil-(nutrient) solution (shift of the plasmolysis boundary to higher nutrient values); controllable release of biogenic elements in the soil solution.

Experiments with fully or partially covalent nitrogen-phosphorus compounds [$(NH_4)HPO_3NH_2$, $NH_4PO_2(NH_2)_2$, $OP(NH_2)_3$, $[NP(NH_2)_2]_3$, $[NP(NH_2)_2]_4$, $[NH_4PO_2NH]_3$] showed that they are better fertilizers than $(NH_4)_2HPO_4$.

Laboratory experiments *inter alia* on oats and barley showed that these covalent compounds are taken up by plants more rapidly than are the pure ionic compounds; furthermore they do not retrograde in soils and plasmolysis phenomena occur only at higher concentrations. Crops 25—35% higher than with $(NH_4)_2HPO_4$ could be achieved in experiments carried and in vessels according to the method of *Mitscherlich*.

Lecture at Stuttgart on April 24, 1969 [VB 206 IE]
German version: Angew. Chem. *81*, 578 (1969)

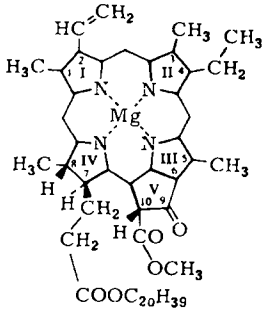
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Recent Investigations on Chlorophylls

By *K. Ballschmiter* [*]

The coordinative properties of the central magnesium atom play a much greater role in intermolecular interactions of chlorophylls than was previously assumed, the coordination number 5 being preferred over 6 [1]. The coordinatively unsaturated magnesium is saturated by molecules of the solvent acting as axial ligands in polar solvents. If a solvent, such as benzene or carbon tetrachloride, is unable to function as a

ligand, the keto group in ring V of a further molecule of chlorophyll-*a* *(1)* enters into coordinative interaction with the magnesium atom[2].



(1)

Molecular-weight determinations show that the dimers, contrary to widespread belief, do not dissociate at higher temperatures (65 °C)[3]. Electronic spectra show that no significant dissociation occurs[4], even in highly dilute solutions (10^{-6} M) in carbon tetrachloride at 23 °C when all polar impurities have been removed — water being the most likely such impurity.

Anhydrous chlorophyll-*a* is readily soluble in aliphatic hydrocarbons such as cyclohexane, *n*-hexane, and hexadecane[5]; solutions can be prepared having concentrations up to 10^{-1} mole/l. IR spectroscopic investigations[6] and molecular-weight determinations[3] show that in these solvents the chlorophyll-*a* dimers combine to form larger aggregates; the highest value measured for *n* in $(Chl_2)_n$ was 12 for a 10^{-1} M solution in *n*-hexane at 25 °C. The aggregation proceeds *via* a new coordination of the magnesium with the free keto groups in ring V. The oligomer C=O/Mg band is shifted toward lower energies compared to the dimer C=O/Mg band in the IR spectrum.

When prepared by the usual methods, which involve precipitation from light petroleum in the presence of water as the last step, chlorophyll-*a* is obtained as the monohydrate[5]. The spectral and other physical properties of the monohydrate are fundamentally different from those of anhydrous chlorophyll-*a*. Water represents an essential structural component of crystalline chlorophyll-*a* and -*b*; in chlorophyll-*a* it is coordinated to the magnesium and is also involved in a hydrogen bond to the keto group in ring V of the neighboring chlorophyll molecule, Mg · · OH_2 · · O=C[6]. This arrangement is retained in aliphatic hydrocarbons.

The specificity of the structure of chlorophyll-*a* with regard to the C=O/Mg and C=O/H_2O/Mg interactions described above has been demonstrated by investigations on pyrochlorophyll-*a*, chlorophyll-*b*, bacteriochlorophyll, and pheophytin-*a*; in all cases deviations from the behavior of chlorophyll-*a* were observed[3,5,6].

Information on the molecular interactions of chlorophylls *in vitro* permit conclusions to be drawn regarding the state of chorophyll *in vivo*[7].

Lecture at Mainz on June 26, 1969 [VB 209 IE]
German version: Angew. Chem. *81*, 629 (1969)

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[1] *J. J. Katz*, Developments appl. Spectroscopy *6*, 201 (1968).

[2] *J. J. Katz*, *R. C. Dougherty*, and *L. J. Boucher* in *L. P. Vernon* and *G. R. Seely*: The Chlorophylls. Academic Press, New York 1966, p. 185.

[3] *K. Ballschmiter*, *K. Truesdell*, and *J. J. Katz*, Biochim. biophysica Acta, in press.

[4] *K. Ballschmiter*, *K. Truesdell*, and *J. J. Katz*, unpublished.

[5] *K. Ballschmiter*, *T. M. Cotton*, *H. H. Strain*, and *J. J. Katz*, Biochim. biophysica Acta *180*, 347 (1969).

[6] *K. Ballschmiter* and *J. J. Katz*, J. Amer. chem. Soc. *91*, 2661 (1969).

[7] *K. Ballschmiter* and *J. J. Katz*, Nature (London) *220*, 1231 (1968).

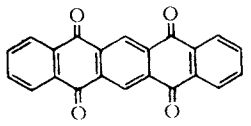
SELECTED ABSTRACTS

The preparation and properties of californium(III) compounds has been reported on by *J. C. Copeland* and *B. B. Cunningham*. Californium(III) oxychloride, CfOCl was prepared by three different methods: from Cf_2O_3 in a HCl/H_2O mixture at 505 °C; by pyrolysis of $CfCl_3 \cdot x\ H_2O$ in H_2 atmosphere at 555–585 °C; and by vacuum pyrolysis of $CfCl_3 \cdot xH_2O$ at 450 °C. The californium oxychloride prepared by each of these three methods crystallizes tetragonally and has the PbFCl type structure with a = 3.956 and c = 6.662 Å. In a N_2/water vapor stream at 500–638 °C, CfOCl reacts to give the cubic (C) modification of californium sesquioxide, which can also be obtained by reaction of the oxychloride in a stream of O_2 at 730 °C. C-Cf_2O_3 crystallizes with a Mn_2O_3 type structure in which a = 10.84 Å. In an O_2 stream partial oxidation to higher Cf oxides takes place; this is recognizable by a reduction of the lattice constant to a = 10.809 Å. / J. inorg. nuclear Chem. *31*, 733 (1969) / –FW. [Rd 45 IE]

The radiation damage in oriented polytetrafluoroethylene caused by a pulsed electron beam has been investigated by *N. R. Lerner* by means of ESR. The orientation (by stretching) of the samples when material is irradiated in air makes it possible to distinguish two ESR signals; the relative intensities of the two signals vary as a function of the radiation dose. When large doses are used the signal ascribable to a $-CF_2-(CF-O-O\cdot)-CF_2$ group predominates; with small doses, the signal due to the $-CF_2-O-O\cdot$ group has the greater intensity. The precursors of these groups, *i.e.* $-CF_2-(CF\cdot)-CF_2$ and $-CF_2\cdot$, are observable if the irradiation is carried out in vacuum. / J. chem. Physics *50*, 2902 (1969) / –Hz. [Rd 41 IE]

The Raman spectra of melts of $InCl_3$ and LiCl, KCl, or CsCl in the temperature range 400–700 °C have been investigated by *J. H. R. Clarke* and *R. E. Hester*. Equimolar mixtures of $InCl_3$ and each of the other three salts give essentially the same spectrum, which can be ascribed to the tetrahedral ion $InCl_4^-$. Further addition of KCl or CsCl gives rise to changes in the spectrum which are indicative of formation of $InCl_5^{2-}$ and $InCl_6^{3-}$; with an excess of LiCl, however, $InCl_4^-$ remains the principal product. / J. chem. Physics *50*, 3106 (1969) / –Hz. [Rd 42 IE]

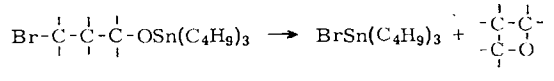
The formation of linear polycyclic diquinones by a new dimerization reaction has been reported by *I. Baxter*, *D. W. Cameron*, and *R. B. Titman*. A few 2-methyl-1,4-quinones dimerize in the presence of *N*-methylcyclohexylamine in ethanolic solution. 2-Methyl-, 3-bromo-2-methyl-, and 3-chloro-2-methyl-1,4-naphthoquinones afford the pentacenediquinone *(1)* (m.p. > 350 °C, pale yellow) in 15% yield on standing for 24 h. 2-Methyl-1,4-anthraquinone gives analogously the 6,8,15,17-heptacenediquinone (golden yellow) in 24% yield.



(1)

After five days' reaction, the red 7,9,18,20-nonacenequinone can be obtained in 35% yield from 2-methyl-1,4-naphthacenequinone. / Chem. Commun. *1969*, 563 / —Ma. [Rd 46 IE]

A new method for the synthesis of oxetanes has been reported by *B. Delmond, J. C. Pommier*, and *J. Valade*. Whereas 3-bromopropoxytributyltin is stable, the substituted homologs *(1)* form oxetanes *(2)* in quantitative yields on heating to *ca.* 170 °C. *(1)* can be obtained from ethoxytributyltin by transalkoxylation with 3-bromopropanols. The oxetane is formed



(1) *(2)*

in 80—90% yield; no by-products are formed. For example: 3-bromo-2-methylpropanol → 3-methyloxetane, 85%; 2-ethyl-3-bromopropanol, 85%; 3-bromo-2,2-dimethyl-propanol, 90%; 3-bromo-2-phenylpropanol, 90%; 3-bromobutan-2-ol, 80%. / Tetrahedron Letters *1969*, 2089 / —Ma. [Rd 49 IE]

A rhodium complex containing CO_2 ligands, *(2)*, has been obtained by *Y. Iwashita* and *A. Hayata* by oxidation of the rhodium(0) complex *(1)* with O_2 in aromatic solvents. Complex *(1)* was prepared from $Rh_4(CO)_{12}$ and $P(C_6H_5)_3$.

$$Rh_2(CO)_4[P(C_6H_5)_3]_4 + O_2 \rightarrow$$

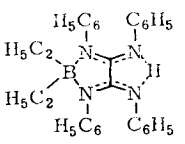
(1) $Rh_2(CO)_2(CO_2)[P(C_6H_5)_3]_3 + CO + O{=}P(C_6H_5)_3$ *(2)*

When the oxidation of *(1)* was carried out with $^{18}O_2$, the CO_2 in complex *(2)* consisted of $^{16}O{=}C{=}^{16}O$, $^{18}O{=}C{=}^{16}O$, and $^{18}O{=}C{=}^{18}O$ in the ratio 1:2:1. ^{16}O- and ^{18}O-triphenyl oxide are formed in the ratio 1:1. These results suggest an intermediate containing four symmetrically arranged oxygen atoms and two symmetrically arranged carbon atoms. The moderately stable yellow complex *(2)*, which still contains solvent (*e.g.* one C_6H_6), decomposes at 118 °C in the presence of oxygen but does not melt below 150 °C in an inert gas. According to the IR spectrum the CO_2 group is angled. / J. Amer. chem. Soc. *91*, 2525 (1969) / —Kr. [Rd 64 IE]

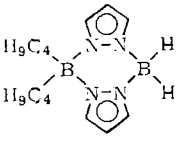
A new group of borylating agents, boryl sulfonates, has been described by *S. Trofimenko*. Dialkylboryl sulfonates *(1)*, the first example of compounds having an RSO_3 group bound to a boron atom, are readily obtained in a one-step synthesis by heating equimolar amounts of trialkylboranes with aromatic or aliphatic sulfonic acids, such as methanesulfonic acid, *p*-toluenesulfonic acid, mesitylenesulfonic acid, *m*- and *p*-nitrobenzenesulfonic acid, *p*-chlorosulfonic acid, and 4,4'-diphenylsulfonic acid, with loss of one equivalent of alkane. Reaction with sulfuric acid yields bis(dialkylboryl) sulfate. Diethylboryl methanesulfonate, b.p. 70—73 °C/2.5 torr, is a pyrophoric liquid. All compounds *(1)* are soluble in aromatic hydrocarbons.

$$R'SO_3H + BR_3 \longrightarrow \underset{(1)}{RH + R'SO_3BR_2} \xrightarrow{Z^-} \underset{(2)}{ZBR_2 + R'SO_3^-}$$

Reactions of *(1)* with nucleophilic compounds afford the borylated derivatives ZBR_2 *(2)*. The reactivity of *(1)* is very similar to that of the difficulty accessible dialkylboryl halides. As examples of syntheses with *(1)* may be quoted the preparation of *N*-(diethylboryl)-*sym*-tetraphenyloxamidine *(3)* from $CH_3SO_3B(C_2H_5)_2$ and the Na salt of *sym*-tetraphenyloxamidine (74% yield) and compound *(4)* from $CH_3SO_3B(C_4H_9)_2$ and $KH_2B(1\text{-pyrazolyl})_2$. / J. Amer. chem. Soc. *91*, 2139 (1969) / —Ma. [Rd 51 IE]



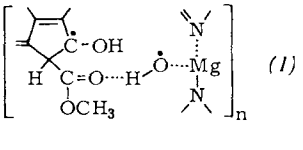
(3)



(4)

The adsorption of hexafluorobenzene on graphitized carbon black has been studied by *C. Pierce*. It may be deduced from the course of the adsorption isotherm that at low surface occupation six-carbon aromatic rings are adsorbed onto fixed sites at certain positions of the graphite lattice. At higher occupations, a change in the curvature of the isotherm indicates a different heat of adsorption and a transition to mobile adsorption until a tightly packed first layer has formed. Taking a value of 47.2 Å² for the adsorption cross-section of benzene on graphite, that of C_6F_6 is found to be 70 Å² for localized adsorption and 55 Å² for mobile adsorption. — The value of 16.2 Å² generally assumed for the cross-section of nitrogen is correct for a close-packed monolayer; for an apparent monolayer of nitrogen on graphite the effective area is 19.3 Å². BET surface areas of graphite should therefore be increased by a corresponding factor. / J. physic. Chem. *73*, 813 (1969) / —Hz. [Rd 67 IE]

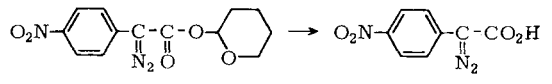
The ESR spectrum of irradiated chlorophyll (Chl) has been investigated under various conditions by *M. Garcia-Morin, R. A. Uphaus, J. R. Norris*, and *J. J. Katz*. Chlorophyll containing no water or oxygen gives no ESR signal in the dark or on irradiation with red light (600—900 nm). Chlorophyll-water micelles, such as are formed in aliphatic hydrocarbons, give a sharp, reversible signal (*i.e.* one that disappears in the dark) on irradiation with red light, which can be explained by delocalization of an electron in the micelle. Under conditions unfavorable for micelle formation, *e.g.* in benzene solution, photooxidation, which is evidenced by a broad, irreversible signal, proceeds much more rapidly than in the presence of micelles. A primary photoproduct of structure *(1)* is proposed in order to explain the experimental findings; it can



(1)

be regarded as precursor of the radical ions $Chl^{\ominus}$ and $Chl^{\oplus}$ which are responsible for the reduction of CO_2 and the oxidation of H_2O during photosynthesis. / J. physic. Chem. *73*, 1066 (1969) / —Hz. [Rd 54 IE]

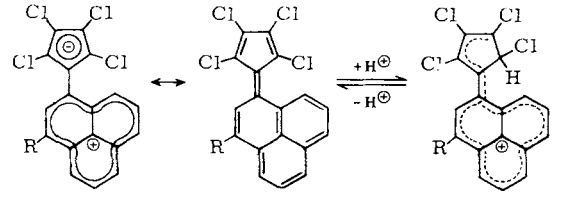
The preparation of a free α-diazocarboxylic acid has been accomplished for the first time by *K. Schank*. Transesterification of tetrahydropyranyl *p*-nitrophenyldiazoacetate *(1)* with glacial acetic acid in the presence of *p*-toluenesulfonic acid with ice-cooling gave 4-nitrophenyldiazoacetic acid *(2)*, m.p.



(1) (2)

125 °C (decomp.) in 77% yield. The constitution of the stable acid was confirmed by the IR spectrum and by conversion into the methyl ester. / Liebigs Ann. Chem. *723*, 205 (1969) / —Ma. [Rd 55 IE]

2-Ethoxy-9,10,11,12-tetrachloropentaphenafulvalene, *(2)*, the first derivative of the hitherto unknown pentaphenafulvalene, has been prepared by *I. Murata, I. Nakazawa,* and *M. Okazaki.* The compound was obtained in the form of dark blue needle-shaped crystals (recrystallized from benzene, m.p. > 250 °C) by reaction of ethoxyphenalenium tetrafluoroborate with sodium tetrachlorocyclopentadienide. The weak base *(2)* dissolves reversibly in 80% sulfuric acid to form the red cation *(3)*. (The position shown for the proton has not

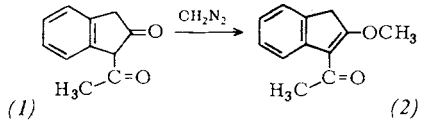


(1) (2) (3)

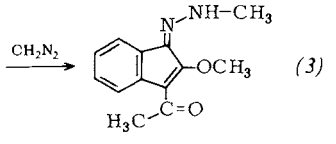
R = C_2H_5O

yet been confirmed unequivocally.) Dipole moment and the NMR spectrum indicate that a dipolar resonance structure such as *(1)* makes a significant contribution to the ground state of *(2)*. Such a contribution is in agreement with HMO calculations on unsubstituted pentaphenafulvalene. / Tetrahedron Letters *1969*, 1921 / — Kr. [Rd 56 IE]

A novel reaction of diazomethane has been observed by *K. Hartke* and *W. Uhde,* who obtained, *inter alia,* 3-acetyl-2-methoxy-1-indenonehydrazone *(3)* (red needle-shaped crystals from cyclohexane; m.p. 120—121 °C, yield 83%) from 1-acetyl-2-indanone *(1) via* 3-acetyl-2-methoxyindene *(2)*. The



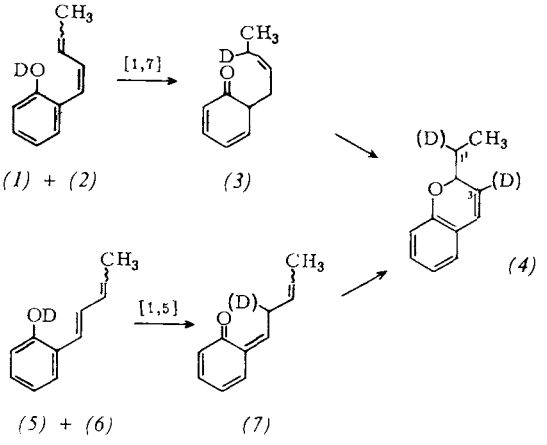
(1) (2)



(3)

result of this reaction corresponds to the coupling of aromatic diazonium salts with CH acidic compounds to give arylhydrazones. 3-Acetyl-2-ethylthio- and 3-acetyl-2-morpholinoindene also form methylhydrazones with diazomethane. / Tetrahedron Letters *1969*, 1967 / —Kr. [Rd 57 IE]

Aromatic [1,7]- and [1,5]-sigmatropic H shifts are the subject of a report by *R. Hug, H.-J. Hanser,* and *H. Schmid.* These authors studied mixtures of isomers that are obtained on reaction of the sodium salt of salicylaldehyde with crotyltriphenylphosphonium bromide (*trans*/*cis* mixture). [*(1)* + *(2)*] = *cis,trans-* + *cis,cis-o*-(1,3-pentadienyl)phenol (7:3) is converted quantitatively into 2-ethyl-2*H*-chromene *(4)* at 121 °C in octane (20 h). [*(5)* + *(6)*] = *trans,trans-* + *trans,cis-o*-(1,3-pentadienyl)phenol gives the same product but only at or

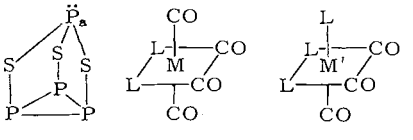


(1) + (2) (3) (4)

(5) + (6) (7)

above 190 °C. Deuterium labeling of the phenolic H atom showed that [*(1)* + *(2)*] is transformed into [1'-D]-*(4)* by a [1,7]-sigmatropic H shift *via (3)*. [*(5)* + *(6)*] affords a compound *(4)* having 0.5 D on C-1' and 0.4 D on C-3, which is formed by [1,5]-sigmatropic H shift *via (7)* or by fast H/D exchange at O and subsequent [1,7]-sigmatropic shift. The 1,3-butadienyl derivatives react in a similar manner. / Chimia *23*, 108 (1969) / —Kr. [Rd 58 IE]

Transition-metal complexes of tetraphosphorus trisulfide *(1)* have been described by *R. Jefferson, H. F. Klein,* and *J. F. Nixon.* $C_7H_8M(CO)_4$ (M = Cr, Mo, W) and $C_7H_8M'(CO)_3$ (M' = Cr, Mo) react with P_4S_3 in boiling CS_2 to give the orange-yellow complexes *cis*-$(P_4S_3)_2M(CO)_4$ *(2)* and *cis*-$(P_4S_3)_3M'(CO)_3$ *(3)*, respectively. Compound *(2)*, M = Mo, reacts with PF_3 to give a poor yield of *cis*-$(PF_3)_2$-$Mo(CO)_4$, but remains unchanged when heated with a small amount of sulfur. P_4S_7 is formed only in the presence of a

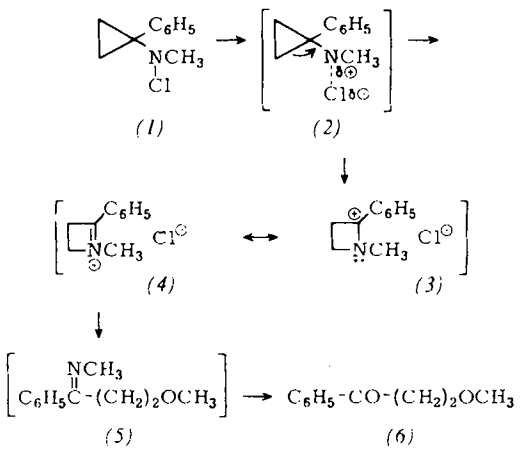


(1) = L (2) (3)

large excess of sulfur. The nickel(0) complex, $Ni(P_4S_3)_4$, is formed on reaction of bis(π-allyl)nickel with P_4S_3 or from nickelocene. The coordination of P_a to the transition metal atom in these compounds was established by NMR spectroscopy. / Chem. Commun. *1969*, 536 / —Kr. [Rd 59 IE]

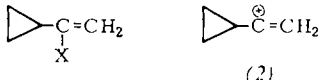
The position of the inner H atoms in phthalocyanin has been established by *B. F. Hoskins* and *S. A. Mason* with the aid of neutron diffraction. They found that these H atoms lie in the plane of the "large ring" — the phthalocyanin skeleton is planar within the limits of experimental accuracy — and that on average 1/2 H is bonded to each of the four pyrrole N atoms. Thus the bonding is similar to that in two porphine structures. The four "half H atoms" lie very close to the connecting line between the centrosymmetric pyrrole N atoms. / Chem. Commun. *1969*, 554 / —Kr. [Rd 60 IE]

***N*-Methyl-1-phenylcyclopropylnitrenium chloride** *(2)*, a nitrogen analog of the cyclopropylmethyl compounds, has been obtained, by *P. G. Gassman* and *A. Carrasquillo,* as an intermediate during the heterolytic cleavage of *N*-chloro-*N*-methyl-1-phenylcyclopropylamine *(1)*, which yields β-methoxypropiophenone *(6)* as main product (85%). The nitrenium



chloride *(2)* is reported not to exist in the form of free ions but to undergo ring expansion yielding *(3)* as the positive charge on the nitrogen begins to increase. Compound *(6)* is then formed *via (4)* and *(5)*. The *p*-methoxyderivative of *(1)* reacts in a similar manner. / Chem. Commun. *1969*, 495 / —Kr. [Rd 61 IE]

The 1-cyclopropylvinyl cation *(2)* has been detected independently by *S. A. Sherrod* and *R. G. Bergmann* and by *M. Hanack* and *T. Bässler*. *Bergmann et al.* produced the cation from 1-cyclopropyl-1-iodoethylene *(1a)* with aqueous-ethanolic $AgNO_3$ at room temperature. Cyclopropyl methyl ketone is formed as final product. The corresponding reaction of the analogous compound 2-iodo-3-methyl-1-butene takes place only under more drastic conditions. Reaction of *(1a)* with Ag acetate and Ag tosylate at room temperature gives the acetate *(1c)* and the tosylate *(1d)*, respectively. *Hanack et al.* treated 1-chloro-1-cyclopropylethylene *(1b)* with $AgClO_4$ in acetic acid at room temperature to give the cyclo-



(1a), X = I
(1b), X = Cl
(1c), X = CH_3COO
(1d), X = OTs

propylvinyl cation *(2)* [final product: cyclopropyl methyl ketone]; with $AgClO_4$/Na acetate and *(1b)* they obtained the acetate *(1c)*. 2-Chloro-3,3-dimethyl-1-butene does not react under these conditions. / J. Amer. chem. Soc. *91*, 2115, 2117 (1969) / —Kr. [Rd 63 IE]

Hexameric $(HF)_6$ is a main constituent, along with the monomer and traces of a dimer, of gaseous hydrogen fluoride at —19 and +22 °C, at which temperatures the gas mixture has the composition HF + $(HF)_6$ and 4.2 HF + $(HF)_6$. This became apparent in electron-diffraction studies by *J. Janzen* and *L. S. Bartell*. The six F atoms of $(HF)_6$ form a puckered six-membered ring, the F—F bond lengths being 2.525 (—19 °C) and 2.533 ± 0.003 Å (22 °C) [2.49 Å in crystalline HF at —125 °C]; the FFF angle is 104 °. Owing to the large deformation amplitudes of the ring, the conformations lying between the boat and the chair forms are rapidly passed through. About half of the FHF bridges are asymmetric with one short HF bond, which is 0.040 Å longer than in monomeric HF. In the other symmetrical FHF bridges the hydrogen appears to prefer a position lying off the FF axis. / J. chem. Physics *50*, 3611 (1969) / —HB. [Rd 65 IE]

A planar tropylium ring having mean C–C bond lengths of 1.401 Å is present in $[C_7H_7Mo(CO)_3]^+[BF_4]^-$, according to an X-ray structure analysis by *G. R. Clark* and *G. J. Palenik*. The Mo atom is surrounded octahedrally by three CO groups (dMoC = 2.035 Å) and the tropylium ring (dMoC$_{ring}$ lying between 2.29 Å and 2.33 Å). The $C_7H_7^+$ ion is bonded as a 6 π-aromatic system and not as a triolefin. The MoC(O) distance is significantly greater than in analogous olefin complexes such as (cycloheptatriene)$Mo(CO)_3$, and the MoC(O) π-bond order is therefore not greater than in $Mo(CO)_6$, unlike the case in olefin complexes. / Chem. Commun. *1969*, 667 / —HB. [Rd 66 IE]

A linear RuNRu bridge with an unusually short RuN bond length of 1.718 Å (σ 0.006) is found, from an X-ray structure determination by *M. Ciechanowicz* and *A. C. Skapski*, to occur in $K_3[(H_2O)Cl_4RuNRuCl_4(OH_2)]$, which crystallizes in the space group C2/m with a = 15.89, b = 7.34, c = 8.16 Å, β = 120.4 °, and Z = 2. The N atom lies in the center of symmetry of the anion; owing to the strong π-character of the RuN bonds two $RuCl_4$ groups are eclipsed, as in $Re_2Cl_8^{2-}$, and distorted towards the H_2O [∢ NRuCl 94.1 and 95.1 ° (σ 0.2), dRuCl 2.363 and 2.364 Å (σ 0.006)]. The H_2O molecules, which are *trans* to the nitrogen, are held by means of long RuO bonds of 2.180 Å (σ 0.026). / Chem. Commun. *1969*, 574 / —HB. [Rd 52 IE]

Trichlorobis(triphenylphosphine)indium *(1)* is the first In complex for which a trigonal-bipyramidal structure could be confirmed by X-ray techniques. According to *M. D. Veidis* and *G. J. Palenik*, complex *(1)* crystallizes orthorhombically in the space group Pcab with a = 18.117 ± 0.002, b = 22.533 ± 0.006, c = 17.198 ± 0.004 Å; Z = 8. The data collected with an automatic diffractometer yield unusually large InP bond lengths; the trigonal bipyramid is slightly distorted, having a PInP angle of 173.0 ± 0.1 °. The average InCl distance (2.383 Å) lies between that in $InCl_4^-$ and that in $InCl_5^{2-}$; the InP distance is 0.2 Å longer than expected for a single bond. / Chem. Commun. *1969*, 586 / —HB. [Rd 53 IE]

BOOK REVIEWS

Analytische Methoden zur Untersuchung von Aminosäuren, Peptiden und Proteinen. (Analytical Methods for the Investigation of Amino Acids, Peptides, and Proteins). By *T. Dévényi* and *J. Gergely*. Vol. 10 in the Series "Methoden der Analyse in der Chemie" (Analytical Methods in Chemistry) edited by *F. Hecht*, *R. Kaiser*, *H. Kriegsmann*, and *W. Simon*. Akademische Verlagsgesellschaft, Frankfurt/Main, 1968, 1st Edit., x + 347 pp., many illustrations; DM 39.– [1].

Protein Chemistry is going through a particularly lively phase today, and this is reflected in the large number of new books concerned with the subject. The analytical side, which is very important, is similarly well covered, and all recent works deal amply with the applications of chromatography and electrophoresis to amino acids, peptides, and proteins. Any further book must therefore be really new and have some novel features. The present book is the translation of a Hungarian compilation from 1963, which was supplemented by (too

few) updating remarks in or after the translation, together with a modern account of gas-chromatographic applications, written by *R. Kaiser* and *A. Prox*. The result is stylistic non-uniformity. Thus, the recent supplement discusses in full even unimportant details, while the main text has gaps, which are sometimes caused by recent progress. Here, the phenol-ammonia atmosphere of the early days of paper chromatography lingers on, thin-layer chromatography is used only for dinitrophenylamino acids, the higly sensitive Dansyl technique receives no mention, and the microgram-scale technique of the Edman degradation of peptides is considered only in solution and not on paper strips. Incidentally, thiazolidone is invariablyshown with a trivalent sulfur. A freely suspended high-voltage arrangement without cooling, said to be devised in 1927 (instead of 1957), is recommended for electrophoresis, but is described elsewhere in the book as unsuitable for the resolution of complex peptide mixtures. Since thin-layer and disk electrophoresis are not included, blood proteins and their separation and characterization by diffusion methods are discussed at length. However, this and the useful tables for ion-exchange resins are insufficient to turn the scales in favor of the book. *T. Wieland* [NB 814 IE]

Handbuch der Lebensmittelchemie (Manual of Food Chemistry). Vol. V, Part I: High-Carbohydrate Foods. Edited by *L. Acker, K. G. Berner, W. Diemair, W. Heimann, F. Kiermeier, J. Schormüller*, and *S. W. Souci*. Springer-Verlag, Berlin-Heidelberg-New York 1967. 1st Edit., XXIV, 819 pp., 398 figures, 7 plates with 63 individual illustrations, stitched DM 228.—, $ 57.00.

The completely revised Manual of Food Chemistry [1] deals mainly with foods containing carbohydrates.

The raw materials are described first, then the components of the material in question and changes that can occur *e.g.* during storage; investigation methods are then reviewed, and this is followed by a section on legal evaluation. The volume begins with grain and grain flour products (*M. Rohrlich* and *B. Thomas*). This is followed by a discussion of flour products and their use, the technique of milling grain, the chemical composition of the products, and their investigation and evaluation. The principles of bakability and the testing of baking quality (Farinograph, Extensograph, Amylograph) are discussed. The next section deals with the starches (*G. Graefe*) and products derived from them, such as swelling starches, thin-boiling starches, dextrins, starch esters, starch ethers, pudding powders, *etc.* The microscopic investigation of starch flours and mill products is described by *A. Th. Czaja*.

The section "Bread, Baker's Produce, and Baking Aids" consists of individual chapters by different authors: "Bread" (*A. Schulz*), "Baker's Produce" and "Aids and Additives for the Production of Bread and Baker's Produce" (*A. Rotsch*), "Investigation and Evaluation of Bread, Baker's Produce, and Baking Aids" (*A. Rotsch* and *A. Menger*). The microscopic investigation of these products (*Th. Czaja*) completes the set of articles, which occupy a total of 400 pages. The section on microscopy contains many extremely beautiful and clear photomicrographs and photographs taken through a magnifying glass.

The section on "Leguminous Plants" (*L. Wassermann*), which is naturally smaller, includes information of the products obtained from soybeans in Eastern Asia, such as soy sauce, tofu, miso, *etc.* The chapter "Microscopic Investigation of Leguminous Plants" (*Th. Czaja*) deals not only with the few generally used seeds, but also with flat peas, adzuki beans, hyacinth beans, and other rare products.

The aricle "Diet Foods Based on Grain" (*R. Franck*) is short, as might be expected, since the raw material has already been described in earlier articles. It deals mainly with digested grain products and diabetic baked goods. The chapter "Dough Products" (*A. Menger* and *L. Acker*) is very thorough, and starts with definitions and raw materials.

The next set of articles deals with sugar and products made from it. The articles "Honey and Artificial Honey" (*H. Duisberg*) and "Cane and Beet Sugar" (*F. Schneider*) are outstanding. The discussion of the microscopic investigation of honey (*J. Evenius* and *E. Focke*) is again accompanied by excellent photomicrographs of pollen grains and extraneous objects in honey. The articles on "Glucose Syrup, Glucose and Dextrose" (*G. Graefe*) and "Other Sugars and Syrups" (*G. Graefe*) are also comprehensive, the chapters on maple syrup and sugar, on sugar alcohols (sorbitol, mannitol, dulcitol, and iditol, xylitol), and on caramel being particularly notable. *H. Viermann*'s short but very informative article on "Malt Extract and Malt Syrup" completes the series of articles on sugars.

The article "Confectionery" (*A. Fincke*) describes the products made from sugar. Briefly, but extremely clearly and systematically, the article deals with fifteen different products, from candy to marzipan nougat, and chewing gum, and with their general and special investigation. The series ends with the article "Ice Cream", which is by several authors. *J. Klose* deals with definitions and evaluation, *E. Loeser* with the technology of ice-cream manufacture, and *W. Pelz* with the investigation of ice cream. Those three chapters again constitute a short monograph. The same is true of the last article in the volume "Baker's Yeast" (*R. Kautzmann* and *W. Zoberst*).

A more or less long bibliography is given at the end of each article, with the titles of the publications cited as well as the usual data. This takes up more space, but it is sometimes of interest to the user of the book to know the subject of the article in question. The bibliography extends up to about 1966. The volume closes with a 30-page subject index. The present, excellently presented volume is a worthy successor to the earlier volumes. It will be of great value to all who are concerned with the chemical, and particularly the food-chemical, problems of products based on seeds containing starch, and on sugar. *H. Thaler* [NB 819 IE]

[1] Cf. Angew. Chem. *80*, 708 (1968); Angew. Chem. internat. Edit. *7*, 743 (1968).

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 4 50 75, Telex 46 1855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 9
SEPTEMBER 1969
PAGES 623–688

Determination of the Structures of Organic Molecules and Quantitative Analyses with the Field Ionization Mass Spectrometer

By H. D. Beckey[*]

Field ionization and electron impact mass spectrometry complement each other well. Whereas bombardment of organic molecules with 70 eV electrons yields many characteristic fragment ions, which give valuable information about the structure of the molecules, the "soft" field ionization even of very unstable substances leads to the formation of relatively intense molecular ions which are often undetectable on ionization by electron bombardment. Field ionization also gives fragment ions that, though not very intense, are often very characteristic, and yield further information about the structure. The field desorption technique greatly reduces the degree of thermal decomposition of solid organic samples.

New activation methods for field ion emitters lead to more intense ion beams and prolong the life of the emitters. Quantitative analyses using the field ionization mass spectrometer are of interest for hydrocarbon mixtures containing a very large number of components (e.g. several hundred). Simplified analyses are possible in particular for high-boiling petroleum fractions.

1. Introduction

The importance of the qualitative and quantitative investigation of organic molecules with the aid of the mass spectrometer has grown steadily in recent years. Earlier articles on the use of the mass spectrometer for the determination of the structures of large organic molecules[1,2] and on the mass-spectrometric investigation of rearrangements of organic ions[3] rightly concentrated on the production of ions by electron bombardment, the technique most commonly used in analytical laboratories. The determination of the structure of a complicated organic molecule requires a large number of specific fragment ions, from which the overall structure of a molecule that is at least partly unknown can be built up like a mosaic after accurate determination of their weights. Large numbers of fragment ions, which are frequently characteristic, are obtained by ionization of organic molecules with electrons having an energy of about 70 eV. An appreciable part of the energy difference between 70 eV and the ionization energy of the molecules (of the order of 10 eV) is transferred from the bombarding electrons to the ionized molecules. The increase in the internal energy of the molecules then leads to numerous fragmentation reactions.

Despite these advantages of the electron bombardment method, the field ionization method has recently shown a steady growth of importance as a frequently ideal complement of the electron bombardment method. This is partly due to the fact that on ionization by electric fields of the order of 5×10^7 V/cm, a much smaller quantity of internal energy is supplied to the molecule, so that this is a "soft" ionization method, and partly to the fact that the field ionization method is specific for the detection of chemical processes on the surfaces of solids, whereas the electron bombardment method is specific for the detection of molecules that are ionized in the gas phase. Finally it has recently been found possible, with the aid of the field ionization mass spectrometer, to study the kinetics of

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[1] *K. Biemann*, Angew. Chem. *74*, 102 (1962); Angew. Chem. internat. Edit. *1*, 98 (1962).

[2] *G. Spiteller* and *M. Spiteller-Friedmann*, Angew. Chem. *77*, 393 (1965); Angew. Chem. internat. Edit. *4*, 383 (1965).

[3] *P. Brown* and *C. Djerassi*, Angew. Chem. *79*, 481 (1967); Angew. Chem. internat. Edit. *6*, 477 (1967).

extremely fast unimolecular decomposition processes [4], and the "atom probe" has now made it possible to analyze a single atom, *i.e.* to determine its atomic weight accurately after it has been made optically visible in the field ion microscope [5].

It should be noted that soft ionization is also possible in the electron bombardment technique if the energy of the electrons is reduced to a value just above the ionization potential of the molecules in question. This yields valuable information about the mechanism of the degradation of organic ions [6]. Characteristic differences nevertheless exist between the mass spectra produced by low-energy electrons and those produced by field ionization. Owing to these differences, each of the two methods has its own specific applications (see Section 4; for reviews on FI mass spectroscopy [*], see [7,8]).

2. Principle of the Field Ionization Method

Field ionization occurs when an atom or molecule is acted upon by an electric field of the order of 10^7–10^8 V/cm. The removal of an electron from a molecule is not a discontinuous process like ionization by electron impact, in which ionization occurs only above a sharply defined bombardment energy, the ionization energy. Field ionization is a process whose probability increases continuously with the field strength. At low field ionization probabilities, however, the field ion current I increases with such a high power of the field strength F ($I \simeq$ const. $\times F^{30}$ according to *Southon* and *Brandon* [9]) that below a relatively well defined "threshold field strength" the field ion current rapidly becomes too small to be measured.

The removal of an electron from a molecule by a high electric field is based on the quantum-mechanical tunnel effect. The process can be most simply explained by considering the field ionization of a hydrogen atom. In a classical electrodynamic treatment, the potential of the electron of the H atom would have to be increased by an amount I (the ionization potential) to become completely separated from the proton in the absence of an electric field (Fig. 1a). In the presence of a high electric field, however, the potential of the atom is deformed (Fig. 1b) in such a way that the electron of the H atom is faced in one direction with a potential barrier of finite thickness. According to the laws of quantum mechanics it is not necessary for the electron to pass over the energy barrier in order to become separated from the proton, since it can also pass through the barrier with a finite probability. It can be seen from Figure 1 that the resulting potential of the atom in a high electric field consists essentially of three components: the atomic potential of the system in the absence of a field; the external potential, which corresponds to the applied electric field; and the image potential, *i.e.* the interaction potential between the electron and the image charges produced by it and the proton in the metal surface producing the field.

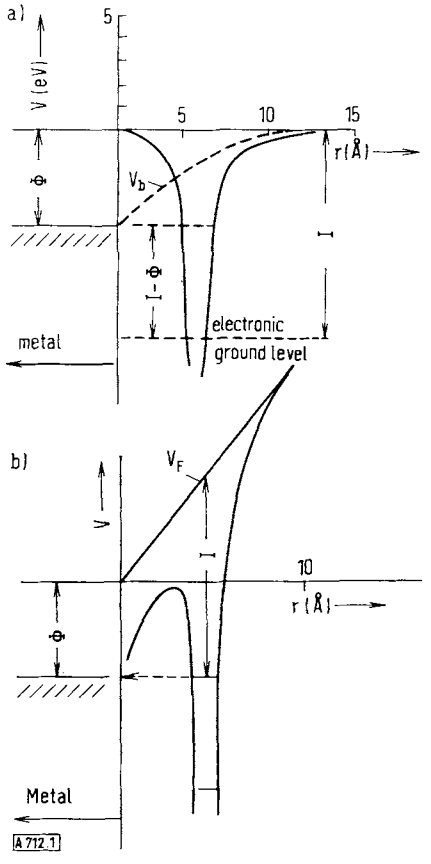


Fig. 1. Potential (V) of an atom in the vicinity of a metal surface. (a) without field, (b) with field.
I = ionization energy, Φ = work function of the metal
V_b = image potential (broken curve)
V_F = external electric potential = eFr (F = field strength).

It can also be seen from Figure 1 that the electron of the H atom must be promoted by the external electric field at least to the potential of the highest occupied level of electrons of the metal to enable it to tunnel through the potential barrier into unoccupied states of the metal producing the field. This leads to a condition for the minimum distance d_{min} from the metal surface at which field ionization is possible:

$$d_{min} \times F \simeq I - \Phi \qquad (1)$$

where Φ is the work function of the metal, and the image potential has been neglected. Thus at a field strength of 5×10^7 V/cm, an H atom cannot undergo field ionization in direct contact with the metal surface producing the field (*e.g.* the surface of a metal spike), but must be at a distance of at least

$$d_{min} \approx \frac{I-\Phi}{F} \simeq 3.4 \text{ Å} \quad (I = 13.5 \text{ V}, \Phi = 5.0 \text{ V}, F = 2.5 \text{ V/Å})$$

[4] *H. D. Beckey, H. Hey, K. Levsen,* and *G. Tenschert,* Int. J. Mass Spectrometry Ion Physics *2*, 101 (1969).

[5] *E. W. Müller, J. A. Panitz,* and *S. McLane,* Rev. sci. Instruments *39*, 83 (1968).

[6] *G. Remberg, E. Remberg, M. Spiteller-Friedmann,* and *G. Spiteller,* Org. Mass Spectrometry *1*, 87 (1968).

[*] The abbreviations FI and EB are used in this article for field ionization and electron bombardment respectively.

[7] *H. D. Beckey*: Field Ionization Mass Spectrometry, Vieweg, Braunschweig 1969, and Akademie-Verlag, Berlin, in press.

[8] *J. Block,* Advances Mass Spectrometry, The Institute of Petroleum, *4*, 791 (1968).

[9] *M. J. Southon* and *D. G. Brandon,* Philos. Mag. *8*, 579 (1963).

For organic molecules having an ionization potential of about 10 V, this distance amounts to about 10 Å at $F = 0.5$ V/Å. The organic molecule can undergo field ionization in the adsorbed state if it is at least 10 Å long, and even shorter adsorbed molecules can be ionized at higher field strengths. This is referred to as "field desorption". The desorption field strengths for single atoms are naturally very high (up to 5×10^8 V/cm [10, 11]).

The strength of the ion current produced is decisively influenced by the supply of neutral molecules to the field ion emitter. For the sake of simplicity let us assume for the moment that the high electric field is produced by a single metal spike having the shape of a hyperboloid of revolution, which is at a high positive potential with respect to a counter-electrode whose surface is large in relation to that of the spike.

The supply of particles to the field ion emission center is made up of two components; the supply from the gas phase and the supply, by surface diffusion, from the particles adsorbed on the shank of the spike. We shall consider the former component first. The number n_0 of particles arriving per second from the gas phase in the absence of an electric field is found to be

$$\dot{n}_0 = \frac{{}^1n\,\bar{c}}{4}\,O \qquad (2)$$

where ${}^1n$ is the number of particles per cm³, $\bar{c}$ is the average molecular velocity, and O is the area of the ion emission center. *Müller* showed some time ago, in connection with field ion microscopy, that the supply of particles can be greatly increased in the presence of high electric fields, since the atoms or molecules are preferentially drawn into the regions of increased field strength as a result of induced or permanent polarization [12]. The multiplication factor σ can have values of up to about 100 for atoms or apolar molecules such as H_2 at very high field strengths (approximately 5×10^8 V/cm), and can be considerable even at about 1×10^8 V/cm in the case of polar organic molecules having large permanent dipole moments.

The factor σ is given by the equations

$$\sigma = 1 + \tfrac{2}{3}\,V_{(F)}/kT \qquad (3)$$

$$V_{(F)} = \frac{\alpha}{2}\,F^2 + \mu F \qquad (4)$$

where k is Boltzmann's constant, T is the absolute temperature, $V_{(F)}$ is the polarization energy, α is the polarizability, and μ is the average permanent dipole moment in the direction of the field. [For strongly polar substances with $\mu \simeq 3$ Debye and at $F \simeq 5 \times 10^7$ V/cm, the second term in eq. (4) predominates.]

At sufficiently high field strengths, practically every molecule that reaches the vicinity of the emission point undergoes field ionization. The ion current is then given by the equation

$$I = e\dot{n}_0\,\sigma \qquad (5)$$

If the point is assumed to have a radius of 1 to 10×10^{-5} cm (emitting area about 10^{-8} cm²) and the gas pressure is 10^{-3} torr, a value of $\sigma = 5$ in eq. (5) gives $I \simeq 5 \times 10^{-10}$ A. The current can be increased to about 5×10^{-6} A by the use of an emitter having numerous micro-points.

The field ion current at low field strengths cannot be represented by a relation as simple as eq. (5). The ionization probability decreases rapidly from unity to smaller values with decreasing field strength.

The second component of the supply of particles consists of the diffusion current of adsorbed molecules from the shank of the spike to its center. The theoretical treatment of this component is more difficult than that of the component from the gas phase [13]. It can be shown in general that the supply from the surface increases with the adsorption energy of the adsorbed molecules and that it can in certain circumstances amount to an appreciable fraction of the supply from the gas phase.

3. Apparatus

3.1. Field Ion Emitter

High electric fields can be produced by strongly curved electrically conducting electrode surfaces at a high electric potential with respect to an oppositely charged electrode. The smaller the radius of curvature of the electrode producing the field (typically 100–10000 Å), the higher is the field strength. Fine metal points, fine wires, and sharp metal edges have been used as field electrodes.

3.1.1. Metal Points as Field Anodes

In the early stages of the development of FI mass spectrometry, fine metal points were used to produce the field [14–16]. The advantages of point emitters are their geometrically well defined surface shape and the possibility of obtaining extremely high field strengths (about 5×10^8 V/cm), at which wire or edge emitters are damaged or destroyed. The disadvantage of point emitters is that they have a very small emitting area in comparison with the other two types, and so give only a small field ion current. Moreover, the random ion emission fluctuations are considerably greater for point emitters than *e.g.* for wire emitters. Wire or edge emitters are therefore generally used for qualitative

[10] *E. W. Müller*, Physic. Rev. *102*, 618 (1956).

[11] *R. Gomer*, J. chem. Physics *31*, 341 (1959).

[12] *E. W. Müller*, Ergebn. exakt. Naturwiss. *27*, 290 (1953).

[13] *H. G. Metzinger* and *H. D. Beckey*, Z. Naturforsch. *22a*, 1020 (1967).

[14] *M. G. Inghram* and *R. Gomer*, Z. Naturforsch. *10a*, 863 (1955).

[15] *E. W. Müller* and *K. H. Bahadur*, Physic. Rev. *102*, 624 (1956).

[16] *H. D. Beckey*, Naturwissenschaften *45*, 259 (1958).

and quantitative organic analyses. Nevertheless, point emitters still have a firm place in FI mass spectrometry, particularly for physico-chemical studies either on phenomena occurring in extremely high electric fields, which can be produced only with single points, or on the dependence of surface reactions on the material from which the point is made (see *e.g.* [17]).

The use of point emitters has recently received new impetus from the development of the "atom probe" by *E. W. Müller et al.* [5]. In this device the mass-spectrometric analysis is preceded by observation of the emitter surface with the aid of a field ion microscope; this is possible only for geometrically well defined and clean single points, and not for wire or edge emitters.

The field strength obtained with a single point is given by

$$F_0 = \frac{V_0}{kr_0} \tag{6}$$

(F_0 = field strength on the surface of the point, V_0 = potential of the point, k = geometric factor, r_0 = radius of curvature at the tip of the point.) The geometric factor depends on the geometrical shape of the point, which may be *e.g.* parabolic or hyperbolic. A typical value is $k = 5$. With $V_0 = 10^4$, $k = 5$, and $r_0 = 10^{-5}$ cm, we obtain $F_0 = 2 \times 10^8$ V/cm.

Fine metal points are mainly produced by chemical or electrochemical etching [18]. Tungsten points are preferred for the production of very high field strengths, since tungsten has a very high tensile strength and the field strengths required for the "field evaporation" of individual surface atoms are higher than for other metals.

By the use of relatively blunt points ($r_0 > 10^4$ Å) ion currents of up to about 10^{-8} A can be produced with polar compounds.

3.1.2. Fine Wires as Field Anodes

Much higher field ion currents can be obtained with fine wires instead of single points as field anodes. This method [19,20] is based on the fact that though the radius of curvature of the wires used is comparable with that of a blunt point, because of the length of the wire (a few mm) its emitting area is greater by a factor of about 10^4 than that of a blunt point. On the other hand, since the field line density in front of a cylindrical electrode is lower than that in front of a paraboloid electrode, the field strength at the surface of a wire would be insufficient for the field ionization of organic molecules but for a local increase in the field strength. Such increases are due to innumerable micro-needle crystals that grow on the surface of a wire during the field ionization process. At the tips of these needle crystals, the field strength is greater by a factor of h/r than the field strength of an ideally smooth wire (h = height, r = radius of the needle crystal). A typical value for the "field intensification factor" h/r is about 7.

The sum of the emitting point surfaces of the needle crystals is naturally only a fraction of the total area of the smooth wire. The optimum value of this fraction is about 1/100, so that the factor relating the area of the smooth wire to that of a point is decreased from 10^4 to about 100. It has in fact been found that well activated (*i.e.* densely covered with needle crystals) wire emitters can give field ion currents of up to 100 times the values obtained with single points ($I_{max} \simeq$ a few μA at a gas pressure of 10^{-3} torr, $V_0 \simeq$ 8—10 kV, r_0 wire = 1.25×10^{-4} cm).

The growth of needle crystals in the presence of organic substances and at high electric fields was first observed with an electron microscope as a secondary process of field ionization. The optimum conditions for the growth of these needle crystals were later studied systematically as a function of various parameters such as pressure, time, voltage, temperature, point material, and nature of the organic substance [21]. Optimum needle growth occurs if the wire is activated as rapidly as possible in a diode arrangement outside the mass spectrometer at a relatively high pressure (about 3×10^{-3} torr), at a voltage of about 10 kV (r_0 wire = 1.25×10^{-4} cm), and in the presence of a strongly polar substance having a low ionization energy.

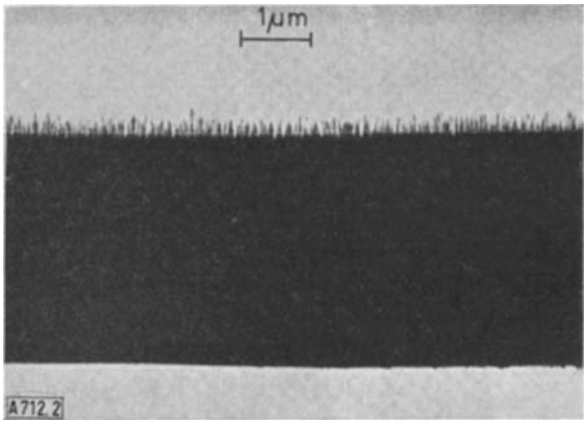


Fig. 2. Electron micrograph of a platinum wire having a diameter of about 3 μm, which has been activated at an acetone pressure of 3×10^{-3} torr and at a voltage of 10 kV. Average length of the micro-needles approx. 2500 Å (electron micrograph by *A. Maas*, Bonn).

Figure 2 shows a very dense, uniform growth of relatively short needles on a platinum filament ($r_0 = 1.25 \times 10^{-4}$ cm) in the presence of acetone. On systematic variation of the organic substance, it was found that needles grown in the presence of benzonitrile give even more intense ion emission [22].

Figure 3 shows needle crystals grown on a platinum wire used as a FI emitter in the presence of benzonitrile. The needles are up to ten times as long as those shown in Figure 2, and their structure is more

[17] *J. Block*, Z. Naturforsch. *18a*, 952 (1963).

[18] *E. W. Müller*, Advances in Electronics and Electron Physics *13*, 83 (1960).

[19] *H. D. Beckey*, Z. Instrumentenkunde *71*, 51 (1963).

[20] *H. D. Beckey*, Z. analyt. Chem. *197*, 80 (1963).

[21] *H. D. Beckey, H. Heising, H. Hey*, and *H. G. Metzinger*, Advances Mass Spectrometry, The Institute of Petroleum, *4*, 817 (1968).

[22] *H. D. Beckey, E. Hilt, A. Maas, M. D. Migahed*, and *E. Ochterbeck*, Int. J. Mass Spectrometry Ion Physics, *2* (1969) in press.

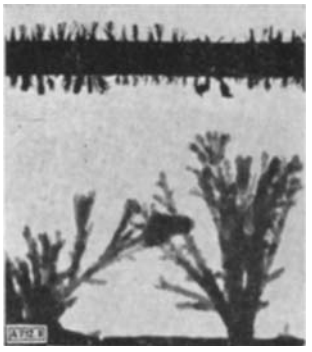


Fig. 3. Electron micrograph of a platinum wire having a diameter of about 2.5 μm, which has been activated with benzonitrile. Average length of the micro-needles about 15000 Å. Bottom: Enlargement of a section (electron micrographs by *A. Maas*, Bonn).

dendritic. The growth rate is considerably greater than when acetone is used (approximately 30 minutes for complete activation). The results of several investigations indicate that these needles consist of organic polymers having low hydrogen contents, and of graphite in the limiting case.

Fine metal or semiconductor wires having high tensile strengths may be used as emitter wires. A detailed comparison has shown that platinum Wollaston wires having a diameter of about 3 μm are particularly suitable [23]. The Wollaston wires are commercially available, and allow relatively high accuracy in the preparation of the emitter. Their average tensile strength, however, is only about 50 kg/mm which is only slightly above the order of magnitude of the mechanical force exerted on the wire by the electric field. These wires are easily broken by improper treatment or by arcing.

Field ionization emitters have recently been made from carbon whiskers about 5 mm long and 2–3 μm in diameter [22] by *Bacon*'s method [24] in a high-current high-pressure carbon arc. These carbon whiskers are single crystals having extremely high tensile strengths (about 750 kg/mm on average). With careful handling, emitters of this type can give weeks or months of service in an FI mass spectrometer. Since graphite whiskers are not commercially available at present and are very difficult to produce, the use of tungsten wires 10 μm in diameter is recommended, since these have a tensile strength about 160 times as high as that of 2.5-μm platinum wire, and since in spite of their large diameter they give a sufficiently high local field strength because of the length of the micro-needles grown with the aid of benzonitrile. The activation method is described in ref. [22].

3.1.3. Sharp Metal Edges as Field Anodes

We also introduced sharp metal edges into FI mass spectrometry [19, 20]. *Robertson* later carried out a detailed investigation on the structure and field strength distribution of such emitters [25–27]. The edges used may be those either of untreated commercial razor blades (from which it may be necessary to remove a coating of grease) or of etched thin foils, preferably of platinum or tungsten.

It is widely held that fine wires could easily break in a high field, whereas this is obviously impossible in the case of metal blades. It must however be remembered that when blades or thin foils are used, arcing to the counter-electrode, which is only a few tenths of a mm away, can often occur at potential differences greater than 10 kV, and this can quickly make the sharp part of the blade unsuitable for ion emission. Moreover, the rear portion of the blade causes electrostatic screening, which leads to a decrease in the field strength as compared with that of a wire emitter. The radius of curvature of the edge must therefore be smaller by a factor of 10 to 100 than that of a wire, and the ion current is accordingly decreased. The variations of the FI current emitted are generally greater with edges than with wires.

Nevertheless, edge emitters are frequently used as well as wires. This is justifiable in particular at some distance from the detection limits and in the purely qualitative detection of ions, where somewhat larger fluctuations of the ion current can be tolerated (for a comparison of point, wire, and edge emitters, see [28]).

3.1.4. Multiple Thin Layer Films as Field Anodes

It should be mentioned that *Gentsch* [29] has recently produced FI emitters in which a thin insulating film a few hundred Å thick is deposited from the vapor on a metal support, and a perforated covering film of metal having a lattice or comb structure is deposited on the insulating film. The physical principle of the field production and field ionization is the same as for the edge emitters described in Section 3.1.3. The system differs however, in that by reduction of the radius of curvature to 10–100 Å and of the distance from the counter-electrode to about 1000 Å, the voltage required to obtain a field strength of 10^7–10^8 V/cm can be reduced from the 10 kV range to about 100 V. A diagrammatic sketch of such an emitter is shown in Fig. 4.

The technological difficulties are that the metal film must not be evaporated by the field, and that electrical breakdown of the thin insulating film must not occur. The diffusion of ions in the insulator must also be kept small. Though these emitters are not yet stable in continuous operation, *Gentsch* has shown in principle that they can be used to produce FI mass spectra. Substantial technological improvements appear entirely feasible.

[23] *K. Levsen, A. Heindrichs*, and *H. D. Beckey*, Messtechnik *78*, 9 (1968).

[24] *R. Bacon*, J. appl. Physics *31*, 283 (1960).

[25] *C. M. Cross* and *A. J. B. Robertson*, J. sci. Instruments *43*, 475 (1966).

[26] *D. F. Brailsford* and *A. J. B. Robertson*, Int. J. Mass Spectrometry Ion Physics *1*, 75 (1968).

[27] *P. A. Blenkinsop, B. E. Job, D. F. Brailsford, C. M. Cross*, and *A. J. B. Robertson*, Int. J. Mass Spectrometry Ion Physics *1*, 421 (1968).

[28] *H. D. Beckey, H. Krone*, and *F. W. Roellgen*, J. sci. Instruments (2), *1*, 118 (1968).

[29] *H. Gentsch*, Ber. Bunsenges. physik. Chem. *71*, 919 (1967).

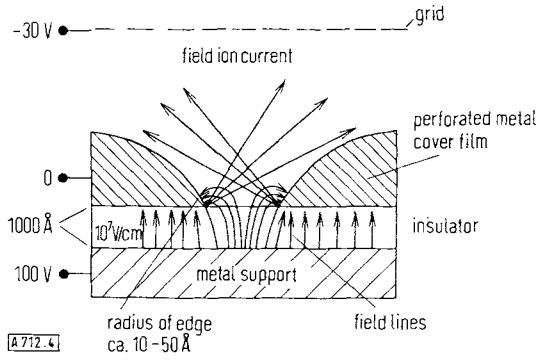


Fig. 4. Multiple thin layer film field ion emitter after *Gentsch* [29] (schematic).

3.2. Field Ion Sources

As was shown in Section 3.1, field ion currents of the order of 10^{-6} A can be produced with well activated wire emitters. This is much higher than the primary ion current produced in electron bombardment ion sources. However, fewer ions reach the collector of the mass spectrometer with field ionization than with electron bombardment, since the ion beam leaving the source is practically parallel in EB, whereas in FI the ions leave the emitter over a very large angle, and after a few thousand Å they have been accelerated to an energy of several kV. Ion beams of this type are difficult to focus into a narrow mass spectrometer entry slit with a small entry angle (about 1 °). It may be assumed as a rule of thumb that the intensity at the detector of the mass spectrometer is smaller by a factor of about 100 for field ionization than for ionization by electron bombardment. With strongly polar substances and very well activated emitters, this factor can be reduced to about ten. Further improvement of the ion optics of FI sources appears possible [30].

The mass resolving power is somewhat lower for FI than for EB sources. This is partly due to the fact that there is a certain potential drop along the length of the micro-needles on an FI emitting wire, this drop depending on the length and diameter of the needles. To obtain a good resolving power, the highest possible voltage must be applied between the FI emitter and the counter-electrode. *Brunnée et al.* [31], for example, obtained a resolving power of $M/\Delta M = 800$ at 18 kV with a single-focusing mass spectrometer (type Varian CH5).

With double-focusing mass spectrometers there is evidently no limit to the resolving power of field ion sources as compared with electron bombardment ion sources. *Chait* and *McLafferty*, for example, obtained a resolving power of 30000 with a double-focusing mass spectrometer having an FI source, and a precision mass determination could even be carried out in the usual manner [32].

[30] *U. Winkler*, Diplomarbeit, Universität Bonn 1968.

[31] *C. Brunnée, G. Kappus*, and *K. H. Maurer*, Z. analyt. Chem. *232*, 17 (1967).

[32] *E. M. Chait, F. W. Shannon, W. O. Perry, G. E. van Lear*, and *F. W. McLafferty*, Int. J. Mass Spectrometry Ion Physics *2*, 141 (1969).

Another problem is the combination of FI and EB sources. As was mentioned earlier, the FI and EB spectra often complement each other very well. It therefore often proves expedient to be able to change quickly from one method to another without the need for mechanical conversion. This problem is easy to solve for measurements on gaseous substances, since the FI emitter can be situated away from the electron beam in a rear part of the source. The gas molecules diffuse uniformly into the electron bombardment and field ionization chambers. After we had produced the prototype of such a source [33] (see Fig. 5), *Brunnée et al.* developed an FI/EB combination source, which also allows alternate measurements on solids by both methods [31] (manufacturer: Varian-MAT).

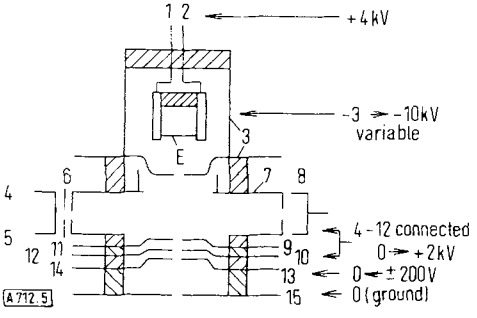


Fig. 5. Prototype of a combined electron bombardment-field ionization source (schematic) [33]. Shaded parts: Insulators. E = FI emitter, 1 and 2 = leads for electric heating of the FI emitter and for the positive high voltage, 3 = counter-electrode, 4 and 5 = cathodes for electron emission. 7 = electron bombardment ionization chamber, 8 = electron collector. Potentials for FI operation are given next to the drawing on the right. Potentials for electron bombardment operation: (7) + 3 kV; accelerating electrodes (9)—(12) and lenses (13) and (14) have the usual potential values. The gas is introduced into the ionization chamber (7).

The electron beam passes through a beam of molecules of the solid evaporating from a furnace. During this EB operation, the FI emitter occupies a rear position. For FI operation, the electron beam is switched off and the FI emitter is moved forward a few millimeters into the molecule beam by a swivel mechanism. The ion source potentials are varied by means of a switch.

4. Determination of the Structures of Organic Molecules with the FI Mass Spectrometer

The electron bombardment method is ideally suited for the determination of the structures of large organic molecules; since the energy transferred to the molecules on electron bombardment is so great that many more or less structure-specific fragments are formed. The procedure for the determination of the structure of an unknown molecule in general is therefore roughly as follows: Some information about the nature of the substance can generally be obtained from the source of the substance or its preparation, and often from preliminary chemical tests. Further information is obtained by physico-chemical methods such as IR,

[33] *H. D. Beckey, H. Knöppel, H. G. Metzinger*, and *P. Schulze*, Advances Mass Spectrometry *3*, 35 (1966).

Raman, UV, and NMR spectroscopy, and a mass spectrometric analysis is carried out with an electron bombardment ion source. This very often provides sufficient information for an unambiguous reconstruction of the structure.

In many cases, however, further information is still required after these steps have been completed, and FI mass spectroscopy can often be of assistance in such cases. The most important data that can be obtained by the FI method in this connection are:

1. the molecular weight of the substance and its empirical formula, and

2. a characteristic fragment-ion spectrum that differs from the EB fragment-ion spectrum.

4.1. Determination of Molecular Weight and Empirical Formula with the FI Mass Spectrometer

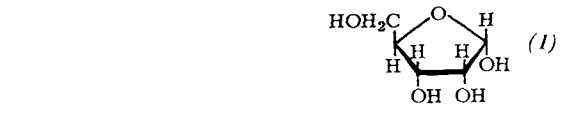
The stability of organic molecules to 70 eV electrons or thermal energy is often so low that no ions of the undecomposed molecules (molecular ions) can be detected in the mass spectrometer. In such cases, the molecular ions can usually be detected in an FI mass spectrum.

In field ionization a molecule is nearly always ionized from the electronic ground state, as can be seen from Figure 1. The probability of tunneling of an electron increases with decreasing height of the potential barrier above an electronic state. The vibrational energy excited in the molecular ion on field ionization is also small. Thus, except where the molecular ions are extremely unstable, they can generally be detected with good intensity even for substances that give vanishingly small molecular ion intensities on ionization with 70 eV electrons.

The decrease in the supply of heat due to lowering of the temperature of the ion source can lead to a considerable increase in the intensity of the molecular ions in electron bombardment mass spectra [6]. Since there are no hot strips for the production of electrons in field ion sources, FI sources are inherently suitable for use as "cold" ion sources. If no molecular ions can be detected for a given substance with an EB source at the lowest possible ion source and substance evaporation temperatures, and with 70 eV electrons, it will not be possible to detect them by reducing the energy of the electrons. Though a decrease in the energy of the electrons increases the intensity of the molecular ions relative to that of the fragment ions the absolute molecular ion intensity is always decreased.

Some substances, such as mono- and oligosaccharides, have high sublimation temperatures and do not give clearly detectable molecular ions on mass-spectrometric analysis with EB sources, even when the temperature and the energy of the electrons are reduced. The field ionization method, on the other hand, gives clearly detectable more or less intense molecular ions for these substances.

Figure 6 shows the EB and FI mass spectra of D-ribose *(1)*. In the EB mass spectrum the molecular ion line M is so weak (<0.2%) that a definite assignment becomes difficult in the presence of a back-ground spectrum or of impurities of the order of 0.2%. In addition to the very intense molecular ion line, the FI mass spectrum contains an (M+1) mass line, which is the



(1)

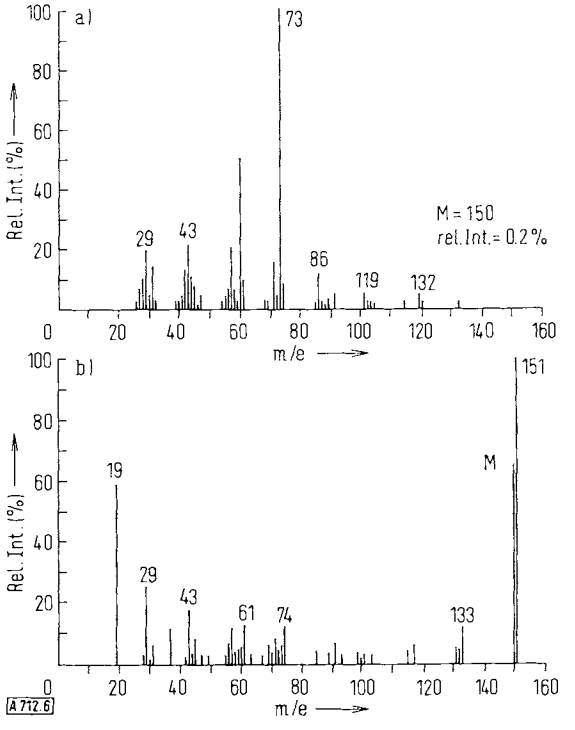
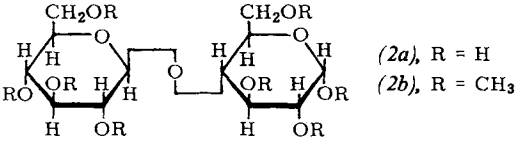


Fig. 6. a) Electron bombardment and b) field ionization mass spectra of D-ribose *(1)* [33].

most intense line in the mass spectrum. This is due to an ion-molecule reaction between two ribose molecules adsorbed on the emitter surface:

$$M^+ + M \rightarrow (M+1)^+ + (M-1)$$

"Hydride ion lines" of this type are very often found for strongly adsorbed polar molecules, and particularly for molecules containing hydroxyl groups.



(2a), R = H
(2b), R = CH_3

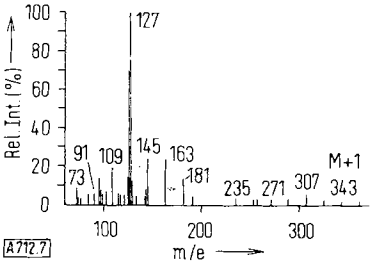
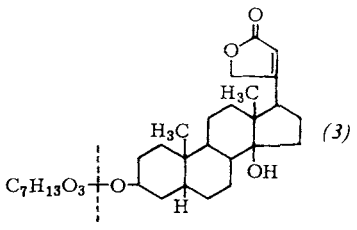


Fig. 7. Field ionization mass spectrum of cellobiose *(2a)*.

There could be doubt in the determination of the molecular weights as to whether the two intense mass lines are M^+ and $(M+1)^+$ or $(M-1)^+$ and M. However, this uncertainty can be readily resolved in view of the fact that with wire emitters the intensity of the $(M-1)^+$ line is usually only a few per cent of the M^+ intensity (generally less than 1%). The fragment ion lines also



(3)

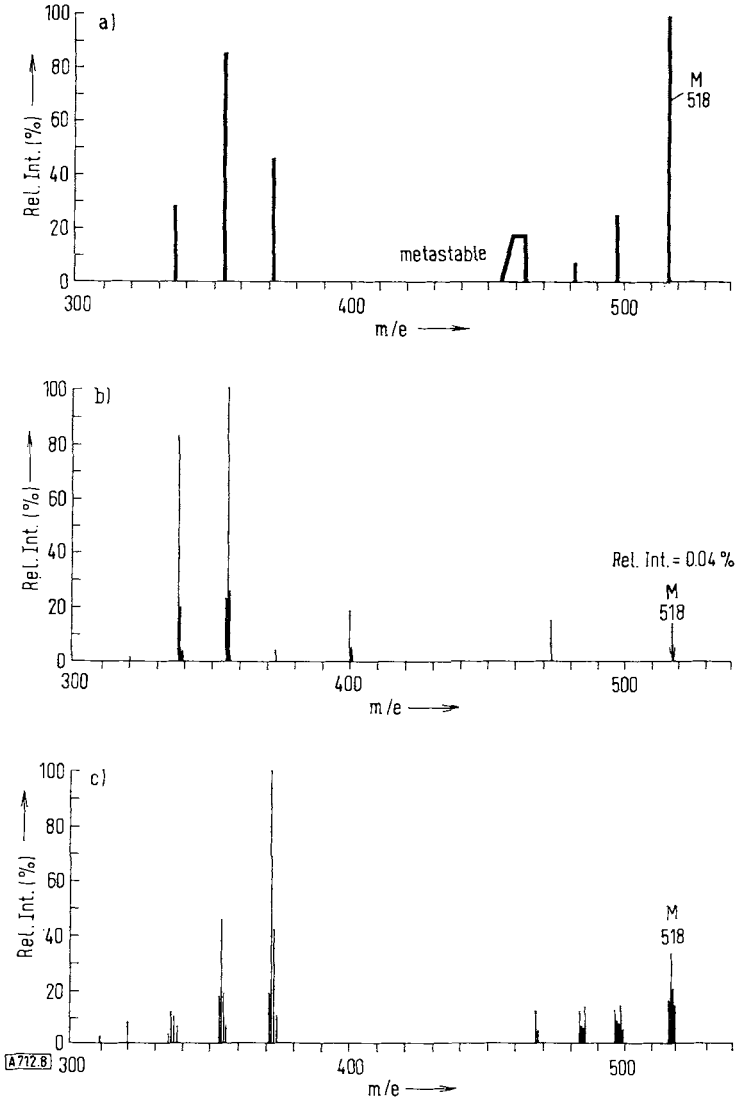


Fig. 8. Mass spectra of somalin *(3)* ($C_7H_{13}O_3$ = cymarose residue) (upper mass range) [34]; a) field ionization, b) electron bombardment ionization, c) electron attachment ionization [36, 37].

lead to definite conclusions concerning the molecular ion peaks.

The intensity of the molecular ion lines of disaccharides in the EB mass spectrum is generally even lower than that of monosaccharides. Consequently, these molecular ion lines usually cannot be definitely detected in the EB spectrum. It can be seen from Figure 7, on the other hand, that the molecular ion line of cellobiose *(2a)* can be detected in the FI mass spectrum [35].

It is interesting to compare the relative molecular ion intensities for electron bombardment, field ionization, electron attachment, and chemical ionization. The last two of these methods, like field ionization, increase the relative molecular ion intensities. Figure 8 shows a comparison of the FI, EB, and EA (electron attachment) spectra of somalin *(3)* [34]. The EA mass spectrum exhibits a certain similarity to the FI spectrum. The EA mass spectrum was recorded by *v. Ardenne*'s method [36] for the addition of slow electrons to molecules [37]. The advantage of the FI method over the EA method is the simple construction of an FI/EB combination source, which allows rapid changes from one type of operation to the other.

Table 1 shows a comparison of the molecular ion intensities of eight isomeric decanes for FI and ChI (chemical ionization).

[34] *C. Brunnée*, Z. Naturforsch. *22b*, 121 (1967).

[35] *H. Krone* and *H. D. Beckey*, Org. Mass Spectrometry *2*, 427 (1969).

[36] *M. v. Ardenne*, Kernenergie *1*, 1029 (1958); Z. angew. Physik *11*, 121 (1959).

[37] *M. v. Ardenne, K. Steinfelder*, and *R. Tümmler*, Z. Chem. *5*, 287 (1965).

Table 1. Relative intensities of the molecular ion lines (in %) of eight isomeric decanes [38, 39].

	FI M^+	ChI [a] $(M-1)^+$
5-Ethyl-2-methylheptane	98.2	20.0
2,3,6-Trimethylheptane	98.0	9.4
3-Isopropyl-2,4-dimethylpentane	95.7	1.9
2,2,4-Trimethylheptane	50.0	5.7
2,2,6-Trimethylheptane	59.2	9.2
3,3,5-Trimethylheptane	42.6	4.5
2,2,3,3-Tetramethylhexane	14.4	0.5
2,2,5,5-Tetramethylhexane	26.3	2.0

[a] ChI = chemical ionization.

The chemical ionization method, which was developed in particular by *Munson* and *Field*[40], consists in allowing a "reaction gas", *e.g.* methane, to undergo an ion-molecule reaction in a mass spectrometer ion source at a relatively high pressure:

$$CH_4^+ + CH_4 \rightarrow CH_5^+ + CH_3$$

(In addition to the CH_5^+ ion, some other reactive ions are formed with decreasing abundance by ion-molecule reactions). The very reactive CH_5^+ ion reacts with the organic molecule to be examined (decane in this case) in accordance with the following overall equation:

$$M + CH_5^+ \rightarrow (M-1)^+ + H_2 + CH_4 \text{ [*]}$$

Very little energy is transferred to the $(M-1)^+$ ions. The $(M-1)^+$ ions in ChI mass spectrometry thus correspond in some measure to the M^+ ions in FI mass spectrometry. It can be seen from Table 1, however, that the relative intensities of the FI molecular ion lines are still considerably greater than those of the corresponding ChI molecule ion lines.

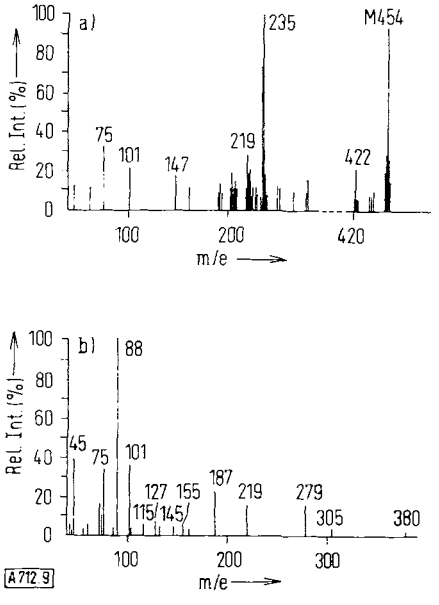


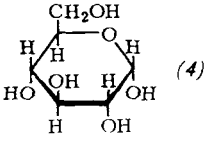
Fig. 9. a) Field ionization and b) electron bombardment mass spectra of octa-*O*-methylcellobiose *(2b)* [35].

The intensity of the molecular ion lines in the FI spectra in relation to those in the EB spectra could be demonstrated for many other examples. However, this effect is limited in molecules that have no stable states in the ionized, positively charged state. This class of molecules appears to include CCl_4 and other perhalogenated organic molecules, in whose FI mass spectra no molecular ions have so far been observed. Some oligosaccharides give such weak molecular ion lines in the FI spectra that it is difficult to assign these lines with certainty. A valuable aid in such cases is the well known technique of methylation, which often makes the molecular ion lines the most intense in the FI mass spectrum, whereas the same substances give only vanishingly small molecular ion lines (if any) in the EB spectrum despite methylation. Figure 9 shows the EB and FI mass spectra of octa-*O*-methylcellobiose *(2b)* [35].

We recently developed a new method [41] that further increases the molecular ion intensity in relation to that found in the normal FI technique, increases the detection sensitivity, and greatly decreases the degree of thermal decomposition of the sample.

Solid organic samples having low vapor pressures are normally introduced into the vicinity of the ionization zone of EB or FI sources through an air lock with the aid of a sliding rod. The substances are then evaporated into the ionization zone as a molecular beam from a micro-crucible by heating.

In thermally unstable substances, the energy required to remove molecules from the lattice is often comparable with the energy required for the thermal removal of smaller molecules from the parent molecule. A well known example is the removal of water molecules from carbohydrate molecules.



(4)

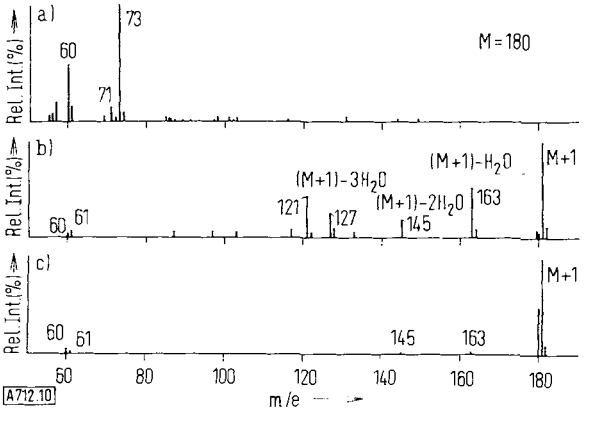


Fig. 10. a) Electron bombardment, b) field ionization, and c) field desorption mass spectra of D-glucose *(4)* [41].

[38] *H. D. Beckey*, J. Amer. chem. Soc. *88*, 5333 (1966).

[39] *F. H. Field, M. S. B. Munson*, and *D. A. Becker*, Advances Chem. Ser. *58*, 167 (1966).

[40] *M. S. B. Munson* and *F. H. Field*, J. Amer. chem. Soc. *88*, 2621, 4337 (1966).

[*] The $(M-H)^+$ ions are denoted in Table 1 and in the following discussion by $(M-1)^+$.

[41] *H. D. Beckey*, Int. J. Mass Spectrometry Ion Physics *2*, 500 (1969).

Figure 10a shows that the molecular ion intensity in the EB mass spectrum of D-glucose is negligible. Though the $(M+1)^+$ intensity is the highest in the FI spectrum (Fig. 10b), species resulting from the removal of one, two, or three water molecules and of a $C_2H_4O_2$ molecule from the glucose molecule are very intense. Thermal cleavage may be assumed to precede the ionization. The thermal breakdown is due to the conversion of the substance from a solid into a gas before the ionization. Some other methods of sample supply must therefore be used if thermal decomposition is to be reduced.

In the new sample supply method, the substance is applied directly from a solution to the field ion emitter and then undergoes field desorption from the adsorbed state. The molecules simultaneously become positively charged, and can then be detected mass-spectroscopically in the usual manner. Though this idea seems obvious in itself, it is only recently that it has become practicable, since the active emitter surfaces available for the adsorption of the molecules had previously been too small to take up enough of the substance for recording of a mass spectrum over a period of a few minutes.

However, our new activation process for field ion emitters, in which benzonitrile is used for activation [22], leads to such a large increase in the active emitter surface that sufficient material can be adsorbed for mass-spectrometric analysis by the field desorption technique.

The advantage of this new supply method is that whereas thermally unstable solids decompose on evaporation, no decomposition occurs when molecules suitable for this method are dissolved in a solvent. The FI wire emitter is dipped into a small drop (1–2 mm in diameter) of a solution (saturated if possible) of the sample, whereupon the molecules of the sample are adsorbed on the FI emitter. They are probably held only weakly by van der Waals forces on a monolayer of the solvent adsorbed on the surface of the emitter. Field evaporation of the physically adsorbed molecules can then occur in the ion source at temperatures so low that the molecules do not suffer appreciable decomposition.

Figure 10c shows the field desorption (FD) mass spectrum of D-glucose *(4)*. In comparison with the FI mass spectrum, it shows considerably less removal of one, two, or three water molecules and of a $C_2H_4O_2$ molecule from the parent molecule. The method is therefore of theoretical as well as practical importance, since it provides an indication of what proportion of certain fragmentation processes is due to the ionization and what proportion to thermal decomposition.

The FD mass spectrum of glucose was recorded with a strongly activated wire [22] having a diameter of 10 μm. After immersion in a saturated aqueous solution of glucose, the wire was inserted into the ion source of an FI mass spectrometer. The spectrometer was evacuated for one hour without heating of the ion source or of the FI wire to remove residual solvent. Again without heating of the FI wire, a background spectrum, which showed only a very small contribution due to D-glucose, was then recorded. The temperature of the FI wire was then carefully raised by passage of a current of a few mA through the wire. The molecular ion line ultimately became sufficiently intense without excessively fast consumption of the small quantity of sample adsorbed on the wire. By optimization of the temperature, it was possible to obtain useful spectra over a period of about 15 min. The intensities then decreased rapidly.

The name "field desorption" is not, strictly speaking, confined to the method used here, but is also applicable to the usual technique of molecular beam evaporation of the sample onto the FI emitter. Some of the molecules are "field ionized" in the gas phase as they approach the FI emitter, while others are first adsorbed and then ionized by "field desorption" [7, 42]. The proportions of these two reactions are not yet accurately known. However, since some of the molecules are field ionized in the molecular beam technique whereas all the molecules are field desorbed in the emitter immersion technique, it is justifiable to speak of field desorption mass spectra in the latter case.

In addition to the increase in the relative molecular ion intensities and the decrease in the thermal decomposition of the sample, the FD technique has the advantage of an increase in sensitivity as compared with the molecular beam FI technique.

On evaporation of the substance from a micro-crucible, a large part of the substances flies past the FI emitter, whereas in the FD technique a large part of the small quantity of solute present in a very small droplet of solution can be deposited on the emitter by evaporation of the solvent. The smallest quantities of substance that can be detected are thus in the microgram range. It had previously been necessary in general to use considerably larger quantities of material in the FI technique, which had therefore been inferior to the EB technique in its detection sensitivity. The elimination of this shortcoming by the FD technique is naturally restricted to substances having relatively low volatilities. One conceivable procedure for more volatile substances would be to cool the FI emitter, adsorb the sample on it, and then carefully heat the emitter.

Strong micro-needle growth can be induced even on the edges of sharp metal blades or of thin metal foils by the benzonitrile activation technique. The field desorption technique can thus also be used with FI emitters of this type.

Good spectra can be obtained in this way *e.g.* by heating a strip of razor blade about 2 mm wide and 8 mm long with a current of about 1 A [41]. However, the use of fine wires as FI emitters offers the advantages of somewhat higher ion current intensities (based on equal pressures) and somewhat better reproducibility of the spectra. In this case currents of the order of only 10 mA are sufficient for heating of the wire.

So far we have discussed only the analysis of relatively nonvolatile solid organic substances, which is carried out either by the molecular beam FI technique or by the FD technique. However, various authors have also

[42] Regarding field desorption see, *e.g.*: *E. W. Müller*, Physic. Rev. *102*, 618 (1956); *R. Gomer*: Field Emission and Field Ionization. Harvard University Press, Cambridge (Mass.) 1961.

investigated many gaseous, liquid, or solid organic substances whose volatility is so great that a normal gas inlet system with a pressure-reduction stage between the gas reservoir and the ion source may be used.

Molecular ions were detectable in the FI mass spectra of all these substances except (as was mentioned earlier) a few halogenated compounds. In some cases molecular ions were found even where the EB mass spectra forced one to conclude that no stable molecular ion state existed. A relevant example is neopentane *(5)*, which gives no molecular ions in the EB spectrum, but gives up to about 8% of molecular ions in the FI spectrum (see Fig. 11). A stable molecular ion state must therefore exist in this case, though with only a small potential trough.

No theoretical explanation has yet been found for the fact that this state is accessible by FI but not by EB. It is possible that an adsorption state of neopentane increases the probability of transition into the stable ionic state, or, as is assumed by *Robertson*[43], that the selection rules are considerably altered in the presence of a very high electric field.

To summarize, therefore, the molecular ions of the great majority of substances that do not give distinct molecular ion peaks on electron bombardment can be detected by the use of the FI or FD techniques. This allows not only the determination of the molecular weights of very small quantities of substance, but also, by the use of a high-resolution mass spectrometer, the determination of the empirical formula (see[1,2]) of the molecules under investigation.

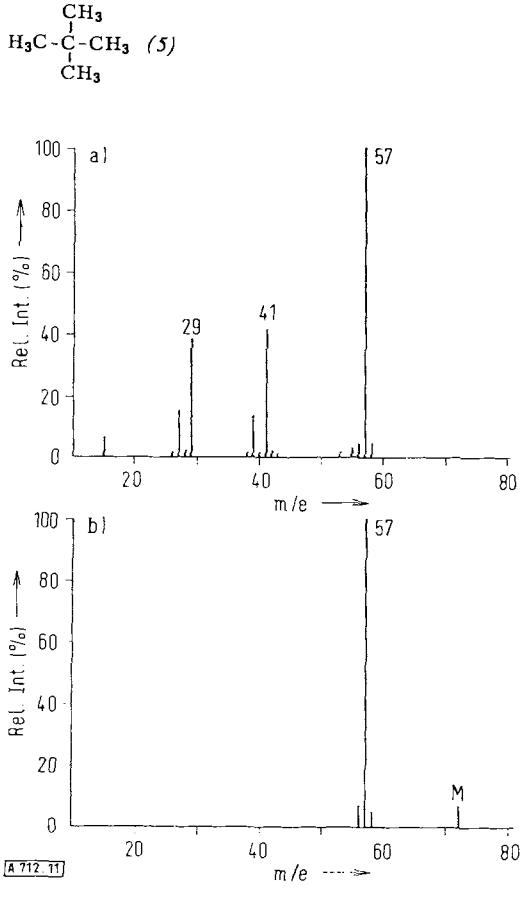


Fig. 11. a) Electron bombardment and b) field ionization mass spectra of neopentane *(5)*.

4.2. Information Obtainable from FI Fragmentation for Structure Determination

The FI mass spectra, like the EB spectra, contain characteristic mass lines of fragment ions that provide clues to the structure of the compounds in question. The intensities of the fragment lines are much smaller for FI than for EB, but the number of these lines is also considerably smaller in field ionization, since the number of possible reaction paths for the decomposition of the molecular ions is very much smaller than on ionization of the molecules with 70 eV electrons. Reactions that proceed in several consecutive steps are rare in FI and give only very low intensities.

The FI fragment ion spectrum often represents a valuable complement to the EB spectrum for two reasons:

1. The intensity distribution of the fragment ions in FI is different from that in EB because of the strong polarization of the molecules, and the spectra are often much easier to interpret because of the small number of lines.

2. There are extremely unstable molecular ions that are characterized in the EB technique, not only by the absence of molecular ion lines, but also by the absence of some fragment ion lines in the mass region slightly below the molecular ion lines. These mass lines, which are often important for the determination of structures, frequently become visible with FI, as will be shown later with the aid of some examples.

In connection with the first of these points it should be noted that the most characteristic fragment lines in FI spectra are those of aliphatic compounds or cyclic compounds with long side chains. In the absence of such side chains, the FI mass spectra of cyclic systems are often not very characteristic.

The FI fragment ions that appear in their normal mass positions in relation to the molecular ions are formed by "field dissociation"[44]. Their intensities increase very rapidly with the field strength. For wire or edge emitters covered with micro-needles, the field strength is about 5×10^7 to 7×10^7 V/cm. (At appreciably higher field strengths the micro-needles break off.) In this range of field strengths *n*-alkanes give fragment ions with a maximum relative intensity of about 1%. With point emitters, on the other hand, with which much higher fields can be produced, the intensity of the $C_2H_5^+$ fragment lines (m/e = 29) can be increased to 100%, as is shown by Figure 12.

The fragment m/e = 29 is the most characteristic fragment in the FI mass spectra of *n*-alkanes, irrespective of their molecular weight. The predominance of this fragment is due to the fact that after ionization, the *n*-alkanes are situated in front of the surface of the point in the extended state. The field tends to displace

[43] *A. J. B. Robertson*, personal communication.

[44] *H. D. Beckey*, Z. Naturforsch. *19a*, 71 (1964).

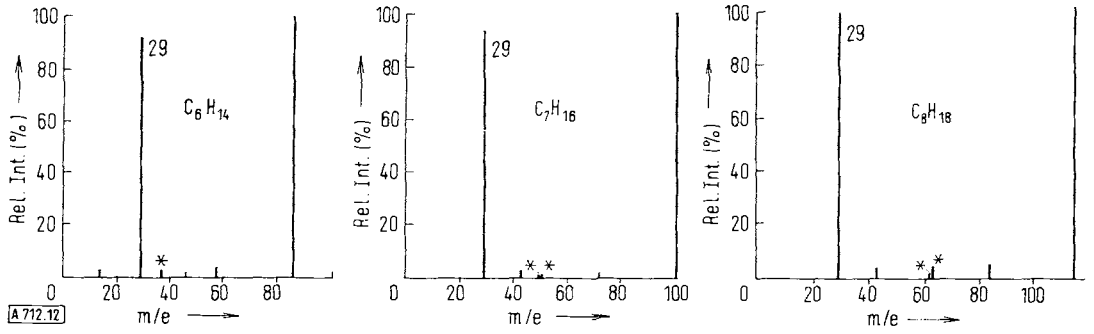


Fig. 12. FI mass spectra of *n*-hexane, *n*-heptane, and *n*-octane with platinum points at high field strengths. Characteristic $C_2H_5^+$ fragment ions (m/e = 29). Metastable ions are denoted by crosses.

the charge to the end of the molecule that is farthest from the point, this tendency being opposed by the decrease in the ionization energy from orbitals nearer the end of the molecule toward orbitals nearer the center of the molecule. An energy balance shows that the removal of a $C_2H_5^+$ ion from the molecular ion is the most strongly favored process[44]. *Lorquet*[45] obtained the same result by a quantum-mechanical calculation of the charge distribution in extended *n*-alkane ions in a high electric field.

Linear primary amines are characterized by the removal of $CH_2NH_2^+$ fragments (m/e = 30). The pronounced unsymmetrical broadening of the lines[46], as shown in Figure 13, is typical of these fragments.

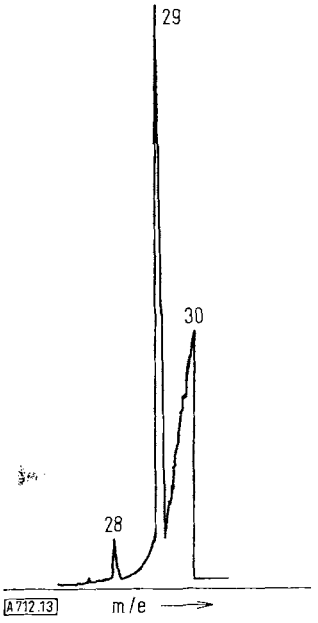
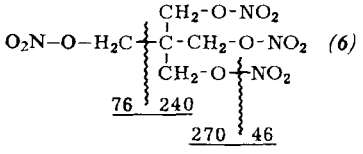


Fig. 13. Section of the FI mass spectrum of 1-pentylamine. Typical broadening of the $CH_2NH_2^+$ mass line (m/e = 30).

Other homologous series of organic compounds have other characteristic fragment lines. Thus primary alcohols[47] are characterized by CH_2OH^+ ions (m/e = 31), and 1-olefins[48] by $CH_2{=}CH_2{-}CH_2^+$ ions (m/e = 41).

Some examples will now be given of cases in which the absence of molecular ions on EB is accompanied by the absence of some important fragment ions from the higher mass range.



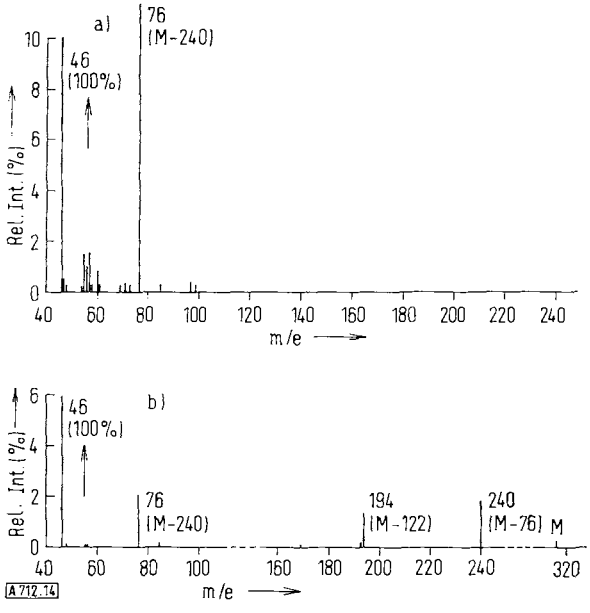


Fig. 14. a) Electron bombardment and b) field ionization mass spectra of pentaerythrityl tetranitrate *(6)* [31].

Figure 14 shows the EB and FI mass spectra of pentaerythrityl tetranitrate *(6)*, an extremely unstable compound used for the ignition of solid rocket fuels and explosives (after *C. Brunnée*[31]). No recognizable fragments are found above m/e = 76 in the EB spectrum, whereas the FI spectrum contains two very characteristic fragment ion lines at m/e = 194 and 240, as well as a weak molecular ion line.

Damico[49] has compared the EB and FI mass spectra of a series of pesticides. Figure 15 shows the spectra of Temik sulfoxide *(7)*. The EB spectrum lacks the molec-

[45] *J. C. Lorquet*, Molecular Physics *9*, 29 (1965).

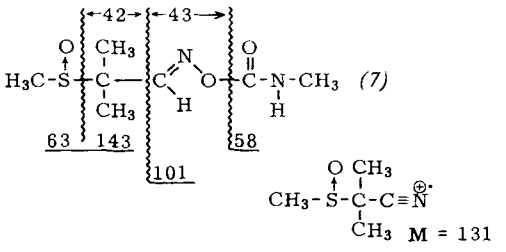
[46] *H. D. Beckey* and *G. Wagner*, Z. Naturforsch. *20a*, 169 (1965).

[47] *H. D. Beckey* and *P. Schulze*, Z. Naturforsch. *21a*, 214 (1966).

[48] *H. D. Beckey* and *P. Schulze*, Z. Naturforsch. *20a*, 1329 (1965).

[49] *J. N. Damico*, *R. P. Barron*, and *J. A. Sphon*, Int. J. Mass Spectrometry Ion Physics *2*, 161 (1969).

ular ion line and the structurally important mass line $m/e = 131$, both of which are present in the FI spectrum. The mass line $m/e = 63$, which is also characteristic, is clearer in the FI spectrum than among the many lines that occur in this mass range in the EB spectrum (for further examples, see [49]).



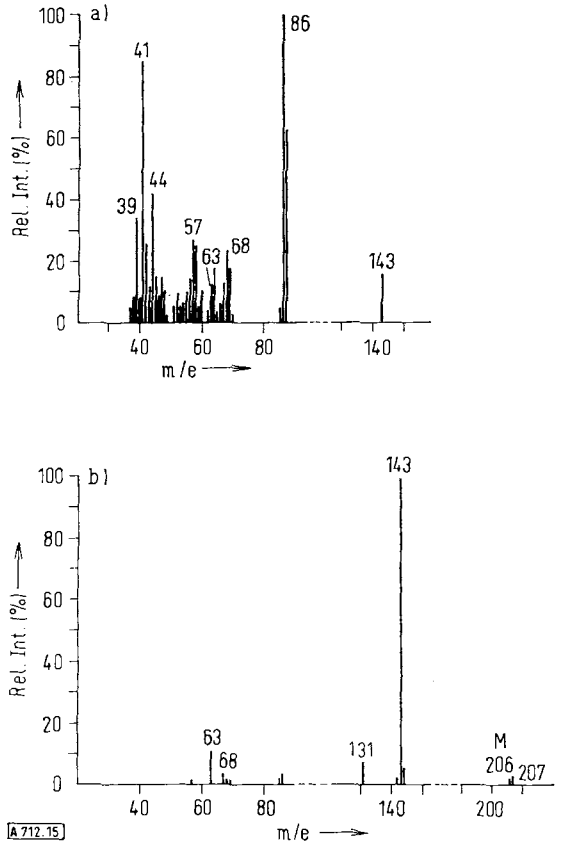


Fig. 15. a) Electron bombardment (70 °C) and b) field ionization (65 °C) mass spectra of Temik sulfoxide *(7)*, $M = 206$ [49].

5. Kinetic Studies with the FI Mass Spectrometer

Questions of the kinetics and the mechanism of the decomposition of organic ions are closely related to the problem of structure analysis. FI mass spectrometry can make new contributions to these problems, which will be briefly discussed here [4].

The most important aspect is the fact that extremely fast decomposition processes can be isolated from the slower processes in the FI mass spectrometer, in contrast with the EB mass spectrometer, which integrates fast and slow reactions over a wide range. Fragment ions that appear at their normal mass numbers (based on the molecular ions) in the FI mass spectrometer must be formed within a time range of 5×10^{-14} to 3×10^{-12} sec. Fragment ions formed later appear either as tails of strongly broadened mass lines or as metastable mass lines. The normal fragment ion mass lines in the EB spectrum, on the other hand, result from decomposition processes occurring in a range of about 5×10^{-14} to 10^{-6} sec after the ionization of the molecule.

The reason for the fact that only extremely rapidly formed fragment ions are detected in the normal mass positions in the FI spectrum is the extremely large potential gradient in front of the FI emitter. For a field of 10^8 V/cm, *i.e.* 1 V/Å, a molecular ion has passed through a potential difference of several volts after traveling a distance of only a few Å. If it then decomposes at this point of lower potential, the fragment ions have a lower kinetic energy than the fragment ions formed at the ionization site. This results in a shift of the mass positions in the spectrum toward lower mass numbers.

Without going into mathematical details [4, 50, 51], it will be shown briefly here how the reaction time Δt of the decomposing ion is found from the observed mass displacement ΔM. The observed ΔM value, together with the fundamental equation for the mass spectrometer, can be used to calculate the potential difference ΔU between the points of ionization and of decomposition. The geometry of the FI emitter and the counter-electrode is used to calculate the potential distribution between these electrodes, and the distance Δx between the points of ionization and of decomposition can be deduced from the ΔU value. The decomposition time Δt is finally found by integration of the equation of motion for the molecular ion. Thus the complete scheme of correlations is

$$\Delta M \rightarrow \Delta U \rightarrow \Delta x \rightarrow \Delta t$$

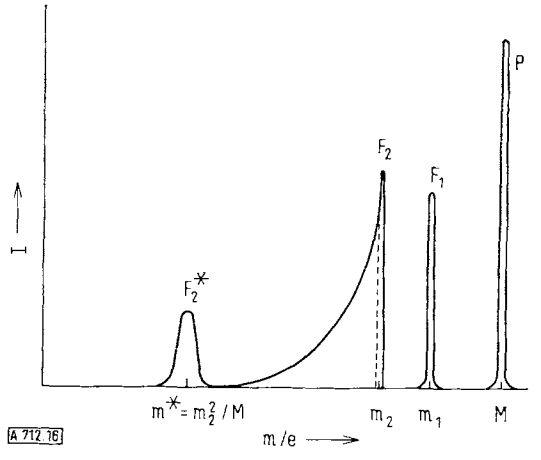


Fig. 16. Schematic representation of the line shapes in FI mass spectra. P = molecular ion line, F_1 = mass line of fragment ions formed on the emitter surface, F_2 = strongly broadened mass line of fragment ions that decompose in the gas phase in the electric field, F_2^* = mass line of metastable ions formed in the field-free space of the mass spectrometer before entry into the magnetic field.

[50] *H. D. Beckey*, Z. Naturforsch. *16a*, 505 (1961).

[51] *H. D. Beckey* and *H. Knöppel*, Z. Naturforsch. *21a*, 1920 (1966).

Figure 16 shows schematically the line shapes for the molecular ions and the various fragment ions in the FI mass spectrometer. The shape of the fragment ions F_1 formed either on the surface of the emitter or in the gas phase within 10^{-13} to 3×10^{-12} sec is as sharp as that of the molecular ions. Strongly broadened fragment ion lines F_2 can be attributed to decomposition processes between 3×10^{-11} and 10^{-8} sec. The "metastable" fragment peak F_2^* contains fragmentations formed within 10^{-8} to 3×10^{-6} sec. As in the EB mass spectrum, these metastable ions occur at an apparent mass number $m^* = m_2^2/M$, where m_2 is the true mass of the fragment and M is the mass of the molecular ion. By evaluation of the strongly broadened mass line as described above and analysis of the decomposition time spectrum of the metastable ions by a retarding potential method [52], it was possible for the first time together with *Tenschert* [4], to follow the mean decomposition times of several organic ions over an extremely wide range of times (3×10^{-11} to 3×10^{-6} sec).

The most important result was the observation that instead of only one or a few discrete rate constants k for these decomposition reactions, there is a whole spectrum of such constants, this spectrum being quasi-continuous to within the accuracy of the measurements. This confirmed one of the fundamental hypotheses of the quasi-equilibrium theory (QET) [53, 54] of mass spectra for large molecules. Similar conclusions were reached by *Hertel*, *Osberghaus*, and *Ottinger* [55–57] on the basis of electron bombardment experiments, though the time range covered in these experiments was not so wide as that covered in the FI experiments described here.

Figure 17 shows the distribution of the mean rate constants as a function of the decomposition time

$$\bar{k}(t) = \frac{1}{N(t)} \cdot \frac{dN}{dt}(t)$$

Possible kinetic applications can be deduced from the fact that it is possible to distinguish between very fast (5×10^{-14} to 3×10^{-12} sec) and slower (3×10^{-12} to 3×10^{-6} sec) decomposition reactions by FI mass spectroscopy.

Rearrangements of organic ions are often associated on the one hand with a low frequency factor and on the other with a low activation energy. If, as in the EB mass spectrometer, the ions have sufficient time available (max. 3×10^{-6} sec), the rearrangement process will be very intense because of the low activation energy, and the corresponding "rearrangement lines"

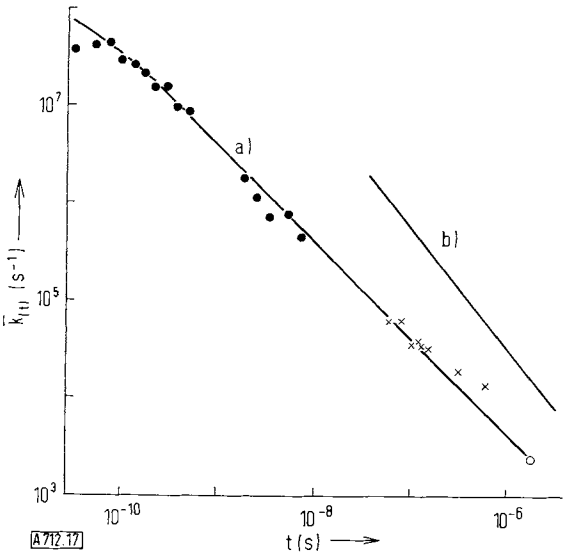


Fig. 17. a) Average rate constants $\bar{k}(t)$ for the decomposition of *n*-heptane ions

$C_7H_{16}^+ \rightarrow C_5H_{11}^+ + C_2H_5$

as a function of time after field ionization. The $\bar{k}(t)$ values were obtained from (●) the strongly broadened fragment-ion line, (×) the mass line produced with a retarding potential, (○) the normal metastable mass line, b) For comparison: $\bar{k}(t)$ values from electron bombardment experiments by *Hertel* and *Ottinger* [56, 57]. (Higher $\bar{k}(t)$ values because of greater energy transfer by 70 eV electrons.)

are often the strongest in the mass spectrum. In field ionization, on the other hand, the molecular ion has a maximum of only about 3×10^{-12} sec available if the rearrangement fragment is to appear in the normal mass position. This time is often insufficient in rearrangement reactions, and the corresponding mass line is then extremely small or completely undetectable. It is of interest for these reasons to compare electron bombardment and field ionization mass spectra of rearrangement reactions. This comparison is carried out by forming the ratio

$$R = \frac{I_{FI}^i / I_{FI}^b}{I_{EB}^i / I_{EB}^b}$$

where the I are the ion intensities and the indices i and b refer to the i-th fragment and to the reference line (the most intense line in the spectrum) respectively. This factor R_r for rearrangements should be very small, whereas the corresponding factor R_d for direct bond rupture should be considerably greater.

Together with *Levsen*, we have shown [4] that the ratio of the smallest R_d factor for a given molecule ($R_{d\,min}$) is always greater than the R_r value for the same molecule in the case of skeletal rearrangements. Figure 18 illustrates this effect for the EB and FI mass spectra of diphenyl ether *(8)*. Even at a very high sensitivity, the FI mass spectrum contains no (M – CO) mass line, whereas the relative intensity of this line in the EB spectrum is 20.3% (see [3]). However, this fragment ion can also be formed in the FI mass spectrometer later in the decomposition. It can then be detected in the mass position of the metastable ion, as is shown in Figure 18.

The mass lines of all skeletal rearrangement processes studied so far were extremely weak in the FI mass

[52] *H. D. Beckey*, *A. Heindrichs*, and *G. Tenschert*, Z. Instrumentenkunde *75*, 195 (1967).

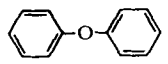
[53] *H. M. Rosenstock*, *M. B. Wallenstein*, *A. L. Wahrhaftig*, and *H. Eyring*, Proc. nat. Acad. Sci. USA *38*, 667 (1952).

[54] *H. M. Rosenstock* and *M. Krauss*, Advances Mass Spectrometry in *F. W. McLafferty*: Mass Spectrometry of Organic Ions. Academic Press, New York 1963, p. 1.

[55] *O. Osberghaus* and *Ch. Ottinger*, Physic. Rev. Letters *16*, 121 (1965).

[56] *Ch. Ottinger*, Z. *Naturforsch. 22a*, 20 (1967).

[57] *I. Hertel* and *Ch. Ottinger*, Z. Naturforsch. *22a*, 1141 (1967).



(8)

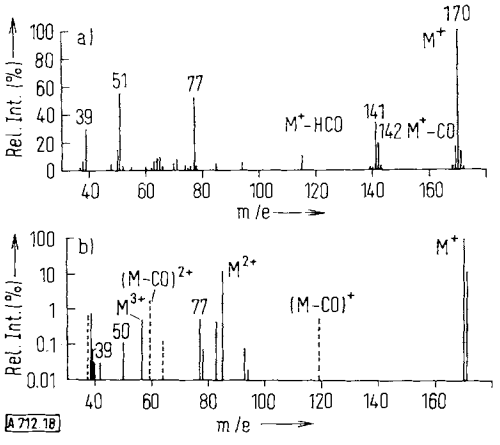


Fig. 18. a) Electron bombardment and b) field ionization mass spectra of diphenyl ether *(8)* (*Levsen* [4]). (Note: Upper intensity scale linear, lower logarithmic.) Metastable mass lines are shown by broken lines in the observed mass position. Temperature of wire 350 °C.

spectra. However, intense lines were found for a number of hydrogen rearrangement processes in the FI spectra [32, 49, 58]. This can be explained in a few cases at the present state of the investigations by assuming that certain states of adsorption favor a rearrangement process already at the surface of the FI emitter. Dissociation of the rearranged molecular ion occurs during field desorption.

In most cases, however, intense H-rearrangement lines do not appear in the FI mass spectrum at the "normal" mass position but are shifted by several tenths of a mass unit towards smaller mass numbers, *i.e.* decomposition occurs after about 10^{-11} sec in the gas phase. This agrees well with the above-mentioned general postulate that the frequency factors for rearrangement reactions, ν_r, are strongly diminished as compared to the frequency factors for direct bond fissions, ν_d, ($\nu_d \simeq 3 \times 10^{13}$ sec^{-1}; $\nu_r \simeq 10^{11}$ sec^{-1} as a result of a rough estimation).

6. Quantitative Analyses with the FI Mass Spectrometer

The electron bombardment mass spectrometer has proved successful over a long period for the quantitative analysis of mixtures of organic compounds. There thus appears to be no need to supplement this method with the field ionization technique for mixtures having relatively few components. The situation is different for mixtures containing a very large number of components (petroleum or gasoline samples with 300–500 components). All the components cannot then be identified by means of the EB mass spectrometer alone, and it is usual to make do with a mass-spectrometric group analysis [59], which gives the relative quantities of *n*-alkanes, *n*-alkenes, cycloalkanes, cycloalkenes, aromatic compounds, *etc.* On the other hand, a complete analysis of such a mixture is possible in principle if all the components are first separated by means of a capillary gas chromatograph and then identified by EB mass spectrometry. In many cases, however, the components are not all separated by gas chromatography. Moreover, when this combination procedure is used, one must be prepared to deal with a large quantity of data.

Frequently, *e.g.* in the characterization of a new fuel, it is unnecessary to identify all 300–500 components, the information required being only slightly more than that provided by a normal group analysis. An important piece of additional information might be *e.g.* the molecular weight distribution within each group. This distribution can be found with the FI mass spectrometer by a method much simpler than the EB method. However, the isomer distribution at a given mass number cannot be deduced from the FI mass spectrum. A combination of molecular weight analysis by the FI method and an EB group analysis is then recommended.

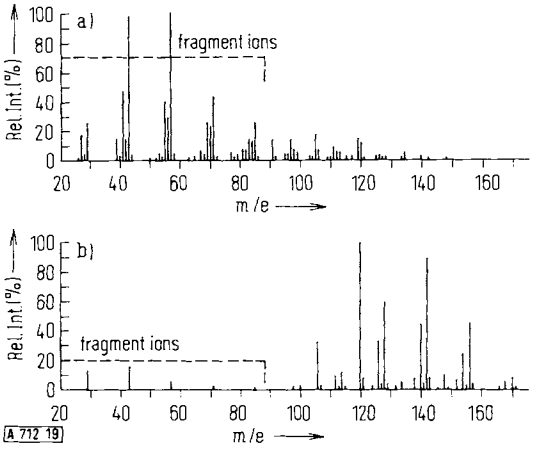


Fig. 19. a) 70 eV electron bombardment and b) field ionization mass spectra of a gasoline sample [62].

Figure 19 illustrates why the determination of the molecular weight distribution is easier with the FI than with the EB mass spectrometer. With electron bombardment, the molecular ion intensities of some components are extremely small, and they may be masked by fragmentations from molecules with higher mass numbers. Both of these difficulties are avoided in the FI method.

For quantitative determination of the molecular weight distribution in a mixture, it is necessary to find the sensitivity coefficients for the various mass groups with the aid of a calibration mixture. The measured heights of the mass lines in the calibration spectrum divided by the quantities of the corresponding substances introduced give directly the average sensitivity coefficients for the substances having the same mass. It is essential for this very simple method that the compositions of the calibration mixture and of the unknown sample should be very similar. If this condition is satisfied a very accurate analysis is possible

[58] *P. Schulze, W. J. Richter,* and *A. L. Burlingame,* 17th Annual Conference on Mass Spectrometry, Dallas (1969).

[59] *G. Franke* in *H. Kienitz:* Massenspektrometrie. Verlag Chemie, GmbH., Weinheim 1968, p. 323.

with the FI mass spectrometer, as is shown by Table 2. This table is based on experiments by *Hippe* [60], in which two synthetic gasoline samples [*] were used, one as the calibration mixture and the other as the sample for analysis.

Table 2. FI mass-spectrometric analysis of a synthetic gasoline mixture.

Mass	Quantity introduced (wt-%)	Analytical results Dec. 16 (wt-%)	Jan. 4 (wt-%)	Mean deviation (wt-%)
68	0.49	0.45	0.48	−0.02
70	3.23	3.04	3.15	−0.13
72	9.38	8.57	9.19	−0.50
78	19.01	18.28	17.88	−0.92
82	0.11	0.08	0.14	0
84	3.01	3.03	3.08	+0.05
86	6.46	6.39	6.70	+0.18
92	13.41	13.90	13.17	+0.12
96	0.11	0.11	0.09	−0.01
98	1.63	1.70	1.65	+0.05
100	5.59	5.95	5.98	+0.38
106	18.24	18.95	18.02	+0.24
112	2.32	2.35	2.31	+0.01
114	5.91	5.93	5.97	+0.04
120	7.68	7.35	7.83	−0.09
126	0.20	0.21	0.20	0
128	1.38	2.02	2.02	+0.64
134	1.39	1.29	1.56	+0.03
142	0.10	0.09	0.11	−0.01
148	0.35	0.31	0.46	+0.03

The composition of a new sample will normally be known only roughly, so that the condition of close similarity of the compositions of the sample and of the calibration mixture will not be satisfied. *Hippe* [60] was able to show that the sensitivity coefficients of substances in the C_1 to C_{10} range in field ionization depend on many more parameters and vary to a much greater degree with these parameters than in electron bombardment ionization. For example, the sensitivity factors of the FI mass lines are strongly dependent, *inter alia*, on the composition of the mixture, the chemical properties of the components, the order in which the components are introduced, and the state of the FI emitter surfaces coated with chemisorbed material. These effects are due to the fact that the molecules are field ionized predominantly in the adsorbed state, in which they are exposed to various interactions with the adsorbent and the neighboring molecules.

For more accurate analyses, therefore, it is necessary to use an iterative process in which *e.g.* all the components are initially present in equal proportions in the calibration mixture. After the result of the analysis has been found to a first approximation, a second calibration mixture having a composition closer to the result of the first analysis is prepared. The calibration mixture need not contain all the components that are present in the sample, but only a few components for each mass number that occurs in the sample. Representative calibration components must be selected for each mass group. The gain resulting from the simplicity of the FI mass spectra is partly offset by the need for the iterative process.

The complications just described obviously do not arise if the sensitivity coefficients of all the components of a mixture are approximately equal. These conditions are apparently satisfied in high-boiling alkane fractions. Firstly, the differences in the probability of field ionization decrease with increasing molecular weight, and secondly these samples do not contain olefins, which strongly influence the sensitivity coefficients.

Mead [61] has used an FI mass spectrometer for the study of alkane fractions in the boiling range 300 to 500 °C. Repeated recording of the spectra showed variations of about ±5% in the relative heights of the mass lines. Each spectrum was therefore recorded three or four times, and the results were averaged. Calibration data were obtained for the principal types of components (*n*-alkanes, iso- and cycloalkanes, and alkylbenzenes). It was found that the sensitivity coefficients of the other groups of compounds are also only within the limits of the measuring error in the C_{20} to C_{40} range. It is therefore possible, for each of the four important groups of compounds (*n*-alkanes, iso- and cycloalkanes, alkylbenzenes) to give an average sensitivity coefficient that is constant in the C_{20}–C_{40} range.

The ratio of *n*-alkanes to isoalkanes naturally cannot be deduced directly from the FI mass spectra, since they give the same molecular ion lines. As was mentioned above, however, this ratio can be found either by the usual electron bombardment group analysis with the aid of characteristic fragment ion lines, or more simply by the molecular sieve technique. In the latter case, an FI mass spectrum is recorded before and after the treatment with the molecular sieve. The *n*-alkanes are adsorbed practically quantitatively by the molecular sieve, so that their relative quantity is given by the difference between the two spectra.

Table 3. Analysis of ASTM Wax No. I.
(EB analysis: average of the results from eight laboratories.)

		EB (wt-%)	FI (wt-%)
n-Alkanes	C_nH_{2n+2}	70.0	65.7 [a]
Isoalkanes	C_nH_{2n+2}	12.8	16.4
Monocycloalkanes	C_nH_{2n}	14.2	14.9
Bicycloalkanes	C_nH_{2n-2}	2.1	1.8
Tricycloalkanes	C_nH_{2n-4}	...	0.3
Alkylbenzenes	C_nH_{2n-6}	0.8	0.7
Indans- and tetralins	C_nH_{2n-8}	0.09	0.2

[a] Absorption by molecular sieve.

Table 3 shows the result of an FI analysis of this type carried out by *Mead* [61], together with the average analytical values obtained in eight laboratories with EB mass spectrometers. The agreement of the results is very good, except in the ratio of the *n*-alkanes to isoalkanes. However, these discrepancies may not be the fault of the field ionization method.

[60] *K. G. Hippe* and *H. D. Beckey*, unpublished results.

[*] The samples were supplied by Dr. *R. D. Behling*, BP-Hamburg.

[61] *W. L. Mead*, Analytic. Chem. *40*, 743 (1968).

[62] *H. D. Beckey* and *G. Wagner*, Z. analyt. Chem. *197*, 58 (1963).

The detection of tricycloalkanes appears to be more definite with FI than with EB, since no data were reported in the latter case. The same is true of the indans and tetralins, whose presence in the sample was reported by some of the laboratories using EB mass spectrometers and not by others. The molecular weight distribution for the groups is given directly by the FI mass spectra.

To summarize, therefore, the analysis of high-boiling hydrocarbon mixtures containing many components by means of an FI mass spectrometer is much simpler if the sensitivity coefficients of the groups of substances are constant. Long calculations are avoided in the evaluation of the spectra, and it is unnecessary to solve extremely large matrix systems or to make allowance for the masking of fragments of heavier components by the lighter components. The detection of trace components in a mixture is more definite with FI than with EB; this observation is not confined to the high-boiling hydrocarbon mixtures discussed here.

Finally, it should be mentioned that *Wanless* [63,64] has constructed "FI metastable maps", which simplify the identification of isomers in hydrocarbon mixtures. On field ionization of apolar compounds, metastable fragments are formed almost exclusively from the molecular ions, and not from primary fragment ions. Accurate measurement of the apparent mass m^* of the metastable fragments ($m^* = m^2/M$, m = true mass of the fragment, M = mass of the molecular ion) allows the definite assignment of the metastable ions to the corresponding molecular ions with the aid of the tables (FI metastable maps). Isomers having the same mass number differ in the abundance distribution of the corresponding metastable ions. Thus a simple correlation is obtained between the structure of the compounds and the metastable ions, without the FI spectrum of mixtures being overloaded with fragment ions that can appear at the same mass number on electron bombardment despite the fact that they are formed from compounds having different molecular weights.

We are grateful to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and Union Rheinische Braunkohlenkraftstoffe for their support of our work in this field.

Received: April 22, 1969 [A 712 IE]
German version: Angew. Chem. *81*, 662 (1969)
Translated by Express Translation Service, London

[63] *G. G. Wanless* and *G. A. Glock jr.*, Analytic. Chem. *39*, 2 (1967).

[64] *G. G. Wanless*, Advances Spectroscopy Fuels Related Materials, in press.

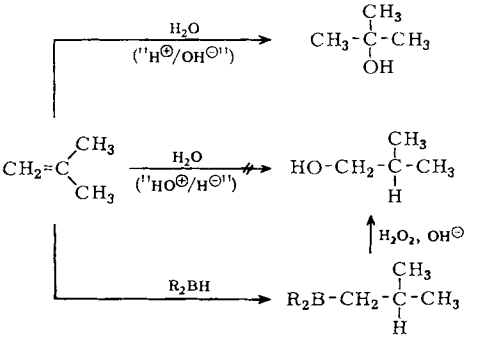
Methods and Possibilities of Nucleophilic Acylation[1]

By D. Seebach[*]

Nucleophilic acylation is the attachment of an $R-\overset{\ominus}{C}=O$ group to an electrophilic center. A brief discussion of the advantages offered by acylations of this type in syntheses is followed by a description of the direct methods (reactions with acylmetal compounds) and the methods proceeding via "masked" acyl anions. The latter methods are based on the use of either metalated vinyl ether derivatives or carbanions derived from acetals. Organyllithiums of sulfur-stabilized carbanions are important reagents of this type.

1. Introduction

The synthetic methods of organic chemistry have always been greatly enriched by the direct or indirect "reversal" of the mode of reaction of a reagent. Thus when water is added to unsymmetrically substituted double bonds, the OH group in the product is always attached to the carbon atom carrying the greater number of alkyl substituents (*Markownikoff*'s rule). A general method allowing the reverse mode of addition would require $HO^{\oplus}$ as an electrophile, the intermediate resulting from the primary attack by this species then being "neutralized" by an $H^{\ominus}$. This is not



Scheme 1.

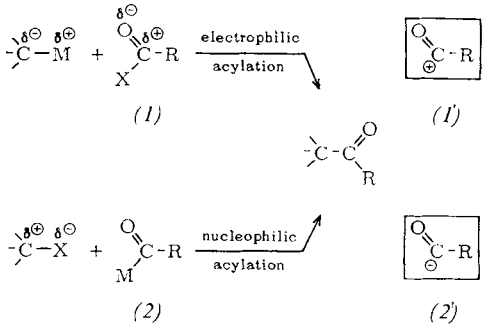
[*] Priv.-Doz. Dr. D. Seebach
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75 Karlsruhe, Richard-Willstätter-Allee (Germany)

[1] A separate review of the dithiane method of nucleophilic acylation has already been published [84].

possible directly, but it can be achieved indirectly, according to *H. C. Brown* [2], by hydroboration.

In this reaction, if one considers only the starting materials and the final products, the mode of reaction of water is reversed. This may also be regarded as "symmetrization" [3] of the reactivity (Scheme 1).

The present article is concerned with reversal of the mode of reaction of the carbonyl carbon atom. In reactions of conventional acylating agents *(1)*, X = halogen, OR, NR_2, *etc.* with carbanions [4], the

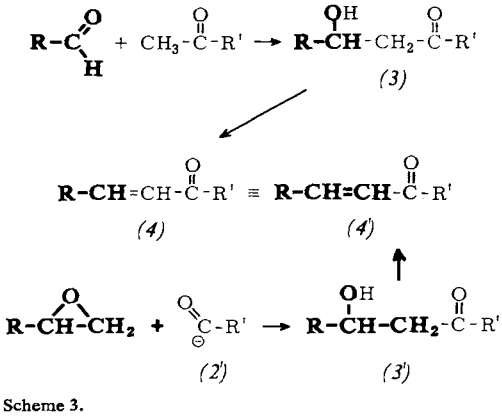


(1) *(1')* *(2)* *(2')*

Scheme 2. M = metal.

acylating component used is formally (though not usually as a "true" intermediate) an acyl cation *(1')*, *i.e.* an electrophile. A nucleophilic acylation should then logically be the addition of an acyl anion *(2')* to a positively polarized C atom. The conventional acylating agents *(1)* are electrophiles, whereas a nucleophilic acylating agent *(2)* appears, at first sight at least, to be an impossibility. Acylating agents of both types should yield identical products [we cannot expect to be able to prepare novel carbonyl compounds with the aid of *(2)*], but the starting materials used may be entirely different (Scheme 2). Instead of a metal derivative having a negatively polarized C atom, a halide with a positively polarized C atom is used. The possibility of using different starting materials is illustrated in Scheme 3 for the preparation of an α,β-unsaturated ketone.

The aldol *(3)* can be prepared by the methods of classical carbonyl chemistry from an aldehyde and a



(3) *(4)* *(4')* *(2')* *(3')*

Scheme 3.

[2] *H. C. Brown*: Hydroboration. Benjamin, New York 1962.

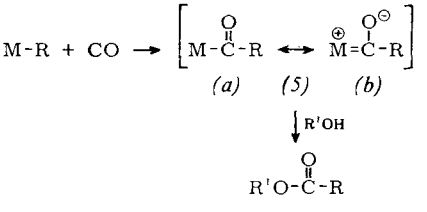
[3] *E. J. Corey*, Pure appl. Chem. *14*, 19 (1967).

[4] Apart from Si- and Ge-acylation, the present article will be concerned only with C-acylation.

methyl ketone; we should be able to obtain the same aldol *(3')* from an epoxide by means of a nucleophilic acylating agent. Elimination of water leads to the identical α-β unsaturated ketones *(4)* and *(4')*. Since the epoxide is readily formed from the olefin, the formation of *(4')* corresponds in its final effect to the replacement of one of the hydrogen atoms on the less substituted C atom of the olefin by an acyl group. One starting compound is often predetermined in a synthesis, so the possibility of varying the building units ("synthons" [3]) can be of great value.

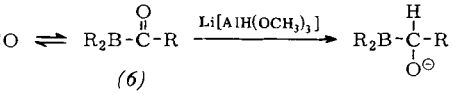
2. "Direct" Acylmetal Compounds *(2)*

The oldest known type of acylmetal compound is obtained by insertion of CO into metal-carbon bonds in which the metal is a transition metal of the group 6 to 8 triads [5]. Like the boryl ketones *(6)* obtained *e.g.* from boranes and carbon monoxide [6] or the silyl and germanyl ketones mentioned below, the acyl derivatives *(5)* which appear from the IR frequency to involve a contribution due to limiting structures *(5b)*, are generally not nucleophilic acylating agents. The transition metal compounds *(5)* react with alcohols



(a) *(5)* *(b)*

to form esters, and the boryl ketones *(6)* react with complex hydride to give alkoxides; the usual electrophilicity of the carbonyl carbon atom is thus evident in both types of compound. Nucleophilic acylations have, however, been observed with ionic compounds of the type *(5)* in which the acyl group is contained in an anion. Thus the reaction of tetracarbonylnickel with aryllithiums [7a,8a] leads to complex salts *(7)*



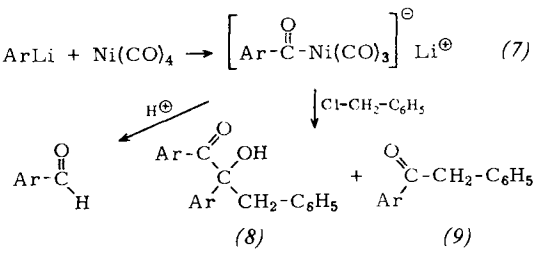
(6)

[5] *J. P. Candlin, K. A. Taylor*, and *D. T. Thompson*: Reactions of Transition-Metal Complexes. Elsevier, Amsterdam 1968, pp. 119 to 134; *J. Tsuji*, Accounts chem. Res. *2*, 144 (1969); cf. *T. Yukawa* and *S. Tsutsumi*, J. org. Chemistry *34*, 738 (1969).

[6] *H. C. Brown*, Accounts chem. Res. *2*, 65 (1969).

[7] a) *M. Ryang, S. Kwang-Myeong, Y. Sawa*, and *S. Tsutsumi*, J. organometallic Chem. *5*, 305 (1966); *Y. Sawa, I. Hishimoto, M. Ryang*, and *S. Tsutsumi*, J. org. Chemistry *33*, 2159 (1968) and other literature cited therein; b) *E. J. Corey* and *L. S. Hegedus*, J. Amer. chem. Soc., in press; c) *91*, 1233 (1969).

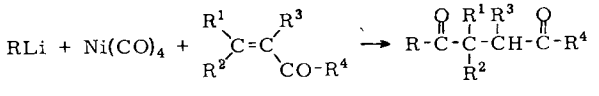
[8] a) Cf. Reaction of phenyllithium with hexacarbonyltungsen to give lithium benzoylpentacarbonyltungstate(0), *E. O. Fischer* and *A. Maasböl*, Angew. Chem. *76*, 645 (1964); Angew. Chem. internat. Edit. *3*, 580 (1964); Chem. Ber. *100*, 2445 (1967); b) *M. Schlosser*, Angew. Chem. *76*, 124 (1964); Angew. Chem. internat. Edit. *3*, 287 (1964) and literature cited therein; c) cf. also, Hg-derivatives: *D. Seyferth* and *R. J. Spohn*, J. Amer. chem. Soc. *91*, 3037 (1969).



(8) (9)

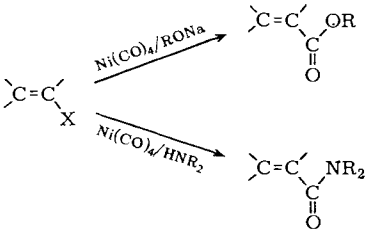
which give aldehydes on treatment with acid and react with benzyl chloride to form the α-hydroxy ketone *(8)* together with a little ketone *(9)*. The ketone *(9)* is the aroylation product of benzyl chloride, and the hydroxy ketone is probably the product of the nucleophilic acylation of the ketone *(9)*.

A useful application of reagents of this type was found by *Corey* and *Hegedus* [7b]. The reagents analogous to *(7)* that are formed in the reaction of methyl-, *n*-butyl-, or phenyllithium with tetracarbonylnickel add on in high yields to α,β-unsaturated carbonyl compounds in the 1,4-position, *i.e.* after the manner of a Michael addition; after hydrolysis, the 1,4-dioxo compounds *(10)* are isolated.



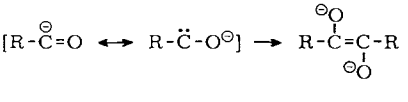
(10)

The alkoxycarbonylations and carbamoylations of vinyl halides with tetracarbonylnickel and alkoxides and amines [7c] are undoubtedly also mechanistically related.

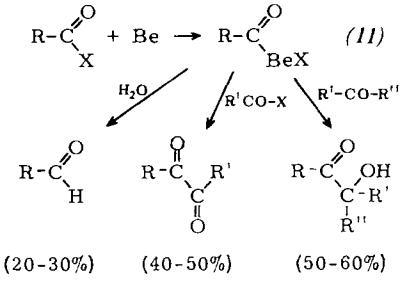


A benzoyl anion intermediate can possibly also be postulated in the reaction of phenyllithium, phenylsodium, or phenylmagnesium bromide with carbon monoxide [8b] to explain the formation of the products (benzhydryl phenyl ketone, benzoin, benzophenone, triphenylmethanol). The formation of benzoin leads to the conclusion that organometallic acylalkali metal compounds, the anions of which are carbenes in one of their limiting resonance structures, can dimerize to give dialkali metal salts of enediols, which are known from the acyloin reaction.

The problem of secondary reactions *e.g. (7)→(9)→(8)* can also arise in all *direct* nucleophilic acylations, since the *free* carbonyl derivatives formed in the reaction with electrophiles are themselves electrophiles.



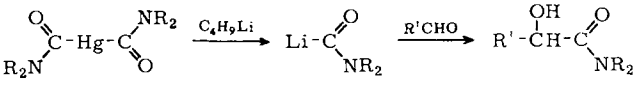
Three years ago, *Lapkin et al.* [9] described the reaction of acyl chlorides, bromides and iodides with beryllium, which, like the formation of Grignard reagents, is exothermic. The resulting ether soluble beryllium derivatives are formulated as *(11)*, and exhibit the expected reactions of acyl anions. Thus hydrolysis leads to aldehydes, acylation to 1,2-diketones, and reaction with ketones to α-hydroxy ketones in the yields indicated. So far as we know, the range of application of these new reagents has not yet been investigated [10].



(11)

(20-30%) (40-50%) (50-60%)

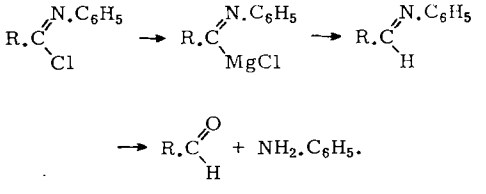
Schöllkopf and *Gerhart* [11] found only recently that treatment of bis(carbamoyl)mercury compounds with two moles of butyllithium yields products *(12)* that can effect nucleophilic carbamoylation; with aldehydes, for example, they form α-hydroxy amides *(13)*.



(12) *(13)*

(11) and *(12)* are the simplest direct nucleophilic acylating agents known at present.

While seeking an aldehyde synthesis more than 60 years ago, *Staudinger* pointed out the possible synthetic value of acylmetal compounds [12]: "If acyl chlorides (bromides) could be converted into the corresponding *Grignard* compounds, this would provide a general method for the reduction of the COOH to the COH group, since the *Grignard* compounds should give aldehydes on cleavage with water:



This process cannot be achieved with acyl chlorides, but a similar reaction takes place with the *imidoyl*

[9] *I. I. Lapkin, G. Y. Anvarova,* and *T. N. Povarnitsyna,* Ž. obšč. Chim. *36*, 1952 (1966); J. gen. Chem. (USSR) (English transl.) *36*, 1945 (1966).

[10] The ease with which *(11)* can be prepared is evidently very strongly dependent on the purity of the metal used (cf. many Grignard reactions). We could not reach these yields with 98.5% beryllium powder; the reaction started only with difficulty.

[11] *U. Schöllkopf* and *F. Gerhart,* Angew. Chem. *79*, 819, 990 (1967); Angew. Chem. internat. Edit. *6*, 805, 970 (1967).

[12] *H. Staudinger,* Ber. dtsch. chem. Ges. *41*, 2217 (1908).

chlorides, since the *chlorine atom* in this case reacts with magnesium [13].

In this little-cited [14] article, *Staudinger* reported that *e.g. N*-phenylbenzimidoyl chloride reacts exothermally with magnesium in ether [15], and that benzylideneanilide can be isolated after hydrolysis; the latter can be readily converted into benzaldehyde. The Grignard compound of the imidoyl chloride would be a carbonyl analog of *(11)* and *(12)* [15].

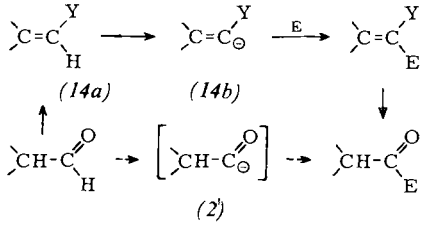
3. Possibilities of Indirect Nucleophilic Acylation

Carbanions (or more precisely organometallic compounds) of such a type that their products can be converted into carbonyl compounds by *hydrolysis*, will be referred to in this discussion as "masked" nucleophilic acylating agents. This requires removal of the hydrogen atom from the carbonyl carbon of an aldehyde, *i.e.* conversion of the aldehyde into its conjugate base.

This should be possible by two general methods.

3.1. Metalated Enol Derivatives

The aldehyde is converted into an enol derivative *(14a)*, which can be metalated to form *(14b)*. *(14b)* is a masked acyl anion, since reaction with an electrophile followed by hydrolysis converts it into a ketone, in which the hydrogen of the aldehyde is electrophilically substituted (dotted arrows). This method is



(14a) *(14b)* *(2)*

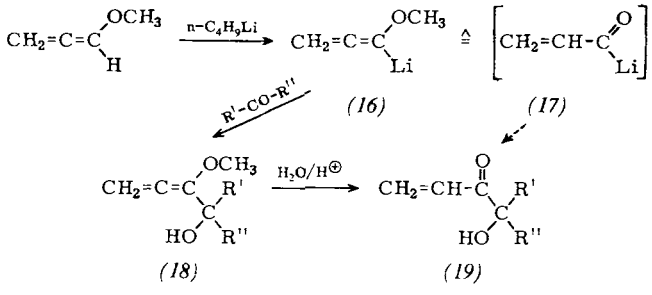
E = electrophile

of limited applicability, since the aldehyde must have at least *one* α-hydrogen atom; for example, nucleophilic benzoylation is not possible by this method because aryl aldehydes cannot be used. The metalation of *(14a)* is favored by anion-stabilizing groups Y. Oxygen rather destabilizes (see below) an α-carbanion, and only one derivative of an α-alkoxy carbanion has been preparatively obtained so far (CH_3-O-CH_2-Li [16]). Though sp^2-bound hydrogen is more acidic than sp^3-bound, enol ethers *(14a)*, Y = OR, can be metalated as indicated above only under very forcing conditions (amylsodium [17a], *tert*-butyllithium / *N,N,N',N'*-tetramethylethylenediamine [17b]). Furan like thiophene (see below), is doubly metalated by amylsodium [to give *(15a)*] [18a]; *(15a)* is the masked succinyl dianion *(15b)*.



(15a) *(15b)*

The ease of metalation of alkyl allenyl ethers [18b] (readily obtainable from propargyl ethers) is particularly interesting; the lithium derivative *(16)* is obtained under "standard conditions" (ether/tetrahydrofuran, −20 °C).



(16) *(17)* *(18)* *(19)*

Deuterolysis, alkylation, hydroxyalkylation, and thiolation lead to the expected products. The product *(18)* obtained by addition to a carbonyl compound is hydrolyzed to the hydroxy ketone *(19)* under very mild conditions (0 to 5 °C, 1 hour); the structure of *(19)* shows that *(16)* is a masked acyllithium derivative of acrolein [*(17)*] (see dotted arrow). *(16)* is the best of the known preparatively usable acylating agents, in that the "demasking" of the products [*e.g. (18)→(19)*] takes place under the mildest conditions. Replacement of the oxygen in enol ethers by sulfur [*(14a)*, *(14b)*, Y = SR] should lead to considerable stabilization of the vinyl anion.

There is no longer any doubt about the stabilizing effect of sulfur, even in the dicoordinate state, on adjacent anionic centers. On metalation of anisole and thioanisole with butyllithium, *Gilman* and *Webb* [19a] found that anisole exchanges an sp^2-bound ring proton α to the oxygen [→*(20)*], whereas thioanisole exchanges an sp^3-bound proton on the methyl group [→*(21)*].

[13] a) Recent attempts to prepare "acyl Grignard compounds" have also been unsuccessful (*A. Eschenmoser*, personal communication); b) reaction of benzoyl chloride with naphthalene-sodium followed by hydrolysis yields benzoin, the formation of which was explained as involving the intermediate formation of benzoylsodium [*W. Schlenk* and *E. Bergmann*, Liebigs Ann. Chem. *463*, 19 (1928)]; the reaction could, however, also proceed by a free-radical mechanism (see ketyls and the acyloin reaction).

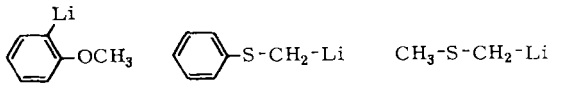
[14] *F. Runge*: Organometallverbindungen. Wissenschaftliche Verlagsgesellschaft, Stuttgart 1944, p. 490.

[15] No Mg-derivative of the imidoyl chloride is formed under the conditions used by *Staudinger* (ether/ethylacetate): on hydrolysis of the reaction product with D_2O we obtained exclusively non-deuterated (according to the ^{1}H-NMR spectrum) benzaldehyde (yield as given in [12]). On varying the reaction conditions (ether, THF; 20–65 °C) we could not detect more than 2% (theoretical) of aldehyde according to the given procedure in the absence of ethyl acetate.

[16] *U. Schöllkopf* and *H. Küppers*, Tetrahedron Letters *1964*, 1503.

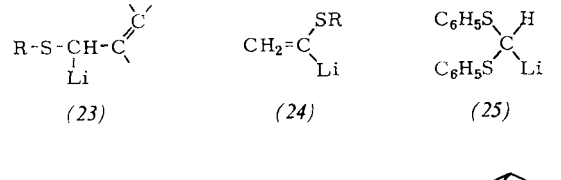
[17] a) *R. Paul* and *S. Tchelitcheff*, C.R. hebd. Séances Acad. Sci. *235*, 1226 (1952); Bull. Soc. chim. France, Documentation *19*, 808 (1952); b) *U. Schöllkopf*, private communication, April 24, 1969.

[18] a) *A. A. Morton* and *C. E. Calff*, J. Amer. chem. Soc. *76*, 4935 (1954); b) *S. Hoff*, *L. Brandsma*, and *J. F. Arens*, Recueil Trav. chim. Pays-Bas *87*, 916, 1179 (1968).

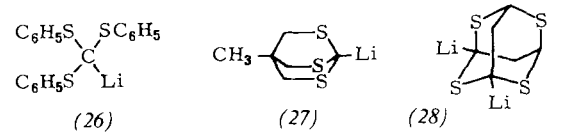


(20) (21) (22)

Amine-activated[21] *n*-butyllithium is necessary for the quantitative production of *(21)*[19b,c] and *(22)*[20] from the corresponding CH compounds, while the derivatives *(23)* of allyl thioethers[22,23], *(24)* of vinyl thioethers[22], *(25)* of thioacetals[19b,24], and *(26)* of orthotrithioformic esters[24–27] can be prepared with butyllithium in tetrahydrofuran. Since *(26)* is formed from tris(phenylthio)methane with tritylithium[26a], the pK_A value of this sulfur compound must be at least two orders of magnitude lower than that of triphenylmethane (pK_A value 28–32, depending on the scale[28]).



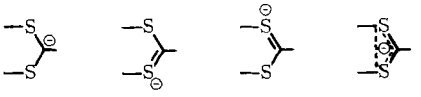
(23) (24) (25)



(26) (27) (28)

It is generally assumed that the stabilization of these anions results from overlap of the "anion orbital" with d shells of the sulfur[28–38]. This picture of d-orbital overlap is possibly too primitive[39], but it is certainly very useful. The looseness of the stereoelectronic requirements for stabilization can be seen from a comparison of the Li derivatives *(21)*–*(28)*. The central C atom in the anions of *(21)*–*(23)*, *(25)*, and *(26)* may be sp^2-hybridized, and p-d overlap then occurs, in *(24)* the $C^{\ominus}$ atom could be sp-hybridized (p-d overlap) or sp^2-hybridized (sp^2-d overlap) while in the anions of *(27)*[26a] and *(28)*[30c,41] the anionic C atom cannot be forced into coplanarity with the neighboring sulfur atoms. so that sp^3-d overlap should occur [cf. the trisulfone derived from *(27)*[42]]; the stabilization of α-sulfonyl carbanions may occur without the participation of d shells[43]. In the undissociated Li compounds *(21)*–*(28)* with the exception of *(24)*, stabilization is possible only by sp^3-d overlap[30c]. The metal atom and the medium used are of decisive importance in stability considerations.

To explain the results of D/H and T/H exchange experiments with thioacetals[33a] and orthotrithioformic esters[33] (see also Table 1), it was assumed[33a] that not only the identical limiting structures *(b)* and *(c)* (which are also decisive for monothiocarbanions), but also delocalization by "1,3-overlap" of the d orbitals of two or three sulfur atoms is involved as indicated in *(d)* for a dithiocarbanion. Dicoordinate selenium, the d shells of which have a higher energy level and should be more diffuse[38] than those of sulfur, also stabilizes carbanions[26d].



(a) (b) (c) (d)

Similar conclusions were drawn from the UV spectra[30c,33a,34,44,45] of thioacetals, where zwitterionic[44] or biradical[33a] excited states with delocalization (d) are assumed. Acceptor properties have also been ascribed to sulfur in the stabilization

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[19] a) *H. Gilman* and *F. J. Webb*, J. Amer. chem. Soc. *62*, 987 (1940); *71*, 4062 (1949); b) *E. J. Corey* and *D. Seebach*, J. org. Chemistry *31*, 4097 (1966); c) see however: *D. A. Shirley* and *B. J. Reeves*, J. organometallic Chem. *16*, 1 (1969).

[20] *D. J. Peterson*, J. org. Chemistry *32*, 1717 (1967).

[21] *G. G. Eberhardt*, Organometallic Chem. Rev. *1*, 491 (1966); *G. G. Eberhardt* and *W. A. Butte*, J. org. Chemistry *29*, 2928 (1964).

[22] *E. J. Corey* and *B. W. Erickson*, unpublished results, 1967.

[23] *J. F. Biellmann* and *J. B. Ducep*, Tetrahedron Letters *1968*, 5629; *J. F. Biellmann*, private communication (May 16, 1969).

[24] *J. F. Arens*, *M. Fröling*, and *A. Fröling*, Recueil. Trav. chim. Pays-Bas *78*, 663 (1959); *A. Fröling* and *J. F. Arens*, *ibid. 81*, 1009 (1962).

[25] *J. Hine*, *R. P. Bayer*, and *G. G. Hammer*, J. Amer. chem. Soc. *84*, 1751 (1962).

[26] a) *D. Seebach*, Angew. Chem. *79*, 468 (1967); Angew. Chem. internat. Edit. *6*, 442 (1967); b) *D. Seebach*, Angew. Chem. *79*, 469 (1967); Angew. Chem. internat. Edit. *6*, 443 (1967); c) *D. Seebach* and *A. K. Beck*, J. Amer. chem. Soc. *91*, 1540 (1969); d) *D. Seebach* and *N. Peleties*, Angew. Chem. *81*, 465 (1969); Angew. Chem. internat. Edit. *8*, 450 (1969).

[27] *G. A. Wildschut*, *H. J. T. Bos*, *L. Brandsma*, and *J. F. Arens*, Mh. Chem. *98*, 1043 (1967).

[28] *D. J. Cram*: Fundamentals of Carbanion Chemistry. Academic Press, New York 1965.

[29] *D. S. Tarbell* and *M. A. MacCall*, J. Amer. chem. Soc. *74*, 48 (1952).

[30] a) *G. Cilento*, Chem. Reviews *60*, 147 (1960); b) *W. G. Salmond*, Quart. Rev. *22*, 253 (1968); c) *D. L. Coffen*, Rec. chem. Progr., in press.

[31] *A. B. Burg* in *N. Kharash*: Organic Sulfur Compounds. Pergamon Press, Oxford 1961, Vol. 1, p. 30.

[32] *C. C. Price* and *S. Oae*: Sulfur Bonding. Ronald Press, London 1962; see also *C. C. Price*, Chem. Engng. News *42*, No. 48, p. 58 (1964).

[33] a) *S. Oae*, *W. Tagaki*, and *A. Ohno*, Tetrahedron *20*, 417 (1964); b) *L. R. Slaugh* and *E. Bergmann*, J. org. Chemistry *26*, 3158 (1961); c) *R. Breslow* and *E. Mohacsi*, J. Amer. chem. Soc. *85*, 431 (1963).

[34] *H. H. Jaffé* and *M. Orchin*: Theory and Application of UV-Spectroscopy. Wiley, New York 1965, p. 466–507.

[35] *A. W. Johnson*: Ylid Chemistry. Academic Press, New York 1966.

[36] *H. A. Bent* in *N. Kharash*: Organic Sulfur Compounds. Pergamon Press, Oxford 1966, Vol. 2, p. 1.

[37] *R. Gleiter* and *R. Hoffmann*, Tetrahedron *24*, 5899 (1968), and private communication from *R. Hoffmann*.

[38] *D. P. Craig*, *A. Maccoll*, *R. S. Nyholm*, *L. E. Orgel*, and *L. E. Sutton*, J. chem. Soc. (London) *1954*, 332; *D. P. Craig* and *E. A. Magnusson*, *ibid. 1956*, 4895; *D. P. Craig*, Chem. Soc. (London), Special Publication No. 12, 343 (1958); *D. W. Cruickshank*, *B. C. Webster*, and *D. F. Mayers*, J. chem. Physics *40*, 3733 (1964).

[39] See the novel bonding models for hypervalent molecules [*J. I. Musher*, Angew. Chem. *81*, 68 (1969); Angew. Chem. internat. Edit. *8*, 54 (1969)] which no longer involve d shells; for more recent articles on hypervalent sulfur compounds, see *M. P. Cava* and *N. M. Pollack*, J. Amer. chem. Soc. *89*, 3639 (1967); *M. P. Cava*, *N. M. Pollack*, and *D. A. Repella*, *ibid. 89*, 3640 (1967); *R. H. Schlessinger* and *I. S. Ponticello*, *ibid. 89*, 3641 (1967); *M. Polk*, *M. Siskin*, and *C. C. Price*, *ibid. 91*, 1206 (1969); *B. M. Trost*, *R. LaRochelle*, and *R. C. Atkins*, *ibid. 91*, 2175 (1969); *M. P. Cava* and *G. E. M. Husbands*, J. Amer. chem. Soc. *91*, 3952 (1969); *J. M. Hoffman* and *R. H. Schlessinger*, *ibid. 91*, 3953 (1969); the stabilization of anions by sulfur is also "plausible" according to the concept of "soft and hard acids and bases" [40] (SHAB).

[40] *R. G. Pearson*, Science (Washington) *151*, 172 (1966); see also *B. Saville*, Angew. Chem. *79*, 966 (1967); Angew. Chem. internat. Edit. *6*, 928 (1967) and literature cited therein; *R. G. Pearson*, Chem. Engng. News *43*, No. 22, p. 90 (1965).

[41] *K. C. Bank* and *D. L. Coffen*, Chem. Commun. *1969*, 8.

[42] *W. v. E. Doering* and *L. K. Levi*, J. Amer. chem. Soc. *83*, 4100 (1961).

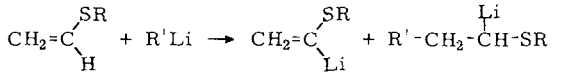
[43] *S. Wolfe*, *A. Rauk*, and *I. G. Csizmadia*, J. Amer. chem. Soc. *91*, 1567 (1969).

[44] *E. A. Fehnel* and *M. Carmack*, J. Amer. chem. Soc. *71*, 84 (1949).

[45] *E. E. Campaigne* and *G. F. Schaefer*, Bol. col. quim. Puerto Rico *9*, 25 (1952).

of sextet species (carbene[26b,26c], nitrene[37]). The mathematical description[30c,37,38,43] of the d orbitals, which are normally unoccupied ("absent"), is therefore difficult, since neither their extent nor their energy is adequately known, and these two quantities are of decisive importance to the result of calculations using the Hückel approximation.

According to this explanation, therefore, anions of the type *(14b)*, Y = SR, *e.g.* as Li derivatives *(24)*, should be much better reagents for nucleophilic acylations than the metalated enol ethers. A careful investigation of *(14)*, Y = SC_6H_5, SC_2H_5, and S-*tert*-C_4H_9, with R'Li = *n*-butyl-, *tert*-butyl- and phenyllithium as metalating agents showed that under optimum conditions only about 80% of the desired H/Li exchange to give *(24)* can be achieved[22]; the competing addition of the Li compounds to form *(29)*[22,46] could not be entirely suppressed. Difficulties of this nature appear to be reduced by the use of butyllithium "activated"

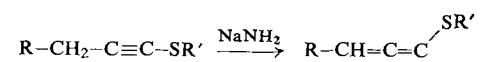


(14a), Y = SR *(24)* *(29)*

with *N,N,N',N'*-tetramethylethylenediamine or triethylenediamine (the basicity of the butyllithium in these complexes is increased at the expense of its nucleophilicity)[47]. The nucleophilicity of the vinyllithium *(24)*, R = C_6H_5, was found to be good; this compound reacts with D_2O, CO_2, CH_3I, aldehydes, and ketones to give the expected products in good yields[22,23]. Thiophene can be metalated to give a disodium compound of the type *(24)*[8b,18a] (see above in connection with furan). The acid hydrolysis[47b–47d] of thioenol ethers (see also Section 3.2.1) to carbonyl compounds proceeds particularly smoothly in the presence of $HgCl_2$[47a,62a].

Anions *(30)* of allenyl thioethers are obtained from alkynyl thioethers and sodamide in liquid ammonia[48,49], *i.e.* under conditions such that even the simple metal derivatives of thioenol ethers should be obtainable, since the nucleophilicity of NH_2 is much less than that of the lithium derivatives used, and the side reaction of addition should be suppressed.

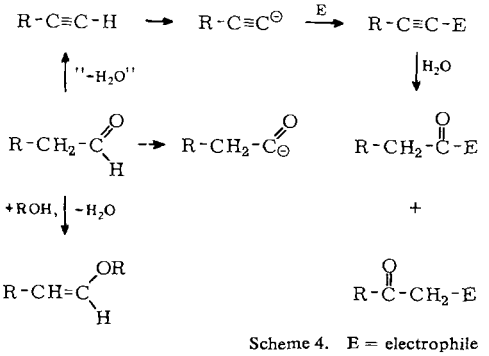
It should in principle also be worth considering the use of compounds containing halogens, such as $CH_2{=}CClLi$[50a]. However, the low stability of such carbenoids and the great resistance of the products to



(30)

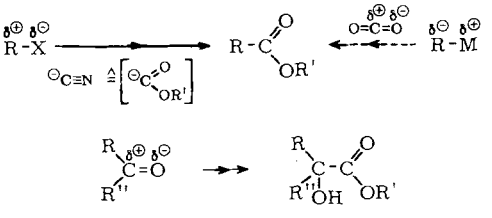
hydrolysis [cf. Cl_3CH with $(CH_3O)_3CH$, $R{-}CCl_2R'$ with $R{-}C(OCH_3)_2{-}R'$, or $CH_2{=}CRCl$ with $CH_2{=}CR(OR)$] have so far prevented their use as nucleophilic acylating agents.

The enol ether-like group of masked acylmetals also includes acetylides. The products of their reaction with electrophiles give carbonyl compounds on *hydrolysis* (addition of water catalyzed by Hg(II) salts). However, the direction of the addition of water cannot usually be controlled[51a]. The reaction yields two isomeric carbonyl compounds, only one of which may be regarded as an acylated electrophile (scheme 4).



Scheme 4. E = electrophile

A well known indirect nucleophilic carboxylating agent, the counterpart of carbon dioxide (dotted arrow in Scheme 5) is the cyanide ion[51b], with the aid of which an ROOC group can be introduced into an



Scheme 5.

electrophilic center. The relatively drastic conditions of the complete acidic or alkaline hydrolysis to the acid stage may be a disadvantage in the synthesis of sensitive compounds (cf. Section 3.2.2).

3.2. Metal Derivatives of Acetals and Related Compounds

3.2.1. Principle and Possible Reagents

In addition to enol derivatives *(14a)*, acetal-like derivatives *(31)* of aldehydes should also be suitable for the production of masked acyl anions *(32)*. The descrip-

[46] *W. E. Parham* and *R. F. Motter*, J. Amer. chem. Soc. *81*, 2146 (1959); *W. E. Parham, M. A. Kalnins*, and *D. R. Theissen*, J. org. Chemistry *27*, 2698 (1962).

[47] a) *J. H. S. Weiland* and *J. F. Arens*, Recueil. Trav. chim. Pays-Bas *79*, 1293 (1960); b) *M. Green*, J. chem. Soc. (London) *1963*, 1324; c) *B. S. Kupin* and *A. A. Petrov*, Ž. org. Chim. *3*, 975 (1967); Chem. Abstr. *67*, 99786 (1967); d) *T. Mukaiyama, S. Fukuyama*, and *T. Kumamoto*, Tetrahedron Letters *1968*, 3787.

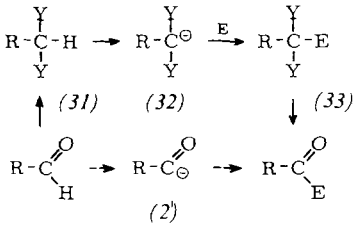
[48] *J. F. Arens et al.*, Recueil Trav. chim. Pays-Bas *80*, 244 (1961); *82*, 1040 (1963); *85*, 580 (1966); *87*, 97 (1968).

[49] *L. Brandsma, C. Jonker*, and *M. H. Berg*, Recueil Trav. chim. Pays-Bas *84*, 560 (1965).

[50] a) *G. Köbrich*, Angew. Chem. *79*, 15 (1967); Angew. Chem. internat. Edit. *6*, 41 (1967) and literature cited therein; b) *P. Blumbergs* and *M. P. LaMontagne*, 157th ACS-Meeting *1969*, ORGN No. 40; c) *G. Köbrich* and *W. Werner*, Tetrahedron Letters *1969*, 2181.

[51] a) *E. g. G. Stork* and *R. Borch*, J. Amer. chem. Soc. *86*, 935 (1964); b) see also the new, extremely reactive aluminum cyanide reagents, *W. Nagata, M. Yoshioka, S. Hari*, and *T. Okumura*, Tetrahedron Letters *1962*, 461; *1966*, 847, 1913

tion "acetal-like" is applied here to derivatives *(31)* and *(33)* that can be converted into the free carbonyl compounds by hydrolysis. Like the vinyl anions *(14b)*,



E = electrophile

anions *(32)* (*i.e.* conjugate bases of aldehydes) should be able to act as acylating agents. They appear less suitable at first sight, since *(32)* is a trisubstituted carbanion, the nucleophilicity of which may be low because of steric hindrance, but whose basicity may be high for the same reason. R could also be a group linked *via* a trisubstituted C atom or an aromatic ring in this case. The restriction on the use of metalated enol ether derivatives (Section 3.1), *i.e.* that the aldehyde must have at least one α-hydrogen atom, is not valid here.

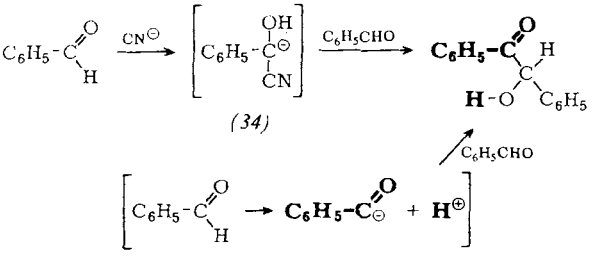
The conversion of an aldehyde *via (31)*, *(32)*, and *(33)* into a ketone (dotted arrows) would, according to the definition in Section 1, be a "reversible symmetrization" of the mode of reaction of the carbonyl group. The electrophilic carbonyl C atom of the aldehyde has become nucleophilic in *(32)*, and after reaction with an electrophile, the electrophilic carbonyl C atom can be restored by hydrolysis of the product *(33)*.

We impose the following requirement for a generally applicable masked nucleophilic acylating agent of the type *(32)*. The groups Y must be such that

1. *(31)* is preparatively readily obtainable.
2. the conversion into the anion *(32)* proceeds easily and quantitatively,
3. the anion is not so stable that it no longer exhibits high reactivity,
4. the carbanionic center is subject to a minimum of hindrance,
5. no carbenoid decomposition [*(32)* → $R-\ddot{C}-Y + Y^{\ominus}$] or other rearrangements occur, and
6. the hydrolysis of the reaction products *(33)* can be carried out under the mildest possible, and also the most specific possible conditions.

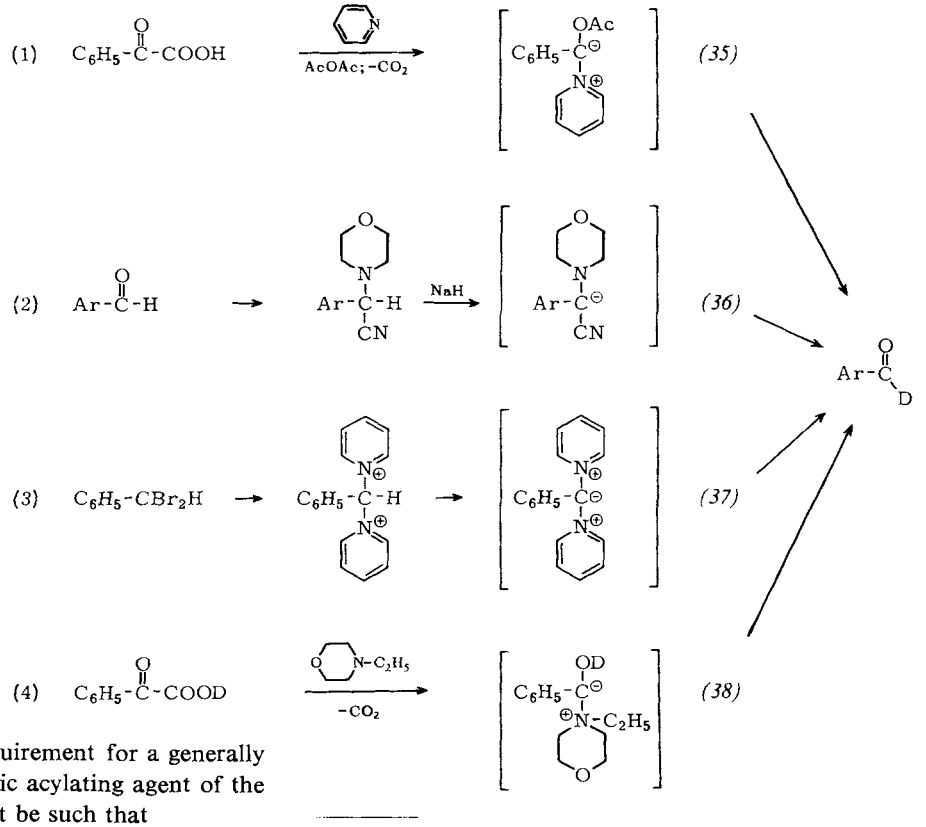
With so many conditions to be satisfied, compromises seem inevitable.

The oldest known reaction involving "masked" acyl anions of the type *(32)* is the preparation of benzoins from aromatic aldehydes [52], as illustrated in Scheme 6



Scheme 6.

for benzaldehyde. The decisive intermediate in this reaction is assumed to be an anion *(34)*, which adds onto an aldehyde molecule. The final product is formally the result of addition of a benzoyl anion and a



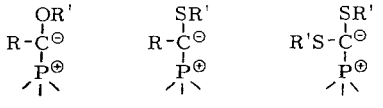
[52] *M. S. Ide* and *J. S. Buck*, Org. Reactions *4*, 269 (1948); cf. also *S. M. McElvain*, *ibid. 4*, 256 (1948).

proton to benzaldehyde; *(34)* is mechanistically equivalent to an acyl anion. The reaction is applicable only to aldehydes having no α-hydrogen atoms (otherwise the aldol reaction competes); attempts to prepare mixed acyloins must be expected to yield mixtures of products. Quantitative production of anions such as *(34)* is not possible.

Several methods for the preparation of deuterated aromatic aldehydes have been published in recent years. Intermediates *(35)–(38)* resembling *(34)* were postulated or prepared in every case [eqs. (1)–(4)].

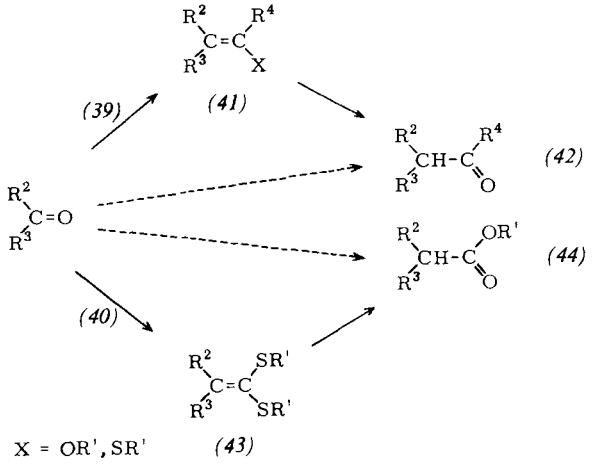
To prove occurrence of these intermediates, they were allowed to react with D_2O, or deuterated starting materials were used; deuterated aldehydes were formed [53–56]. The compounds *(35)–(38)* cannot be used as generally applicable reagents for the introduction of acyl groups, since they are not formed in high concentrations and/or they exhibit strong steric hindrance [for example, *(37)* is of the triarylmethyl type], *i.e.* they do not satisfy the above conditions; even the acylation of $D^{\oplus}$ has so far been preparatively developed for several examples only by the reaction described in eq. (2) [54].

Alkoxy-(alkylthio-) *(39)* and dialkylthiomethylene phosphoranes *(40)* are also nucleophilic acylating or carboxylating



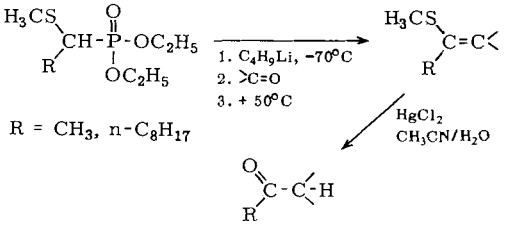
(39a) *(39b)* *(40)*

reagents in a certain sense. Reaction with carbonyl compounds leads in the one case to enol ethers (thioenol ethers), *(41)* [47d,57–59], and in the other case, which has so far been observed only with the sulfur derivatives *(40)*, to ketene thioacetals *(43)* [26b,60–62]. The hydrolysis [47,62a,84] yields the carbonyl compounds *(42)* and *(44)*. In the final effect (dotted arrows), the only respect in which these reactions differ from the nucleophilic acylations is in the absence of the α-hydroxyl group in the final product; the oxygen atom is removed with the phosphorus in the olefination step.



X = OR', SR' *(43)*

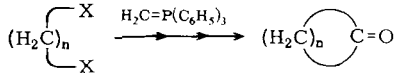
A more recent application of this principle, using phosphonates [62a] is shown in the following Scheme.



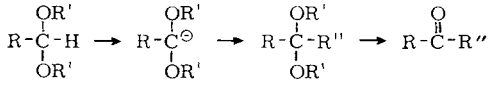
Scheme 7.

If one considers only the overall reaction in Scheme 7 (dotted arrow), the reaction sequence shown here is also a nucleophilic acylation [35].

However, the final product, *i.e.* the free carbonyl compound, is formed by an oxidative process in this case. Cyclanones can be prepared in good yields by this method [63] (cf. below, dithiane method [82,84]).



Since the acetal grouping is readily hydrolyzed, an anion *(45)* would be a welcome masked acylating agent, the products of which would also satisfy the condition that the free carbonyl group should be easily obtainable under mild and specific conditions by hydrolysis. It is well known that acetals are stable in alkaline solution, but can be readily hydrolyzed with acids. As was mentioned in connection with the



(45)

[53] *T. Cohen* and *I. H. Song*, J. Amer. chem. Soc. *87*, 3780 (1965).

[54] *D. J. Bennett*, *G. W. Kirby*, and *V. A. Moss*, Chem. Commun. *1967*, 218.

[55] *R. A. Olofson* and *D. M. Zimmerman*, J. Amer. chem. Soc. *89*, 5057 (1967).

[56] *J. C. Craig* and *L. R. Kray*, J. org. Chemistry *33*, 871 (1968).

[57] *S. G. Levine*, J. Amer. chem. Soc. *80*, 6150 (1958); *G. Wittig* and *E. Knauss*, Angew. Chem. *71*, 127 (1959).

[58] For a summary see [35].

[59] See also halogeno- and dihalogenomethylene phosphoranes, *e.g. A. J. Speziale*, *K. W. Ratts*, and *D. E. Bissing*, Org. Syntheses *45*, 33 (1965), and [35].

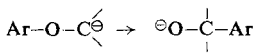
[60] The reaction proceeds only with aldehydes. Triphenylphosphorane: *D. M. Lemal* and *E. H. Bannit*, Tetrahedron Letters *1964*, 245. Trimethoxyphosphorane [61]: *E. J. Corey* and *G. Märkl*, *ibid.* 1967, 3201.

[61] The ylid $(CH_3O)_3P=C(SC_6H_5)_2$ is obtained from $(C_6H_5S)_3SLi$ [26] and trimethyl phosphite, and derivatives *(43)*, $R^3 = H$, $R' = C_6H_5$, can be prepared in this way [62b].

[62] a) *E. J. Corey* and *J. I. Shulman*, unpublished results, 1969; b) *D. Seebach* and *H.-D. Herrmann*, unpublished results.

[63] *A. Monden*, Liebigs Ann. Chem. *603*, 115 (1957); *H. J. Bestmann* and *H. Häberlein*, Z. Naturforsch. *17b*, 787 (1962); *P. T. Keough* and *M. Grayson*, J. org. Chemistry *29*, 631 (1964); *K. V. Scherer* and *R. S. Lunt*, *ibid. 30*, 3215 (1965); *H. J. Bestmann* and *E. Kranz*, Chem. Ber. *102*, 1802 (1969).

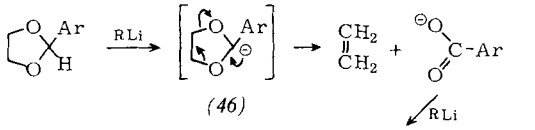
metalated enol ether derivatives, however, α-alkoxy and α-aryloxy carbanions are not generally obtainable; the ether oxygen does not stabilize negative charges, whereas it is an excellent stabilizer for carbonium ions. Aryloxy carbanions can undergo Wittig rearrangement [64]. The only simple alkoxy carbanion derivative



that can be obtained preparatively is methoxymethyllithium, which was mentioned earlier [16]. No dialkoxy carbanions of the type *(45)* have been obtained as yet.

As is known from H-isotope exchange experiments [33] (see also Table 1) and from conductivity measurements [24], the kinetic and thermodynamic acidity [28] of aldehyde acetals is so low that it cannot be measured directly; it has been shown by indirect methods that the kinetic acidity of an α-alkoxy proton (>CH–OR) is about six orders of magnitude lower than that of an α-alkylthio proton (>CH–SR) [33]. This tells us nothing about the thermodynamic stability of corresponding carbanions. Attempts to metalate dialkoxyacetals with strong bases have either been unsuccessful or led to cleavage of the compound used. Thus when organolithium compounds and 2-aryldioxolanes are brought together at room temperature in ether, an exothermic reaction occurs; the products indicate that this reaction proceeds *via* an anion *(46)*. As indicated in eq. (5),

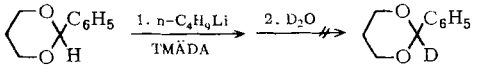
(5)



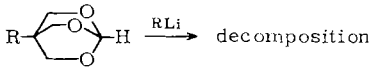
(46)

secondary products

(6)

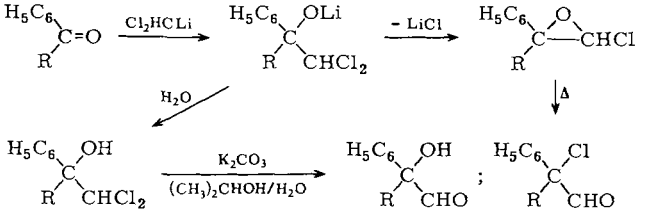


(7)



this decomposes into ethylene and arenecarboxylate [65] (cf. the olefin synthesis described by *Corey* and *Winter* [66]). Even in experiments with 2-phenyl-1,3-dioxane [eq. (6)], the anion of which cannot "fragment" in this way, with the very effective metalating agent *n*-butyllithium/*N*,*N*,*N*′,*N*′-tetramethylethylenediamine [21], in tetrahydrofuran at −78 to +20 °C it was not possible to detect an anion, which should be stabilized, like *(46)*, as a benzyl-like carbanion by conjugation with the aromatic system [62b]. (Under the same conditions, toluene is metalated to give benzyllithium [21,67]; the kinetic acidification due to an α-phenyl group is about ten times as large as that due to an α-ethylthio group [33a].) The orthoformic acid derivative [eq. (7)] also failed to give a directly detectable anion, but decomposed with butyllithium in ether *via* carbenes or carbenoids [65a]. Thus, in none of these cases can the desired metalated acetals or ortho esters be produced under conditions such that they are still stable.

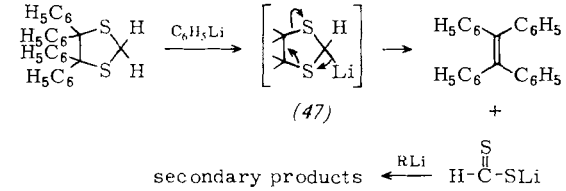
The use of chloro- and bromocarbenoids [50] (R–CCl_2–Li, R–CBr_2–Li) as masked acyllithium compounds is somewhat limited, the reasons being the same as in the case of vinyl halogenocarbenoids (see Section 3.1). Only recently has it been shown [50b,c] that arylketones can be converted into α-hydroxy- and α-chloroaldehydes by dichloromethyllithium, which is stable at temperatures below −90 °C:



In view of the observations described in Section 3.1 on the stabilization of carbanions by adjacent dicoordinate sulfur [see Li derivatives of the anions *(21)* to *(28)*,] it is not surprising that preparatively useful reagents of the type *(32)* have been found among the thioacetals [68]. [The methylene groups in corresponding "diphosphinoacetals", *e.g.* bis(diphenylphosphino)-methane $(C_6H_5)_2P–CH_2–P(C_6H_5)_2$, appear to be much more active than those in thioacetals [69,70]; nothing is known about the possibility of using metalated derivatives *(32)*, Y = PR_2, for nucleophilic acylation.]

Schönberg et al. [71] were probably the first to produce a dithiomethyllithium compound *(47)* when they treated tetraphenyl-1,3-dithiolane in ether with phenyllithium [eq. (8)]. They observed the olefin formation discovered much later for dioxolanes [eq. (5)].

(8)



(47)

secondary products

[64] *G. Wittig*, Angew. Chem. *66*, 10 (1954); see also [28], pp. 230–233.

[65] a) *K. D. Berlin* and *B. S. Rathore*, Tetrahedron Letters *1964*, 2547; *K. D. Berlin*, *B. S. Rathore*, and *M. Peterson*, J. org. Chemistry *30*, 226 (1965); b) *P. S. Wharton*, *G. A. Hiegel*, and *S. Ramaswami*, *ibid. 29*, 2441 (1964).

[66] *E. J. Corey* and *R. A. E. Winter*, J. Amer. chem. Soc. *85*, 2677 (1963); *E. J. Corey*, *F. A. Carey*, and *R. A. E. Winter*, *ibid. 87*, 934 (1965); *E. J. Corey* and *J. I. Shulman*, Tetrahedron Letters *1968*, 3655.

[67] Cf. also [19b, 20] and *J. F. Eastham* and *G. W. Gibson*, J. Amer. chem. Soc. *85*, 2171 (1963); *C. G. Screttas* and *J. F. Eastham*, *ibid. 87*, 3276 (1965); *88*, 5668 (1966); *M. Schlosser*, J. organometallic Chem. *8*, 9 (1967).

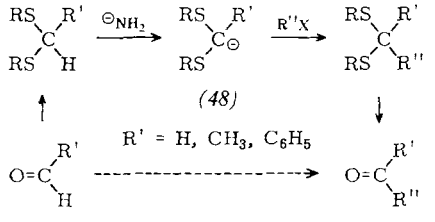
[68] *E. J. Corey* and *D. Seebach*, Angew. Chem. *77*, 1134, 1135 (1965); Angew. Chem. internat. Edit. *4*, 1035, 1037 (1965).

[69] *K. Issleib* and *S. Häusler*, Chem. Ber. *94*, 113 (1961).

[70] *D. J. Peterson*, J. organometallic. Chem. *8*, 199 (1967) and literature cited therein.

[71] *A. Schönberg*, *D. Černik*, and *W. Urban*, Chem. Ber. *64*, 2577 (1931).

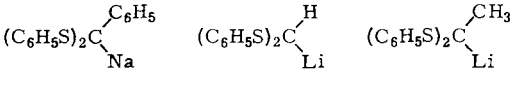
In 1959 and 1962, *Arens* and *Fröling*[24] described the preparation of solutions containing alkali metal derivatives of dithio carbanions *(48)*. Treatment of open-chain aldehyde thioacetals in liquid ammonia with alkali metal amides yields colored solutions, and ketone thioacetal can be obtained on addition of an alkali metal halide. The authors recognized the significance of the reaction sequence as a novel method for the preparation of higher aldehydes from formaldehyde (R′ = H) and of ketones from aldehydes (dotted arrow in Scheme 8). They also found, however, that this method is of limited application, and no further investigations were carried out. The limitations of the method were that (i) only thioacetals of formaldehyde, acetaldehyde, and benzaldehyde could be metalated in this way, (ii) to obtain good yields it was necessary



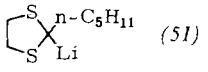
Scheme 8.

to use excess amide, and hence also excess halide, (iii) only the anion of formaldehyde bis(phenylthio)acetal *(48)*, R = C_6H_5, R′ = H, reacted (in moderate yields) with carbonyl compounds, (iv) very reactive electrophiles, such as acyl chlorides, cannot be used in the medium in question, and (v) the hydrolysis of thioacetals, *i.e.* the last step of the cycle, is generally believed to be difficult[72].

Truce and *Roberts*[73] who concluded from literature references[71,74] that phenyllithium and *n*-butyllithium cleave thiacetals, prepared the sodium derivative *(49)* of benzaldehyde bis(phenylthio)acetal in dimethylformamide with the aid of sodium hydride; *(49)* could



(49) *(25)* *(50)*



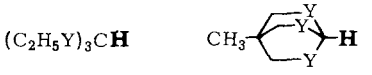
(51)

be alkylated and acylated. They obtained sulfur-free products by hydrolysis and desulfurization (Raney Ni or $NiCl_2/NaBH_4$). *Normant* and *Cuvigny*[75] obtained the Na derivative *(49)* with NaH in hexamethylphosphoric triamide (HMPT), whereas other thioacetals are cleaved by sodamide in this solvent. *n*-Butyllithium in tetrahydrofuran gives excellent results in the preparation of bis(phenylthio)methyllithium *(25)* from the CH_2 compound[19b]; however, this simple method fails in attempts to obtain *(50)* by metalation of the corresponding acetaldehyde derivative. Under these conditions, thioacetals having a dithiolane structure give the same results as were obtained by *Schönberg, i.e. (51)* decomposes[76] under the conditions of its formation (−20 °C) [cf. eqs. (5) and (8)].

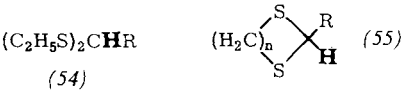
3.2.2. Dithiane and Trithiane Method

Though the relative acidities (as was mentioned, kinetic acidities often give no reliable information on the thermodynamic stabilities of the metal derivatives or their anions) listed in Table 1 gave no reason to expect any very pronounced difference between open-chain and six-membered ring thioacetals [cf. *(54b)* with *(55e)*], *Corey* and *Seebach*[68,76] found that the 1,3-dithianes *(55)*, *n* = 3, occupy a special place.

Table 1. Relative rates of D/H or T/H exchange for acetals, thioacetals, orthoformic esters, and trithioorthoformic esters with K *tert.*-butoxide in *tert.*-butanol [33a]. H = D or T.



(52) *(53)*



(54) *(55)*

Compound	Y	*n*	R	Relative rate
(52a)	O			[a]
(52b)	S			1.5×10^4
(53a)	O			[a]
(53b)	S			1.8×10^7
(54a)			H	40
(54b)			C_2H_5	1
(55a)		2	H	515
(55b)		2	C_2H_5	20
(55c)		3	H	215
(55d)		3	CH_3	0.4
(55e)		3	C_2H_5	1.5
(55f)		3	$(CH_3)_2CH$	1.3
(55g)		3	$(CH_3)_3C$	1.2
(55h)		4	C_2H_5	5.4

[a] No exchange in 20 hours at 110—140 °C.

Under the conditions mentioned above (tetrahydrofuran, *n*-butyllithium, −20 °C, 1–5 hours), many dithianes *(56)* with a wide range of groups R can be quantitatively metalated to give the 1,3-dithian-2-yllithium compounds *(57)*, which are stable below 0 °C. The reagents *(57)* exhibit good nucleophilic properties, and the products of their reactions with electrophiles can be hydrolyzed under mild conditions. s-Trithian-2-yllithium compounds *(58)* can also be used[76–78].

[72] *L. F. Fieser* and *M. Fieser*: Organische Chemie. Verlag Chemie, Weinheim 1965, p. 525.

[73] *W. E. Truce* and *F. E. Roberts*, J. org. Chemistry *28*, 961 (1963).

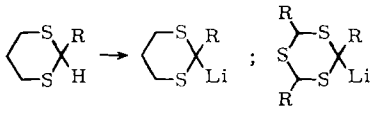
[74] *E. E. Reid*: Organic Chemistry of Bivalent Sulfur. Vol. III, Chem. Publishing Co., New York 1960, p. 332.

[75] *H. Normant* and *T. Cuvigny*, Bull. Soc. chim. France *1965*, 1881.

[76] *E. J. Corey* and *D. Seebach*, unpublished results, 1965/1966.

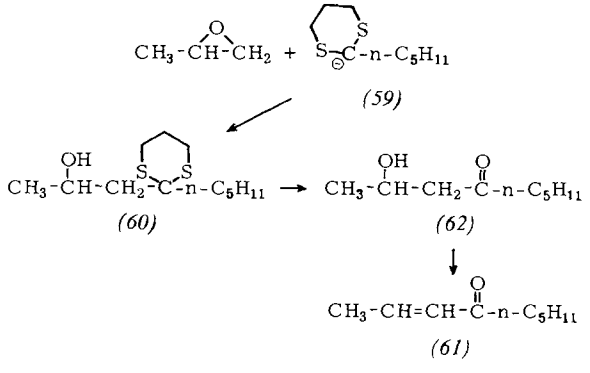
[77] *D. Seebach* and *D. Steinmüller*, Angew. Chem. *80*, 617 (1968); Angew. Chem. internat. Edit. *7*, 619 (1968).

[78] *D. N. Crouse* and *D. Seebach*, Chem. Ber. *101*, 3113 (1968).



(56) (57) (58)

The dithiane method is the most extensively studied of all the nucleophilic acylation methods. It has proved successful in the preparation of 1-deuterated aldehydes [79], silyl and germanyl ketones [80], optically active aldehydes and ketones [77,81], and cyclic carbonyl compounds and hydrocarbons [82], as well as in the most prolific prostaglandin synthesis known at present [83]. One advantage is the chemical stability of the dithianyl protective group for the carbonyl group under various conditions, so that reactions on the C-2 substituents of the dithiane or trithiane system with the reaction products of *(57)* and *(58)* can be carried out. The free carbonyl compound is obtained, when desired, by hydrolysis. Since a comprehensive review of the chemistry of 1,3-dithian-2-yllithium compounds is at present being published [84], we shall merely demonstrate their application to the preparation of aldols and α,β-unsaturated carbonyl compounds as mentioned in the introduction [68,76,77].

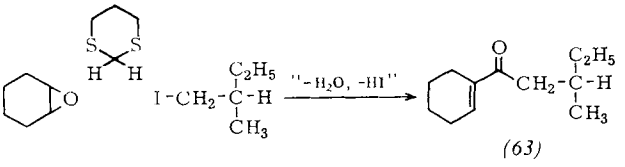


(59)

(60) (62)

(61)

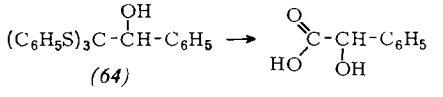
The Li compounds *(57)* add onto epoxides in high yields; the *n*-hexanal derivative *(59)* and propylene oxide give the dithiane derivative *(60)* of an aldol (90%). Hydrolysis with mercuric chloride/mercuric oxide yields the free aldol *(62)* (90%), which is then dehydrated to obtain the aldol condensation product *(61)* (85%). [The mild and extremely specific hydrolysis does not lead directly to the dehydrated product *(61)*!] The aldehyde from which the thioacetal *(56)* is derived is not required for the preparation of a dithianyllithium *(57)*. For example, successive reaction of unsubstituted dithiane [82] with (*S*)-(+)-1-iodo-2-methylbutane and 1,2-epoxycyclohexane in a single reaction



(63)

vessel, followed by hydrolysis and dehydration leads to the optically active ketone *(63)* in an overall yield of 40% from simple starting materials.

Metalated orthotrithioformic esters, *e.g (26)* and *(27)* can be used in a similar manner for nucleophilic carboxylation. Hydrolysis of the product *(64)* obtained from *(26)* and benzaldehyde to mandelic acid can be achieved merely by stirring a solution in acetone in the presence of mercuric salts at room temperature [26a]



(64)

The requirements listed above for a "good" masked nucleophilic acylating agent are only incompletely satisfied by the trithiocarbanion derivatives. Unlike the Li dithianes, these compounds tend to undergo carbenoid decomposition [24–27].

The above outline of the methods of nucleophilic acylation is intended to direct the attention of synthetic chemists toward this variant of carbonyl chemistry, which permits the use of little-noticed "short cuts" in syntheses. For this reason, the development of new methods and the extension of the known principles of nucleophilic acylation should not be neglected.

Received: June 19, 1969 [A 714 IE]
German version: Angew. Chem. *81*, 690 (1969)
Translated by Express Translation Service, London.

[79] *D. Seebach, B. W. Erickson,* and *G. Sing,* J. org. Chemistry *31,* 4303 (1966).

[80] *E. J. Corey, D. Seebach,* and *R. Freedman,* J. Amer. chem. Soc. *89,* 434 (1967); *A. G. Brook et al., ibid. 89,* 431 (1967); *90,* 1076 (1968).

[81] *D. Seebach, D. Steinmüller,* and *F. Demuth,* Angew. Chem. *80,* 618 (1968); Angew. Chem. internat. Edit. *7,* 620 (1968);

[82] *D. Seebach, N. R. Jones,* and *E. J. Corey,* J. org. Chemistry *33,* 300 (1968); *T. Hylton* and *V. Boekelheide,* J. Amer. chem. Soc. *90,* 6887 (1968).

[83] *E. J. Corey et al.,* J. Amer. chem. Soc. *90,* 3245, 5947 (1968); *91,* 535 (1969).

[84] *D. Seebach,* Synthesis, in press.

Non-Enzymatic Activation of Molecular Nitrogen

By G. Henrici-Olivé and S. Olivé[*]

Several transition metal complexes that can absorb nitrogen from the gas phase are now known. Some of the N_2-metal complexes are stable enough to be isolated and their structure elucidated, the N_2 molecule remaining chemically inert. In other cases reduction to N^{3-} is possible, but the structure of the reactive intermediate N_2-metal complex can be approached only by mechanistic studies. In the stable complexes the nitrogen is bound via a lone pair of electrons in the direction of the molecular axis ("end-on"), in the reducible complexes possibly "edge-on".

1. Introduction

The problem of the enzymatic fixation of nitrogen in nature is of interest to chemists, biochemists, and biologists alike. Whereas in nature the nitrogen is taken from the air under very mild conditions with the aid of microorganisms and incorporated, *via* ammonia, into organic nitrogen compounds that are important to life, temperatures of 300 to 600 °C and nitrogen pressures of several hundred atmospheres are required in industry to overcome the inertness of the nitrogen molecule and convert N_2 into NH_3 (Haber-Bosch process).

Whereas biochemists are trying to probe the secrets of nature by extracting the nitrogen-fixing enzymes from the biological cell environment and investigating them separately, chemists have been trying for a number of years to imitate nature *in vitro* by fixing nitrogen on synthetic compounds and complexes. The biochemical investigations have shown that certain transition metals, particularly iron and molybdenum, are always present in the natural systems, and are presumably directly involved in the process of the fixation and reduction of nitrogen. Transition metals, in fact, are the deciding factors also in most synthetic systems.

The research carried out in both directions during the past few years has been summarized by *Murray* and *Smith*[1], and smaller areas of the field have been reviewed by other authors[2–4].

The present article is confined to the non-enzymatic fixation of nitrogen. In order to mark the trends and to illustrate how far the frontiers of science have advanced in this field, a brief account on the relevant research is given. The main part of the article, however, is concerned specifically with mechanistic aspects of the fixation and activation of nitrogen, and hence particular attention is devoted to the processes occurring at the transition metal center.

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[1] *R. Murray* and *D. C. Smith*, Coordinat. Chem. Rev. *3*, 429 (1968).

[2] *J. Chatt*, Proc. Roy. Soc. (London) *B 172*, 327 (1969).

[3] *J. Chatt*, Platinum Metals Rev. *13*, 9 (1969).

[4] *M. Ziegler*, Chemiker-Ztg. *93*, 133 (1969).

2. The Characteristics of the Nitrogen Molecule

The nitrogen molecule is well known to be particularly resistant to chemical attack, with the result that it has become accepted as an ideal inert gas. Its dissociation energy is very high (225.8 kcal/mole), and no appreciable dissociation into atoms occurs at normal pressure even at 3000 °C. Apart from biological activation, only one reaction of nitrogen at room temperature was known until recently; this was the reduction to Li_3N by metallic lithium.

The part played by transition metals in the activation of this inert molecule, both in enzyme systems and in the Haber-Bosch process, almost certainly involves the formation of a metal-nitrogen complex, leading to weakening of the multiple bond. Processes of this type are familiar from homogeneous catalysis on transition metal centers, as in the polymerization of ethylene on titanium complexes. The possibility of the existence of such complexes of the $N \equiv N$ molecule had been predicted on theoretical grounds in 1960, both by *Ruch*[5] and by *Orgel*[6]. No evidence of their occurrence was, however, found until 1965 (see Section 3); and relatively few complexes of N_2 are known even now, in comparison with the innumerable coordination compounds of the isoelectronic CO.

What is the reason for this inertness as compared with other compounds containing triple bonds, such as $H-C \equiv C-H$ or $R-C \equiv N$, and why is the tendency to complex formation so small?

SCF–LCAO–MO[*] calculations have shown[7–9] that the nitrogen molecule has the electronic configuration

$$(1\sigma_g)^2\,(1\sigma_u)^2\,(2\sigma_g)^2\,(2\sigma_u)^2\,(1\pi_u)^4\,(3\sigma_g)^2$$

[5] *E. Ruch*, Monograph: "10 Jahre Fonds der Chemischen Industrie", Verlag der Chemischen Industrie e.V., Fond der Chemischen Industrie, Düsseldorf 1960, p. 163.

[6] *L. E. Orgel*: An Introduction to Transition Metal Chemistry. Methuen, London 1960, p. 137.

[*] Self consistent field – linear combination of atomic orbitals – molecular orbitals.

[7] *C. W. Scherr*, J. chem. Physics *23*, 569 (1955).

[8] *B. J. Ransil*, Rev. mod. Physics *32*, 239 (1960).

[9] *J. W. Richardson*, J. chem. Physics *35*, 1829 (1961).

[10] See, *e.g.*, *H. B. Gray*: Electrons and Chemical Bonding. Benjamin, New York 1965.

The highest occupied orbital is thus a σ orbital, and not the degenerate π orbital as in *e.g.* acetylene. According to these calculations, the 3 σ_g orbital consists essentially of the $2p_\sigma$ orbitals of the N atoms (about 25 % s-character). The first empty MO is the degenerate antibonding π orbital $1\pi_g$. These calculations are confirmed by spectroscopic observations [7,8,10].

Figure 1 shows the surface of the MO's that are important to any complex formation or reaction (after *Chatt* [2]).

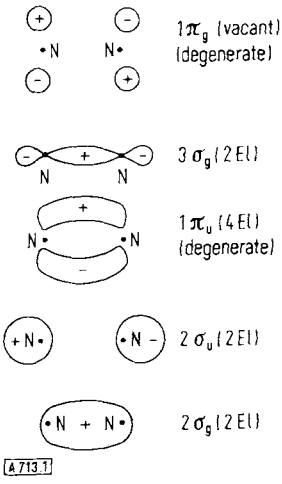


Fig. 1. Schematic representation of the LCAO—MO's in the nitrogen molecule (after *Chatt* [2]).

Chatt [3] has suggested that the low reactivity of N_2 is essentially due to the energetically unfavorable position of the highest occupied orbital. The $3\sigma_g$ orbital of the N_2 molecule, which has an energy of −15.5 eV, is much more stable than *e.g.* the degenerate pair of π orbitals of acetylene (−11.4 eV).

Jaffé and *Orchin* [11] proposed a qualitative MO scheme to explain the difference in the complex-forming tendencies of N_2 and CO. The model is based in principle on the fact that the 2s orbital of oxygen is very low in energy in relation to the 2s orbital of carbon, so that $2p_\sigma$ of oxygen is better suited, on energy grounds, for combination with 2s of carbon. The lone pair of electrons on the carbon consequently has a relatively high energy, is predominantly of p-character, points in the opposite direction to the C=O bond, and is therefore available for complex formation. In N_2, on the other hand, the lone pairs of electrons on the two N atoms, according to this model, occupy low-lying orbitals having predominantly s-character.

According to more recent calculations of the two molecules by *Edmiston* and *Ruedenberg* [12], however, this picture does not appear to be quite correct. Localized molecular orbitals (LMO's) were calculated on the basis of the SCF–LCAO–MO's for the two molecules N_2 and CO. It was found that the two isoelectronic molecules can be represented by almost the same schematic diagram (Fig. 2), *i.e.* each of the atoms carries a localized lone pair of electrons; these electron pairs are predominantly 2s, but they have sufficiently strong $2p_\sigma$ components to enable them to point "backward" (at 180° to the bond). Between the two atoms are three equivalent banana-shaped bonding orbitals (which are slightly polarized toward the O in CO).



Fig. 2. Schematic representation of the LMO's for N_2 and CO (after *Edmiston* and *Ruedenberg* [12]).

It can be seen from Table 1, however, that the calculated s-character of the lone pairs of electrons shows a trend parallel to that assumed by *Jaffé*. The figures show that the s-character of the bonding orbitals steadily decreases from left to right in the periodic system (C, N, O), whereas that of the lone pair of electrons increases.

Table 1. Variation of the s character in the bonding LMO's and in the LMO's for the lone pairs of electrons on C, N, and O in N_2 and CO [12].

Atom	2 s character	
	bonding [a]	lone pair
C	0.60	0.60
N	0.46	0.75
O	0.25	0.79

[a] In the three equivalent bonding orbitals.

The comparison of the two schematic representations of MO's in Figures 1 and 2 may at first sight seem rather confusing. The chemist whose theoretical background is not so extensive has a strong tendency to attach an excessively concrete physical significance to a calculated set of SCF—MO's or to the qualitative pictures of the surfaces built up from these MO's, and to forget that another set can represent an equally correct solution. Roughly speaking, it may be said that the "electron cloud" in a given molecule can be divided into different regions by mathematical tricks, so that different calculation methods may give a different pattern.

The localized molecular orbitals (LMO's) are constituted in such a way as to minimize interorbital electronic interaction. In contrast with the SCF SCF–LCAO–MO's on which they are based (cf. Fig. 1), orbitals localized on *one* atom are often found here for the lower shells and for lone pairs of electrons, as well as bonding orbitals localized between the two atoms. These calculations are thus much more closely allied to the chemist's concept of chemical bonding.

It can be concluded from a comparison of the electronic situations in N_2 and CO that the differences between the two molecules should be quantitative rather than qualitative (cf. [6]). There is, however, a possibly important difference in the energies of the highest occupied orbitals of the two molecules; the difference is about 1.4 eV in favor of CO [9,13]. Another difference is the polarity of CO. Nevertheless, the problem of the fixation of nitrogen on transition metal

[11] *H. H. Jaffé* and *M. Orchin*, Tetrahedron *10*, 212 (1960).

[12] *C. Edmiston* and *K. Ruedenberg*, J. chem. Physics *43*, 97 (1965).

[13] *R. Sahni*, Trans. Faraday Soc. *49*, 1246 (1953).

complexes looks hopeful, and several such complexes with N_2 ligands have, in fact, already become known (see Section 3).

There still remains the question how such complexes are to be pictured. By analogy with CO, one would expect bonding to occur *via* the lone pairs of electrons (end-on). On the other hand, comparison with other substances containing triple bonds, such as the alkynes, forces us to consider a complex bond normal to the axis of the N_2 molecule (edge-on), particularly since it has been shown that the biological systems that are to be imitated here can reduce acetylene (to ethylene) as well as N_2.



Bonding in the direction of the molecular axis (end-on)

Bonding normal to the molecular axis (edge-on)

Some indications clearly favor bonding in the direction of the molecular axis in a number of isolable, stable complexes (cf. Section 4.2). However, this does not tell us anything definite about the configurations that really activate the nitrogen molecule.

3. Present State of Research on the Fixation of Nitrogen

In 1965, *Allen* and *Senoff*[14] reported the first isolable ruthenium complex containing an N_2 molecule as a ligand:

$[Ru(NH_3)_5N_2]^{2\oplus}$ *(1)*

anions: $Br^{\ominus}$, $I^{\ominus}$, $BF_4^{\ominus}$, $PF_6^{\ominus}$

The nitrogen had not in fact been absorbed from the gas phase in this case, but had been formed in the reaction of $RuCl_3$ with hydrazine in aqueous solution by disproportionation of the hydrazine, with simultaneous formation of NH_3. Soon afterwards, however, *Shilov et al.*[15] showed that free molecular nitrogen can also be taken up as a ligand in Ru(II) complexes.

Several other methods for the preparation of the complex *(1)* and a series of similar complexes were subsequently described. Only a few important developments will be mentioned briefly here.

Isolable complexes are so far confined to Group VIII of the periodic system. Complexes with elements of the first period appear to be relatively unstable, and difficulties are often encountered in their isolation An interesting cobalt complex has been described, in which N_2 and H_2 can be reversibly exchanged[16]:

$$[CoH_3(P(C_6H_5)_3)_3] + N_2 \rightleftarrows [CoH(N_2)(P(C_6H_5)_3)_3] + H_2$$

The osmium analog of *(1)* has been found to be particularly stable[17]. The nitrogen is so strongly bound in this complex that it withstands boiling in strong hydrochloric acid.

The unexpected thermodynamic stability of such nitrogen complexes is also shown by the fact that even water can be displaced by nitrogen in some cases[18]:

$$[Ru(NH_3)_5H_2O]^{2\oplus} + N_2 \rightarrow [Ru(NH_3)_5N_2]^{2\oplus} + H_2O$$

It should be mentioned, finally, that binuclear complexes in which the nitrogen molecule forms a bridge between two transition metal units have also been found. In the case of Ru^{II}, a complex of this type is formed as follows:

$$[Ru(NH_3)_5H_2O]^{2\oplus} + [Ru(NH_3)_5N_2]^{2\oplus} \rightarrow [(NH_3)_5RuN_2Ru(NH_3)_5]^{4\oplus} + H_2O$$

again by displacement of water. The compound was isolated from aqueous solution with $[BF_4]^{\ominus}$ as the anion[18]. A nitrogen-nickel(0) complex of this type is formed[19] on reduction of bis(2,4-pentanedionate)-nickel(II) with trimethylaluminum in the presence of tricyclohexylphosphine and nitrogen; this complex is formulated as follows:

$$[(C_6H_{11})_3P]_2NiN_2Ni[P(C_6H_{11})_3]_2$$

These novel compounds naturally present a temptation to hopeful comparisons with the biological activation of nitrogen. Might this not be an analog at least of the fixation step? Unfortunately, no evidence has so far been found to indicate that the nitrogen, once fixed in these stable complexes, is susceptible to chemical attack. Early success reports, according to which the nitrogen in *(1)* had been reduced to NH_3 by $NaBH_4$[14] were found to be fallacious since *Chatt* showed that when $^{15}N_2$ is used, the NH_3 liberated from the complex contains no ^{15}N[3].

An entirely different line of investigation is based on the observation by *Volpin* and *Shur*[20] that Ziegler-Natta systems and similar combinations of a transition metal compound and an organometallic reducing agent take up gaseous nitrogen and reduce it to $N^{3\ominus}$. After hydrolysis, the nitrogen is collected as NH_3. Up to 0.4 N_2 molecule per transition metal center was fixed and reduced in these early experiments.

This approach was adopted by a number of authors and developed in different directions[21–26].

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[14] *A. D. Allen* and *C. V. Senoff*, Chem. Commun. *1965*, 621.

[15] *A. E. Shilov*, *A. K. Shilov*, and *Yu. G. Borodko*, Kinetika i Kataliz *7*, 768 (1966).

[16] *A. Yamamoto*, *S. Kitazume*, and *S. Ikeda*, J. Amer. chem. Soc. *90*, 1089 (1968).

[17] *A. D. Allen* and *J. R. Stevens*, Chem. Commun. *1967*, 1147.

[18] *D. E. Harrison*, *E. Weissenberger*, and *H. Taube*, Science (Washington) *159*, 320 (1968).

[19] *P. W. Jolly* and *K. Jonas*, Angew. Chem. *80*, 705 (1968); Angew. Chem. internat. Edit. *7*, 731 (1968).

[20] *M. E. Volpin* and *V. B. Shur*, Nature (London) *209*, 1236 (1966), and literature cited there.

[21] *H. Brintzinger*, J. Amer. chem. Soc. a) *88*, 4305, 4307 (1966); b) *89*, 6871 (1967).

[22] *G. Henrici-Olivé* and *S. Olivé*, a) Angew. Chem. *79*, 898 (1967); Angew. Chem. internat. Edit. *6*, 873 (1967); b) Angew. Chem. *80*, 398 (1968); Angew. Chem. internat. Edit. *7*, 386 (1968).

[23] *R. Maskill* and *J. M. Pratt*, Chem. Commun. *1967*, 950.

[24] *E. E. Tamelen*, *G. Boche*, *S. W. Ela*, and *R. B. Fechter*, J. Amer. chem. Soc. *89*, 5707 (1967).

The reactions proceed at room temperature and at nitrogen pressures of 1 to 150 atm; because of the presence of the organometallic component in the system (*e.g.* Grignard reagent, alkylaluminum, or alkali metal naphthalide), organic solvents (usually ethers) must be used. The nitrogen molecule is presumably coordinately fixed to the transition metal and reduced by the organometallic component which is always present in great excess (cf. Sections 4.4 and 4.5). The disadvantage of this reaction is that the nitrogen appears to adhere very strongly to the transition metal species in the nitride form; with one exception, which will be described later, the only method found so far for the removal of the reduced nitrogen from the metal is hydrolysis or alcoholysis.

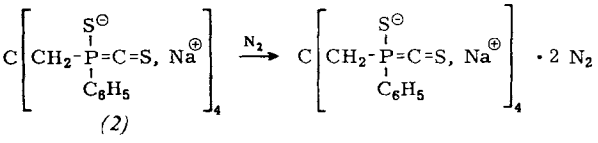
The conversion in the fixation process has been increased to 100% with respect to the metal, *i.e.* one N_2 molecule per transition metal center. This was achieved with VCl_3 and Li naphthalide in tetrahydrofuran [22a]. *Van Tamelen et al.* [25,26] developed a similar process into a cycle of fixation, reduction, and alcoholysis. The fixing and reducing system is a combination of titanium tetraisopropoxide and Na naphthalide in tetrahydrofuran. $N^{3\ominus}$ is converted into ammonia with an accurately measured quantity of isopropyl alcohol, and is thus separated from the metal. The original combination is regenerated by introduction of fresh Na naphthalide (or simply of Na, since the naphthalene is still available in the system). By five such cycles it was possible to convert up to 1.7 molecules of N_2 per titanium center into ammonia at normal pressure.

Volpin et al. [27] recently managed to remove the nitride nitrogen from the transition metal in a batch procedure, so making it available for further fixation. These authors used the reducing combination of Al and aluminum bromide, which is well known *e.g.* from the Fischer-Hafner synthesis of aromatic complexes of transition metals [28]. When this combination was used with salts such as $TiCl_4$ or $CrCl_3$, they found that more than 100 nitrogen molecules per transition metal center could be reduced to $N^{3\ominus}$ by the use of a large excess of aluminum and Lewis acid (for example, Ti : Al : $AlBr_3$ = 1 : 600 : 1000, 30 hours, 130 °C, 100 atm of N_2; 142 molecules of N_2 were reduced per titanium atom). The nitrogen is presumably present as $N^{3\ominus}$ attached to an aluminum species; it is liberated as NH_3 on hydrolysis.

Another development that could show promise also comes from *Volpin*'s laboratory. With phenyllithium as the reducing agent together with $(C_5H_5)_2TiCl_2$ in ether, some aniline was found as well as NH_3 on hydrolysis (0.65 mole of NH_3, 0.15 mole of $C_6H_5NH_2$ per mole of Ti complex at 20 °C and 100 atm of N_2) [29].

A carbon-nitrogen bond was thus obtained for the first time in this case, though only to a small extent.

Transition metal compounds, however, are no longer the only synthetic nitrogen fixers. In 1967 it was reported for the first time that the phenylsulfenium cation ($C_6H_5S^+$) takes up gaseous nitrogen [30]; the reaction products could not be isolated. *Ellermann et al.* [31], however, recently prepared an organic compound, again containing ionic sulfur, that "avidly absorbs molecular nitrogen". The reaction product, which contains two nitrogen molecules per complex unit, has been isolated. The authors assumed that the nitrogen molecules were bound in a spirocyclic complex by the compound *(2)* which acts as a doubly bidentate chelating agent.



(2)

These new compounds may raise the question whether the transition metal centers are really of decisive importance in the enzymatic fixation of nitrogen, as has been assumed until now.

4. Attempts to Elucidate the Mechanism of the Activation of Nitrogen

4.1. Metal Surfaces

From the point of view of the industrial activation of nitrogen (Haber-Bosch), great efforts were made to establish the reaction mechanism of this industrially important process, but these have not yet led to any satisfactory conclusion. The active species and the rate-determining step are still in dispute (for reviews see [1,32,33]). Most of these investigations were carried out on extremely pure metal surfaces (Group VIII). Two studies that are related in some measure to the nitrogen complexes will be mentioned.

Eischen and *Jacknow* [34] investigated the fixation of nitrogen by nickel on silica supports. The authors found with the aid of IR spectroscopy that N_2 is chemisorbed on nickel at room temperature. A number of interesting conclusions are drawn from the presence of a strong absorption band at 2202 cm^{-1}. The free nitrogen molecule gives a band at 2331 cm^{-1}, which is due to an N≡N stretching vibration; owing to the symmetry of the N_2 molecule, this band does not ap-

[25] *E. E. van Tamelen, G. Boche,* and *R. H. Greeley,* J. Amer. chem. Soc. *90,* 1677 (1968).

[26] *E. E. van Tamelen, R. B. Fechter, S. W. Schneller, G. Boche, R. H. Greeley,* and *B. Åkermark,* J. Amer. chem. Soc. *91,* 1551 (1969).

[27] *M. E. Volpin, M. A. Ilatovskaya, L. V. Kosyakova,* and *V. B. Shur,* Chem. Commun. *1968,* 1074.

[28] *E. O. Fischer* and *W. Hafner,* Z. Naturforsch. *10b,* 665 (1955).

[29] *M. E. Volpin* and *V. B. Shur,* Bull. Acad. Sci. USSR. Div. Chem. *1966,* 1819.

[30] *D. C. Owsley* and *G. K. Helmkamp,* J. Amer. chem. Soc. *89,* 4558 (1967).

[31] *J. Ellermann, F. Poersch, R. Kunstmann,* and *R. Kramolowsky,* Angew. Chem. *81,* 183 (1969); Angew. Chem. internat. Edit. *8,* 203 (1969).

[32] *P. H. Emmet*: Catalysis. Reinhold, New York 1955.

[33] *E. K. Rideal*: Concepts in Catalysis. Academic Press, New York 1968.

[34] *R. P. Eischen* and *J. Jacknow,* Proc. 3rd Intern. Congress on Catalysis. North Holland Publ. Co., Amsterdam 1964, p. 627.

pear in the IR spectrum, but is observed only in the Raman spectrum. The relatively high extinction coefficient of the observed IR band suggests that considerable polarization of the N_2 molecule must have occurred. The frequency shift, on the other hand, indicates chemisorption with (at least partial) chemical bonding between the metal and the N_2 molecule. (No shift would occur if the polarization was due to the action of asymmetric surface electric fields on a purely physically adsorbed molecule.) If the isotope $^{15}N_2$ is chemisorbed instead of $^{14}N_2$, the IR band appears at 2128 cm^{-1}. A mixture of the three isotopes $^{14}N_2$ $^{14}N-^{15}N$, and $^{15}N_2$ gives three bands in the correct intensity ratio. This shows that no atomic species are present. It is concluded from the observations as a whole that the nitrogen molecule is attached end-on to the nickel(0). It can be calculated from the isotopic shift of the IR band that the force constants for this structure are 19×10^5 dyne/cm for the N–N bond and 3×10^5 dyne/cm for the metal-N bond [35]. The end-on structure would be conclusively proved if it were possible to separate the IR bands of $Ni \leftarrow {}^{14}N \equiv {}^{15}N$ and $Ni \leftarrow {}^{15}N \equiv {}^{14}N$, for which a difference of 5–6 cm^{-1} is predicted from theory [34]. However, the resolution of the instrument used was not sufficient for this.

Another interesting investigation that also points to end-on binding of the nitrogen, in this case to iron, was carried out by *Brill et al.* [36], who studied the action of nitrogen on an iron point in a field electron microscope. The point was exposed to a nitrogen atmosphere at 76 °K. After heating for a short time at 400 °C, the micrograph shows a distinct prominence of the 111 faces of the iron. It is thus concluded that the nitrogen is preferentially chemisorbed on these faces, with the result that their surface energy is reduced, and these non-equilibrium faces consequently grow. The authors interpret the preferential deposition of the N_2 molecule on the 111 face as follows: The iron atoms are arranged in these faces in such a way that the atoms of the top layer surround holes having trigonal symmetry. It is assumed that the surface atoms make unoccupied orbitals available, and that these can be used for the construction of molecular orbitals having π character with respect to the axis of the trigonal hole. These can then interact with the occupied π orbitals of an N_2 molecule arranged along the trigonal axis (π bonding).

4.2. Complexes with Nitrogen Ligands

The first N_2 complex *(1)* isolated gave a strong IR band at 2118 to 2167 cm^{-1} (depending on the anion), and all other complexes having an N_2 ligand also give this band, the wave number of which differs by 150 to 300 cm^{-1} from the (Raman-active) stretching vibration of the free nitrogen molecule. As in the case of N_2 on metal surfaces (Section 4.1), therefore, the end-on configuration is also assumed for the coordinately bound nitrogen. This has been proved by X-ray analysis in two cases, *i.e. Allen* and *Senoff*'s ruthenium complex (octahedron with linear Ru–N–N grouping [37]) and the complex $[Co(N_2)(P(C_6H_5)_3)_3]$ (trigonal bipyramid with H at one apex and N_2 at the other; 5° deviation from linearity in the grouping Co–N–N [38]).

The nitrogen-metal bond in these complexes is formulated by *Chatt* [2,3] as a sort of double bond, unlike that discussed by *Brill et al.* [36] for the chemisorption on iron. *Chatt*'s interpretation agrees with the formulation normally given for the carbonyl complexes [6]. An occupied σ orbital (this refers to one of the lone pairs of electrons according to Figure 2, and to the orbital $3\sigma_g$ according to Figure 1) interacts with an unoccupied d_σ orbital of the metal (d_{z^2} or $d_{x^2-y^2}$ in the octahedral complex). Electron back-donation (see Fig. 3) occurs *via* an occupied $d\pi$ orbital of the metal (d_{xy}, d_{xz}, d_{yz} and the empty antibonding $1\pi_g$ orbital of the nitrogen (π symmetry with respect to the M–N–N axis).

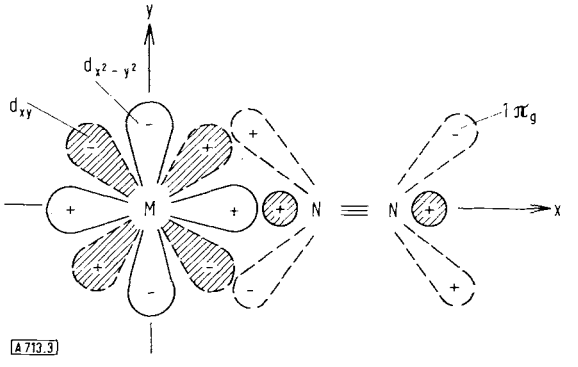


Fig. 3. Double-bond-like interaction between metal and nitrogen molecule (shaded: occupied orbitals).

The electron density passing in this way into the antibonding nitrogen orbital should weaken the bonding between the two nitrogen atoms. The displacement of the stretching vibration $\nu(N \equiv N)$ by 150–300 cm^{-1} indicates that this indeed has happened. However, the weakening is evidently not enough to make the coordinately bound nitrogen accessible to chemical reactions (*e.g.* hydrolysis or reduction). Even in complexes of the type $M-N_2-M$ [18,19], in which one should expect double weakening of the $N \equiv N$ bond according to these views, the nitrogen molecule still remains in the unreactive state. It should be noted that for these complexes, because of the symmetry of the molecule, the $N \equiv N$ stretching vibration is only Raman-active, as in the free N_2 molecule.

The energy conditions for the formation of an N_2 complex seem to be extremely critical. *Chatt et al.* [3] have shown that small changes in the other ligands of the metal center can make the isolation of a stable complex impossible. For example, the iridium complex

$IrCl(N_2)[P(C_6H_5)_3]_2$

[35] See *H. Siebert*: Anwendung der Schwingungs-Spektroskopie in der anorganischen Chemie. Springer, Berlin 1966.

[36] *R. Brill, E. L. Richter,* and *E. Ruch,* Angew. Chem. *79,* 905 (1967); Angew. Chem. internat. Edit. *6,* 882 (1967).

[37] *F. Bottomley* and *S. C. Nyburg,* Chem. Commun. *1966,* 897.

[38] *J. H. Enemark, B. R. Davies, J. A. McGinnety,* and *J. A. Ibers,* Chem. Commun. *1968,* 96.

is very easy to prepare. The corresponding iodide, on the other hand, is too unstable to be isolated in the pure state. The same is found when one attempts to replace the triphenylphosphine ligands with ethyldiphenylphosphine. (It should, however, be remembered that the isolability of the complex is not necessarily related to the chemical reactivity of the coordinately bound N_2 molecule; cf. also Section 5.)

Undoubtedly it will be interesting to follow the weakening of the N≡N bond (as indicated by the displacement of the IR band) as a function of the other ligands in the complex [39].

4.3. The System Bis(π-cyclopentadienyl)titanium Dichloride/Ethylmagnesium Bromide

The combination bis(π-cyclopentadienyl)titanium dichloride/ethylmagnesium bromide in ether was one of the first systems with which *Volpin* and *Shur* [20] observed the fixation and reduction of gaseous nitrogen in 1964. Several attempts have been made since then to explain the mechanism of this reduction.

The first important contribution was made by *Shilov et al.* [40]. These authors showed by experiments with deuterated Grignard reagent and with deuterated ether that the nitrogen is present as nitride, and is liberated as NH_3 only on hydrolysis. *Volpin* had assumed at first that the coordinately bound nitrogen could take up hydrogen from the solvent or the Grignard reagent [20]. On hydrolysis of the (undeuterated) reaction solution with heavy water, *Shilov et al.* also found that the isotope distribution in the hydrogen-deuterium mixture liberated indicated the presence of a metal hydride. This was in fact later definitely confirmed by *Brintzinger* [21a] by electron spin resonance measurements.

At that time, *Shilov et al.* assumed that the active species was an unstable intermediate occurring during the reduction; this could not be confirmed by other authors. *Maskill* and *Pratt* [23] showed that the quantity of nitrogen fixed does not change appreciably if the components of the system are first allowed to react under argon, the nitrogen only being introduced later (cf. also Table 2).

Further information was provided by our own investigations of the same system in benzene [41]. ESR measurements on the nitrogen-free system gave the same signal as had been observed by *Brintzinger* using ethereal solvents [21a,42] (see Fig. 4).

This signal is a 1:2:1 triplet, in which each of the three lines shows further multiplet splitting due to the ring protons of the cyclopentadienyl groups. The triplet is due to the interaction of the unpaired electron of a Ti(III) species with two equivalent protons, and so points to a hydride structure. The intensity of this signal increases for 1 to 1.5 hours from the moment of mixing of the two components, and then remains constant. The titanium has thus been reduced to the ESR-active state Ti^{III} ($3d^1$) during this period, and then remains in this state. The reduction is probably similar to that in the Ziegler-Natta system $Cp_2TiCl_2/C_2H_5AlCl_2$, with alkylation of the titanium followed by decomposition of the relatively unstable alkyltitanium compound (see *e.g.* [43]).

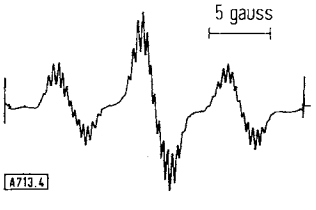


Fig. 4. ESR signal in the reaction solution Cp_2TiCl_2/C_2H_5MgBr in benzene. Mg/Ti = 12; high dilution; $T = 20$ °C. Cp = cyclopentadienyl.

Measurement of the magnetic susceptibility of such a system after about 2 hours shows that the Ti(III) concentration is only about 50% of the original Ti(IV) concentration. Since all the experiments with this system were carried out with a large excess of Grignard reagent [20,21,40] (Mg/Ti = 12 in the experiments described here), it is hardly to be expected that only partial reduction has occurred. It is probable, therefore, that part of the titanium has been reduced beyond the Ti(III) stage.

The system Cp_2TiCl_2/C_2H_5MgBr in benzene also fixes and reduces nitrogen. The process is again independent of whether the components are brought together under nitrogen or exposed to nitrogen only at the time of maximum hydride concentration (after about 1 hour). This can be seen from Table 2.

Table 2. Fixation of nitrogen on the system Cp_2TiCl_2/C_2H_5MgBr in benzene. [Ti] = 10×10^{-3} mole/l; Mg/Ti = 12; $T = 22$ °C; 110 atm of N_2 [41].

No.	N_2 added	Time	NH_3/Ti (h)
1	immediately	17	1.0
2	after 1 h	17	0.88
3	immediately	70	0.96
4	after 1 h	70	1.0

The ESR signal of the reaction solution was recorded at the end of experiment 1. The hydride signal was still present with a comparable intensity at this time, although one nitrogen atom per titanium was already present in the reduced form. This again shows clearly that the hydride hydrogen is not involved in the reduction process [*]. It can also be seen from Table 2 that the fixation of nitrogen has already reached its final value of $NH_3/Ti \simeq 1$ after 17 hours; this value cannot be increased by the use of either a higher Mg/Ti ratio or of higher pressures. Since not more than one N_2 molecule can be fixed per two titanium centers, we believe that the process takes place on a binuclear complex.

Brintzinger had initially assumed the binuclear structure *(3)* for the hydride [21a], but later became convinced that the hydride is better described by formula

[39] *J. Chatt* and *R. L. Richards*, personal communication.

[40] *G. N. Nechiporenko, G. M. Tabrina, A. K. Shilova*, and *A. E. Shilov*, Doklady Akad. Nauk SSSR *164*, 1062 (1965).

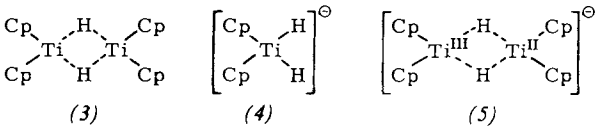
[41] *G. Henrici-Olivé* and *S. Olivé*, unpublished.

[42] *H. Brintzinger*, J. Amer. chem. Soc. *89*, 6871 (1967).

[43] *G. Henrici-Olivé* and *S. Olivé*, Angew. Chem. *79*, 764 (1967); Angew. Chem. internat. Edit. *6*, 790 (1967).

[*] *Brintzinger* had thought at first that the ESR data pointed to participation of the hydride hydrogens [21b], but he himself disproved this by further detailed investigations [42].

(4) [42]. The results of our work reported here, particularly in conjunction with the data for the similar system described in the next section, lead us to assume that the active species is a binuclear complex containing titanium in different valence states [structure *(5)*].



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

It is possible, in our view, that the nitrogen is fixed to the Ti(II) side of the complex, and that the ESR activity of the Ti(III) side is consequently not appreciably changed.

4.4. The System Cp_2TiCl_2/Alkali Metal Naphthalide

If an alkali metal naphthalide (*e.g.* Li^+Np^- or Na^+Np^-) is used as the reducing agent instead of a Grignard reagent, fixation of nitrogen occurs even at normal pressure. In the system Cp_2TiCl_2/LiNp in tetrahydrofuran, for example, 0.96 molecule of NH_3 is obtained per titanium center after 16 hours with Li/Ti = 6 and under one atmosphere of nitrogen [22b]. The ratio NH_3/Ti again cannot be increased beyond about 1 under any conditions. The fixation takes place slowly; under the same conditions, 0.5 NH_3 molecule per titanium is obtained after 2 hours, and 0.7 molecule after 4 hours.

ESR studies again provided a number of clues as to the mechanism in this system.

Let us first consider the system in the absence of nitrogen. A readily resolvable ESR signal is observed (see Fig. 5), but in contrast with the Grignard system, the ratio of reducing agent to titanium component is critical here. The signal is observed only at molar ratios $3 \leqslant$ Li/Ti $\leqslant 4$. Its intensity passes through a maximum at Li/Ti = 3.5, and is almost 0 at Li/Ti = 4.0. At higher values of the ratio, the lithium naphthalide signal appears. The stronger reducing agent LiNp is evidently capable of reducing the ESR-active Ti(III) species further.

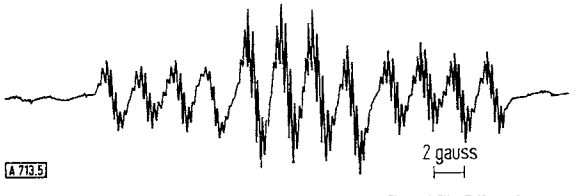
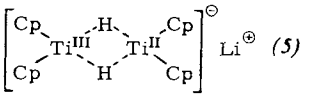


Fig. 5. ESR signal of the reaction solution Cp_2TiCl_2/LiNp in tetrahydrofuran. Li/Ti = 3.5; high dilution. $T = -40$ °C [22b].

The predominant hyperfine splitting is again a 1:2:1 triplet indicating the presence of two equivalent protons. The coupling constant is similar to that of the hydride in Figure 4 [21a, 22b]. In this case, however, each line is further split into four components of equal intensity; the only possible cause for this is a lithium nucleus (^{7}Li, nuclear spin $I = 3/2$). Since the Li coupling constant is relatively large and is practically independent of temperature in an interval of 100 °C, it may be assumed that the lithium is fairly firmly bound, presumably in the inner coordination sphere of the titanium. (The same is true of Na [22b].) Finally the interaction with the ring protons of the Cp groups again occurs, leading to splitting of each of the twelve principal lines into a multiplet. From these data, and taking into account the fixation of nitrogen, the most probable formula for the ESR-active species, as in the last section, is found to be *(5)* [*]. The exact location of the lithium ion is not yet known.



(5)

Unlike in the Grignard system (preceding section), the bridge hydrogen in this case comes from the solvent. This is shown by the fact that an identical spectrum is obtained with LiNp prepared from $C_{10}D_8$ [41]. The hydride formation mechanism is thus evidently different in this case. A conductometric titration was carried out to clarify this mechanism. NaNp was used to avoid interference by the soluble LiCl (NaNp and LiNp behave almost identically in these reactions [22b]). It can be seen from Figure 6 that the conductivity increases rapidly in the range $2 \leqslant$ Na/Ti $\leqslant 3$, indicating the occurrence of ionic species.

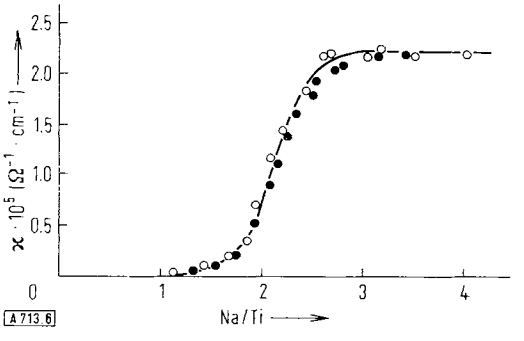
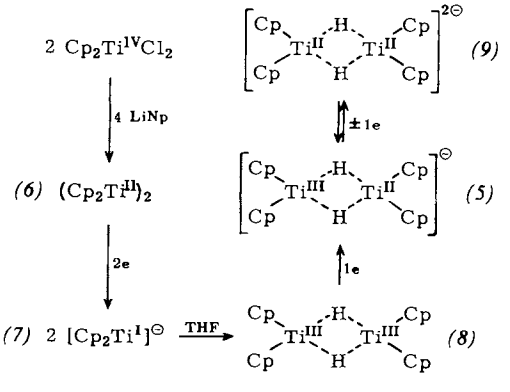


Fig. 6. Conductometric titration of Cp_2TiCl_2 with NaNp in THF. $[Cp_2TiCl_2]_0 = 10 \times 10^{-3}$ mole/l. ○, ●: two sets of measurements [41].

Combination of all the data mentioned leads to the following reaction scheme for the nitrogen-free system:



(9) *(6)* $(Cp_2Ti^{II})_2$ *(5)* *(7)* $2\,[Cp_2Ti^{I}]^{\ominus}$ *(8)*

[*] Complexes containing two Ti(III) centers can also be ruled out on the basis of various ESR consideration [22b, 42].

The reaction of 2 Cp_2TiCl_2 with 4 LiNp leads to the formation of dimeric titanocene *(6)*, the synthesis of which by this route is known from the literature [44]. Since titanocene is stable in tetrahydrofuran, the further reaction must be attributed to excess naphthalide. It is assumed that the ionic Ti(I) compounds *(7)* are formed as intermediates, and that these attack the solvent. The dimeric hydride species *(8)* are formed, as well as ionic reaction products of tetrahydrofuran. The latter are considered to be responsible for the electric conductivity, the occurrence of which in this range was shown by conductometric titration (Fig. 6).

The consumption of a total of four LiNp per titanium shows that further reduction of *(8)* is to be expected. The complex *(5)* is the ESR-active form. The disappearance of the ESR signal in the range $3.5 \leqslant Li/Ti \leqslant 4$ requires a further reduction to the diamagnetic complex *(9)*. Above Li/Ti = 4, as was mentioned earlier, the excess LiNp appears in the ESR spectrum, *i.e.* the reduction process is complete.

It is of interest in connection with the nitrogen fixation mechanism that the system fixes nitrogen both at Li/Ti = 3.5 [maximum ESR signal, complex *(5)*] and at Li/Ti = 4.0 [no ESR signal, complex *(9)*] ($NH_3/Ti \simeq 0.2$). In the former case, however, the signal disappears on addition of nitrogen. Since only one of the two species *(5)* and *(9)* is presumably responsible for the fixation, we have assumed that an equilibrium exists between them.

According to observations on polymerization catalysis (for example, ethylene can be polymerized on Ti^{III}/Ti^{IV} or on Ti^{II}/Ti^{III} complexes), the species *(5)*, in which the titanium atoms have different valences, seems the more likely candidate. The difference in the numbers of ligands means that the two titanium centers will differ in their symmetries. A proposal that agrees with the ESR data is shown in Figure 7. The Ti^{III} has a tetrahedral environment, whereas the Ti^{II} is situated in a trigonal bipyramid. (The equivalence of the two bridge hydrogens requires that the lithium be symmetrically placed in relation to these atoms.)

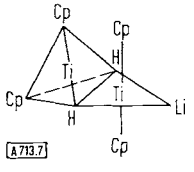


Fig. 7. Suggested configuration of the ESR-active species *(5)*.

On entry of a nitrogen molecule, the Ti(II) part of the complex could be opened out to octahedral symmetry (Fig. 8). It is not yet possible to tell whether the nitrogen is end-on, as in the stable complexes (Section 4.2), or edge-on. Again by analogy with the polymerization of ethylene on titanium complexes, an edge-on formulation is chosen for these assumed reactive intermediates. *Cis*-migration of the lithium (or insertion of the N_2 at the site of the lithium) could lead to the azo structure. (This would explain the disappearance of the ESR signal on addition of N_2.) The –N=N– grouping is well known to be unstable in the presence of alkali metal naphthalide, and would immediately be reduced further to two N^{3-}. One of the two N^{3-} evidently remains attached to the Ti center and so blocks the path to further fixation of nitrogen.

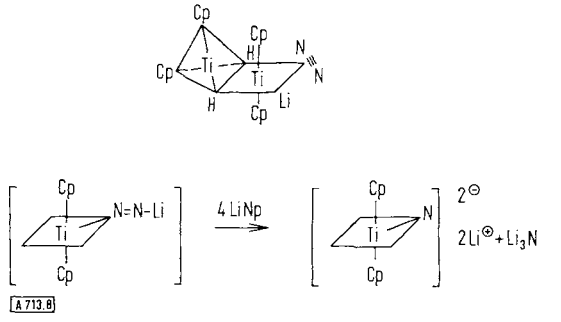


Fig. 8. Suggested mechanism for the fixation of nitrogen in the system Cp_2TiCl_2/LiNp. (The tetrahedral Ti(III) portion has been omitted from the bottom two complexes.)

As was mentioned, the fixation-reduction process in this system takes several hours. Since the ESR signal disappears rapidly on admission of N_2 and the reduction to the azo compound should also be relatively fast, the rate-determining step could be the supply of the active species from the equilibrium.

4.5. "Electron Reservoir" Complexes of Transition Metals

A somewhat different mechanism occurs if simple halides of the transition metals are used with lithium naphthalide instead of the bis(cyclopentadienyl) compound [22a]. This is shown by the fact that, under favorable conditions, two NH_3 molecules can be obtained per transition metal center in this case (Table 3). Thus one N_2 molecule is fixed per transition metal center; the active species cannot, therefore, be binuclear complexes.

The fixation-reduction process again takes a certain time, as can be seen from Figure 9. Particularly at 1 atm of N_2, the time taken appears to be of the same order of magnitude as for the system Cp_2TiCl_2/LiNp discussed in the last section.

Table 3. Fixation of nitrogen on reduced transition metal solutions, solvent THF [22a].

Salt	LiNp/metal	N_2 pressure (atm)	NH_3/metal
VCl_3	3	120	0.9
	5	120	1.2
	7	120	2.0
	10	1	0.9
$CrCl_3$	10	120	1.2
	10	1	0.4
$TiCl_4$ [a]	10	120	1.3
	15	120	1.7

[a] In toluene.

[44] *N. Hirota*, J. Amer. chem. Soc. *89*, 32 (1967).

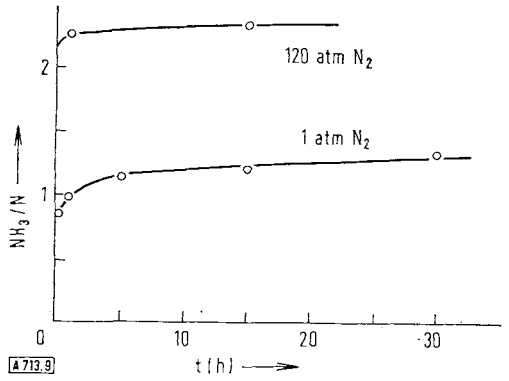


Fig. 9. Time-dependence of the N_2 fixation reaction in the case of the system VCl_3/LiNp [41].

ESR measurements show that in these systems the metal is reduced to the zerovalent stage and beyond. On addition of three reduction equivalents (Li/V = 3), the signal of the bis(naphthalene)vanadium(0) sandwich complex is observed in the reaction solution, and at higher Li/V ratios another signal, which can be assigned to a V(−II) species, is observed [45]. In the $CrCl_3$/LiNp system, it is found that as the Li/Cr ratio is increased, the ESR signal of bis(naphthalene)-chromium(I) appears first, and then that of bis(naphthalene)chromium(−I) [41]. Free LiNp can be detected in the ESR signal only above Li/M = 6 in both cases (M = metal). The intensity of the ESR signal, however, is still low in relation to the quantity of LiNp introduced. Evidently a further electron transfer occurs from LiNp to M(0), with formation of negatively charged M(−x) species, which are held in solution by the naphthalene ligands.

On hydrolysis of the reduced metal solutions, considerable quantities of hydrogen are liberated, as can be seen from Figures 10 and 11. The preparation and hydrolysis were carried out under argon in these experiments. (LiNp does not liberate hydrogen during the hydrolysis, but reacts to form dihydronaphthalene [46].)

It is significant in connection with the fixation of nitrogen that considerably less hydrogen is evolved if

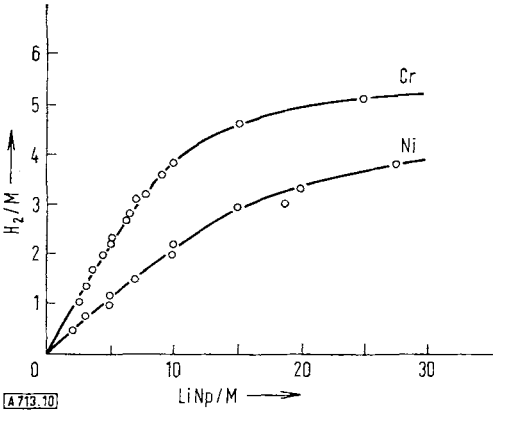


Fig. 10. Evolution of hydrogen during hydrolysis in the systems $CrCl_3$/LiNp (top) and $NiBr_2$/LiNp (bottom) [45].

[45] *G. Henrici-Olivé* and *S. Olivé*, J. organometallic Chem. *9*, 325 (1967).

[46] *G. E. Coates*: Organometallic Compounds. Methuen, London 1960.

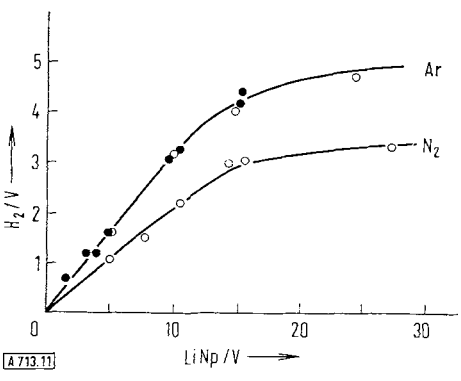


Fig. 11. Evolution of hydrogen during hydrolysis in the system VCl_3/LiNp; reaction carried out under argon (top) and under nitrogen (bottom).

● in dimethoxyethane; ○ in tetrahydrofuran [41].

the reduction is carried out under nitrogen (see Fig. 11; a similar observation was reported by *Shilov et al.* for the Grignard system [40]). This decrease in the quantity of hydrogen liberated does not, however, occur in systems that are not able to fix nitrogen, such as $NiBr_2$/LiNp (see Table 4).

Table 4. Hydrolysis of transition metal solutions reduced under argon or under nitrogen LiNp/metal = 10; T = 20 °C; 1 atm of N_2 [22a].

M	H_2/M under Ar	H_2/M under N_2	NH_3/M found
V	3.1	1.9	0.9
Cr	3.6	2.8	0.4
Ni	2.0	2.0	–

Information about the source of the gas evolved can be obtained by the use of heavy water. Figure 12 shows the results of the mass-spectroscopic analysis of the deuterolysis gases for the $CrCl_3$/LiNp system.

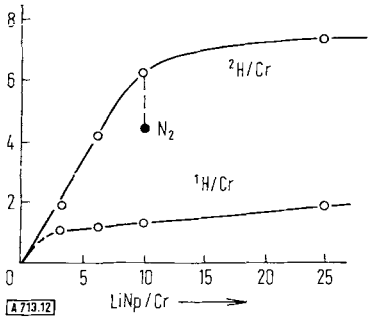


Fig. 12. Results of deuterolysis for $CrCl_3$/LiNp. ○: reduction under argon; ●: reduction under nitrogen [41].

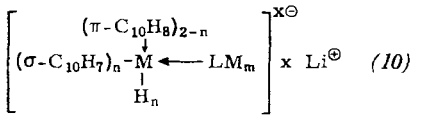
It can be seen that by far most of the gas evolved is deuterium; it must therefore have been formed by decomposition of the heavy water.

The fact that some hydrogen is liberated points to the presence of metal-hydrogen bonds. The number of hydrogen atoms per metal atom is in the neighborhood of 1 up to Li/M = 10, but increases slightly and appears to tend toward a limiting value of two.

Figure 12 also shows the results of a comparison experiment in which the reduction was carried out under

nitrogen, *i.e.* under conditions such that the system fixed nitrogen. It is found that the quantity of deuterium liberated decreases, but not the quantity of hydrogen.

From all these observations, the formulation *(10)* can be deduced for the nitrogen-fixing species.



(10)

The presence of naphthalene is shown by the ESR experiments. The presence of metal-hydrogen bonds is interpreted as resulting from the removal of H from π-bonded naphthalene and simultaneous transition into a σ-naphthyl-metal bond (cf. similar processes on an Ru(0)–Np complex studied by *Chatt et al.* [47]).

Solvent molecules (LM) must also be introduced, their number *m* being such as to satisfy the symmetry requirements of the metal in question. The hydrolysis experiments show that the complex can accept further electrons supplied by LiNp molecules These extra charges are presumably delocalized, particularly in the antibonding π orbitals of the aromatic ligands, and compensated for by Li^+ cations. The maximum number of these extra charges appears to be 6. This is shown by the deuterolysis experiments (Fig. 12), taking into account the well known fact that finely divided zerovalent Cr or V decomposes heavy water in accordance with

$$M^0 + 2\,{}^2H_2O \rightarrow M^{II} + {}^2H_2 + 2\,O^2H^{\ominus}$$

The fixation of nitrogen may be assumed to involve coordination of the N_2 molecule to the metal center, with displacement of a solvent molecule.

The extra charges are used to reduce the nitrogen in accordance with

$$N_2 \xrightarrow{6e} 2\,N^{3-}$$

Several complexes with different charges *x* are presumably present in equilibrium, but only one species (*e.g.* that with $x = 6$) is capable of attacking the nitrogen molecule. This would explain why the ratio NH_3/M can reach a value of 2 only when LiNp is present in a large excess. The supply of the active species from the equilibrium could again be the rate-determining step. Since the ratio NH_3/M cannot be increased above 2, it must be assumed that the reduced $N^{3\ominus}$ again remains in the complex, and is liberated only on hydrolysis.

5. Outlook

Nitrogen has evidently lost some of its eminence as an inert gas in recent years. On the one hand it is to be expected that the number of new stable complexes with N_2 ligands will grow steadily. On the other hand nitrogen has been reduced to $N^{3\ominus}$ under mild conditions (with regard to temperature and pressure) with strong reducing agents in aprotic solvents.

One might ask whether this can be expected to mean competition for the industrial processes for the production of ammonia. In view of the present price of NH_3, the answer to this must be no. However, the question as asked is wrongly phrased, since ammonia is only the industrial starting point for the chemistry of nitrogen. A more sensible question would be whether any competition is to be expected with the current processes for the production of amines, amides, nitriles, *etc.* In view of the outstanding progress that has been made in homogeneous catalysis on transition metal complexes in the course of the last 10–20 years, this possibility must be taken very seriously.

The $N^{3\ominus}$ stage attached to the transition metal is probably of no more value in this respect than the isolable stable N_2 complexes. If we may be allowed a (possibly somewhat daring) comparsion with olefin chemistry, a large number of stable complexes of olefins with transition metals are known, but these are not generally catalysts. The catalytically active intermediates formulated for reactions such as the oxo process, the Wacker process, cyclooligomerization of butadiene, Ziegler-Natta polymerization, *etc.*, on the other hand, in which the olefin is supposed to be coordinately bound to the transition metal center, have so far never been isolated.

Let us turn again briefly to the question of end-on or edge-on bonding. In all the stable complexes studied so far, the nitrogen is most probably attached end-on. However, edge-on attachment of N_2 molecules cannot be detected as easily as end-on attachment, which is indicated by the IR band at $\simeq 2100\ cm^{-1}$. The only relatively simple method of recognizing complexes of the edge-on type, apart from elemental analysis, would be from their Raman spectra. Who knows whether edge-on complexes have already passed through the hands of chemists without being recognized? Concerning the active species in the reduction process $N_2 \rightarrow 2\,N^{3-}$, the question of end-on or edge-on must necessarily remain open, since these intermediates cannot be isolated.

Concluding this report, it may be said that the investigation of the systems known at present has yielded some information about the interrelations between transition metal species and the nitrogen molecule. Above all, however, it has shown which directions lead to dead ends and which should be followed in further work.

We are grateful to Professor H. H. Zeiss, Monsanto Research S.A., who brought the interesting subject of the fixation of nitrogen to our notice, and to Professor J. Chatt, University of Sussex, for stimulating discussions.

Received: June 16, 1969 [A 713 IE]
German version: Angew. Chem. *81*, 679 (1969)
Translated by Express Translation Service, London

[47] *J. Chatt* and *J. M. Davidson*, J. chem. Soc. (London) *1965*, 843.

Phosphorus

From Elemental Light to Chemical Element

By F. Krafft[*]

Exactly 300 years ago in the city of Hamburg, a certain Hennig Brand, self-styled doctor medicinae, and chymist, discovered a strange substance in human urine, which was later called phosphorus (light bearer), a name then common to various luminous substances, and which created much excitement in the latter years of the 17th century on account of its properties. However, it was not Brand who profited from the discovery but others: Johann Daniel Krafft, Johann Kunckel, and Gottfried Wilhelm Leibniz, men who knew only too well how to exploit the weaknesses of the discoverer. "Cold fire", Brand's own name for the new substance, was originally regarded as elemental light or fire, and it was not until the conception of the antiphlogistic theory by Antoine Laurent Lavoisier that the proper position of phosphorus among the chemical elements was recognized. In fact, the element played a decisive role in the overthrow of the phlogiston doctrine, a little over one hundred years after its discovery and almost two hundred years ago.

1. The Year of the Discovery

In his paper 'Historia inventionis phosphori' [1], which was published in 1710, *Gottfried Wilhelm Leibniz* writes: "Inter inventa nostri saeculi non minimum habendum est phosphorus igneus . . ." "Not least amongst the discoveries of our time is phosphorus igneus, which differs from other substances in that it is nothing other than a hidden fire (ignis quidam tectus) that manifests itself in light and smoke and bursts into flames when rubbed. This discovery became public knowledge around the year 1677 (Id inventum circa annum 1677 prodiit . . .). . ."

Johann Daniel Krafft (Kraft, Crafft; 1624–1697), however, Councillor of Commerce to the Saxon elector at Dresden, had already demonstrated the substance, together with three other kinds of "phosphorus," at the court of the Grand Elector *Friedrich Wilhelm von Brandenburg* at Berlin on April 24, 1676, but without making any reference to the discoverer or to the origin of the substance. The demonstration is recorded by the Court Physician *Johann Sigismund Elsholz* (1623–1688) in a document entitled 'De phosphoris quatuor observatio' and dated May 20, 1676 [46]. In September 1677 the same *Krafft* informed *Robert Boyle* (1627–1691) that one of the samples of phosphorus he had received from *Brand* had continued to luminesce for two years [2].

At the same time, *Johann Kunckel* (1630–1703), one of the most highly esteemed "chymists" of the day, was also in possession of this substance. A friend of his, *Georg Caspar Kirchmaier* (1637–1700), Professor of Rhetoric at Wittenberg, gives an account in his short treatise 'Noctiluca constans et per vices fulgurans, diutissime quaesita, nunc reperta', the foreword to which is dated September 11, 1676 (Chapter 3: De noctiluca aliqua constanti):

"Almost six months have passed since he (*i.e. Kunckel*) first revealed to me that he possesses the 'eternal light' . . . I will not say how long this skilled man spent in collecting and preparing the starting material, but will be content to have mentioned that when he repeated the work – not before July 25 – he obtained but little more than half an ounce, in spite of the fierce fire which was kept burning for many hours."

Kunckel himself reports later in his 'Collegium physico-chymicum experimentale' [3], which was published posthumously, that he learned of *Brand*'s phosphorus while staying at Hamburg just a few weeks after the discovery of *Balduin*'s phosphorus. He states, incorrectly, that the latter, a calcined calcium nitrate, was discovered in the year 1677. In fact, the Saxon magistrate *Christoph Adolph Balduin* (1632–1682) had already reported on his discovery in 1674 in 'Miscellanea curiosa medico-physica Academiae naturae curiosarum sive Ephemerides medico-physicae Germaniae' [4] and written a special treatise in the following year [5]; in neither case, however, does he disclose the method of preparation.

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[1] *G. W. Leibniz*: Historia inventionis Phosphori. Miscellanea Berolnensia ad incrementum scientiarum *1*, 91–98 (Sumptibus J. Ch. Papenii, Berlin 1710).

[2] *R. Boyle*: A Short Memorial of some Observations made upon an Artificial Substance, that shines without any precedent Illustration (Sept. 1677). Lectures and Collections made by Robert Hooke, Secretary of the Royal Society, London 1678, p. 57–66 (reprinted in *R. T. Gunther*: Early science in Oxford, Vol. VIII. Oxford University Press, Oxford 1931, p. 273–282).

[3] *J. Kunckel*: Collegium physico-chymicum experimentale oder Laboratorium Chymicum. Hamburg-Leipzig 1716 (²1722), p. 660–665.

[4] *Ch. A. Balduin* in: Miscellanea curiosa medico-physica Academiae naturae curiosarum sive Ephemerides medico-physicae Germaniae. Annus quartus et quintus 1673/74, p. 121.

[5] *Ch. A. Balduin*: Aurum superius et inferius aurae superioris et inferioris hermeticum et phosphorus hermeticus sive magnes luminaris. Frankfurt-Leipzig 1675.

Thus the seventeenth-century printed sources cited here suggest early 1676 as the date of the discovery of phosphorus igneus, as it was called by *Leibniz*. Even in 1784, *Lorenz Crell* referred to these data in a note accompanying his paraphrased translation of *Leibniz*' 'Historia'[6]. He had, however, understood the year 1677 given by *Leibniz* to be the year of the discovery, for he paraphrases the passage quoted above as: "Phosphorus, that remarkable invention of our century, was discovered in 1677." (The same conclusion is reached by *J. S. T. Gehler*[7], *J. C. Fischer*[8], and others.) On the basis of the sources cited, *J. R. Spielmann* had previously, in 1766, decided in favor of the year 1674 or 1675 for *Brand*'s discovery[9], followed shortly by *J. C. Wiegleb*[10].

Thus it is hardly surprising that to our time these years are continually given as the supposed date of the discovery of phosphorus: *E. Färber (Farber)*[11,12], *J. R. Partington*[13]; *A. Wolf*[14] on the other hand writes: "the dates given vary from 1667 to 1674", and simply takes an average: "sometimes about 1670" (with which *P. Walden*[15] also concurs). Even the authors of the historical section of the latest (1965) edition of 'Gmelins Handbuch der anorganischen Chemie'[16] still shared the opinion of *Spielmann* and *Wiegleb* stating: "that ... the years 1674 and 1675 come into question as the date of the discovery of phosphorus."

However, "it is in the interest of science that the history of memorable discoveries (historia inventionum memorabilium) be handed down accurately", as *Leibniz* states in the opening passage of his 'Historia'. In this treatise *Leibniz* himself actually sets the date of the discovery as 1669, provided that one correctly interprets the information that he gives. Unlike *Kunckel*, who lost no opportunity to play down, in a rather ungentlemanly fashion, the credit due to *Brand* in favor of his own claims to the discovery, or at least to the independent rediscovery of phosphorus, and on whose information, both written and oral, all other contemporary versions of the history of the discovery are directly or indirectly based, *Leibniz* takes great pains to provide an objective report, in spite of later differences with *Brand*. He was well acquainted with the Hamburg chymist, recognized also by *Krafft* and *Kunckel* as the first discoverer, or at least better acquainted than those who had met him during a single visit to Hamburg, for he corresponded with him over a considerable period of time, visited him in Hamburg, and on two occasions was able to persuade him to visit Hanover for a relatively long time to prepare phosphorus. Moreover, *Leibniz* himself made no claim to the discovery.

On April 30, 1962, *Wilhelm Homberg* (1652–1715) presented a report to the Paris Academy dealing with the discovery and the purported rediscovery of phosphorus by *Kunckel*. In *Leibniz*' opinion, this paper contains several grave errors which he immediately critized, apparently in vain for no correction ever appeared. Thus, "Itaque ne veritas rei gestae, non multis fortasse hodie nota, intercedat" he published his 'Historia inventionis Phosphori'. Before proceeding to correct the various errors he presents a Latin version of Homberg's report[17]:

"Prima inventio huius Phosphori casui debetur, ut multa alia pulchra inventa. Chymista quidam Germanus, cui nomen *Brand*, Hamburgi degens, homo obscurus, humilis originis, ingenio moroso et phantastico, et in omnibus, quae agebat, mysteriosus, materiam hanc luminosam aliud quaerens invenit. Vitrariae artis deditus erat a iuventute, sed hanc deseruerat, ut lapidi philosophico vacaret, cuius spes animum eius invaserat. Cum ergo sibi persuasisset, secretum Lapidis in praeparatione urinae consistere, diu et multipliciter in ea laboravit frustra: tandem anno 1669 post fortem urinae destillationem in recipiente invenit materiam lucidam, quae postea Phosphori nomen obtinuit. Hanc monstravit amicis quibusdam, et inter alios *Kunkelio* Chymistae Electoris Saxoniae, sed cavit, ne quid diceret, inde compositio cognosci posset, obiitque secreto suo nemini communicato. Post obitum eius *Kunkelius* tam pulchrum arcanum perire non aequo animo ferens, resuscitationem inventi aggressus est, et considerans *Brandium* tota vita in urina laborasse, suspicatus est, in ea Phosphorum esse quaerendum. Huic ergo operam dedit, et post pertinacem quadriennii laborem, tandem, quod quaerebat, invenit. Non aeque mysteriosus fuit ac *Brandius*, arcanum ne nonnullis communicavit circa annum 1679. In Gallia et Anglia *Kraftius* Medicus Dresdensium, inventor huius Phosphori habetur, quoniam eum primus illuc attulit. Sed revera non nisi dispensator eius fuit, quem a *Kunkelio* acceperat, ut eruditis exteris ostenderet. Immo ignorabat compositionem *Kraftius* tunc, cum itinera sua obiret."[*]

[6] *L. Crell*: Lorenz Crells Neues Chemisches Archiv, Vol. 1, 2. 213 (1784).

[7] *J. S. T. Gehler*: Physikalisches Wörterbuch oder Versuch einer Erklärung der vornehmsten Begriffe und Kunstwörter der Naturlehre ... 3. Theil. Schwickertscher Verlag, Leipzig 1790, p. 481.

[8] *J. C. Fischer*: Physikalisches Wörterbuch oder Erklärung der vornehmsten zur Physik gehörigen Begriffe und Kunstwörter ... Dritter Theil. J. Chr. Dieterich, Göttingen 1800, p. 872.

[9] *J. R. Spielmann*: Institutiones Chemiae. 2nd Edit., Strasbourg 1766, p. 223.

[10] *J. Chr. Wiegleb*: Geschichte des Wachstums und der Erfindungen in der Chemie, in der neuern Zeit. Ersten Bandes erster Theil, von 1651 bis 1700. F. Nicolai, Berlin and Stettin 1790, p. 39–42.

[11] *E. Färber*: Die geschichtliche Entwicklung der Chemie. J. Springer, Berlin 1921, p. 56.

[12] *E. Farber*: The evolution of chemistry. A history of its ideas. methods, and materials. Ronald Press Co., New York 1952, p. 83,

[13] *J. R. Partington*: A short history of chemistry. 3rd. Edit. MacMillan, London 1957, p. 62.

[14] *A. Wolf*: A history of science, technology and philosophy in the 16th and 17th centuries, Vol. 1. 2nd. Edit. MacMillan, New York 1959, p. 348.

[15] *P. Walden*: Chronologische Übersichtstabelle zur Geschichte der Chemie von den ältesten Zeiten bis zur Gegenwart. J. Springer, Berlin 1952, p. 17.

[16] Gmelins Handbuch der Anorganischen Chemie. 8th Edit. System-Nummer 16: Phosphor; Teil A. Verlag Chemie, Weinheim/Bergstr. 1965, p. 8.

[17] Cf. ref. [1], p. 92.

[*] "Like so many other beautiful discoveries (inventa), the discovery of this phosphorus was due to a coincidence. A German chemist named *Brand* who lived at Hamburg, an unknown man of humble origin, of a morose and fanciful nature, and secretive in all that he did, discovered the luminous substance while searching for something else. From his youth he had occupied himself with the art of glassmaking but had forsaken this art in order to devote time to the philosopher's stone, upon which he had set his hopes. When he reached the conclusion, that the secret of the stone consisted in the treatment of urine, he frequently spent long periods working vainly with the latter. At length, in the year 1669, after vigorous distillation of the urine, he found a luminous material in the receiver which was later given the name phosphorus. This he showed to some friends and, among others,

If this report is compared with information given by *Kunckel* in his own works on the discovery of phosphorus and with that contained in letters to and from *Leibniz* and *Brand* – particularly in the correspondence between *Brand, Leibniz, Krafft*, and *Kunckel* of 1676 to 1679, which was first cited by *H. Peters* in 1902 [18] and then published in its entirety in 1916 [19] it becomes clear that *Homberg* must have heard the details from *Kunckel* himself. *Homberg* also states that he visited *Kunckel*, who had been appointed "Chymist" in the service of the Grand Elector in 1679, in Berlin, and received from him the procedure for the preparation of phosphorus [20]. Thus the mere fact that the name *Brand* and the year 1669 can be traced back to *Kunckel* imparts credibility to these statements. Moreover, *Leibniz*' detailed corrections – the death, the character, and the ability of *Brand*, and concerning *Brand*'s reports to *Krafft* and *Kunckel* – which follow the reprinted passage, make no further mention of the date. It must therefore agree with that which *Brand* had told him (*Kunckel* too can only have heard it from *Brand*), and the fact that *Brand* himself had told *Leibniz* of his discovery is clear from several details that are retold only by *Leibniz*, and particularly from the report that the motivation for his investigations on urine came from a printed work on alchemy: "Inciderat Brandius in processum quendam chymicum in libro typis edito, exantem, qui ex urina parare docebat liquorem aptum (si credimus) particulae argenti in aurum muturandae" [21].

Since phosphorus igneus remained unknown outside Hamburg until 1676, when *Krafft* and *Kunckel* were shown it by *Brand* and given samples, and since no earlier date is given in connection with or by *Krafft* – who only occasionally failed to mention the name of the discoverer but never claimed to be the same – or by *Kunckel*, there was no reason for *Brand* to subsequently pre-date his discovery. So long as no new contradictory sources become available there appears to be little reason for scepsis concerning *Brand*'s claim to have discovered the substance which he called "my fire" or "cold fire" in the year 1669, exactly three hundred years ago.

Kunckel, Chymist to the Saxon Elector, but took care to say nothing that could reveal the composition, and died without having told anyone his secret. After his death, *Kunckel*, who was not indifferent to the loss of such a beautiful secret, set about the resuscitation of the discovery; and considering that *Brand* had spent his whole life working with urine, he suspected that phosphorus was to be found in this substance. He therefore directed his attention to the latter, and, after four years' intense work, discovered that which he sought. He was not so secretive as *Brand* and he made the secret public around the year 1679. In France and in England, *Kraft*, a Dresden physician, is held to be the discoverer of phosphorus since it was he who first took it to those countries. In fact he was merely the distributor of the phosphorus that he had received from *Kunckel* to show to foreign scholars. *Kraft* was not even aware of the preparation when he undertook his journeys."

[18] *H. Peters*, Chemiker-Ztg. *26*, 1190 (1902).

[19] *H. Peters*, Arch. Gesch. Math., Naturwiss. Techn. *7*, 85 (1916).

[20] *W. Homberg*, Manière de faire le phosphore brulant de Kunckel. Mémoires de l'académie royale des sciences à Paris, depuis 1666, jusqu'à 1699 *10*, 57 (Paris 1730).

[21] Cf. ref. [1], p. 93.

The year 1677 (circa annum 1677) given by *Leibniz* does not refer to the discovery of phosphorus but to the disclosure of the discovery (prodiit!) – and outside Hamburg this actually took place in the year 1676/1677. *Leibniz* himself first became acquainted with phosphorus during a demonstration to the Hanoverian court by *Krafft* in mid-1677, and he immediately reported what he had seen in 'Journal des Savants' [22]. There he states: "...if the liquid is placed on any object outside the phial then the light disappears within a short time ..., but if it remains in the closed phial it is preserved for several years. *And it has actually been kept for two years*", *i.e. Leibniz*, too, recognized the discovery as being of an earlier date. (The year 1669 is also given in [7, 8, 23–32], but in no case does the author give any proof.)

2. The Discoverer

In the 17th and 18th centuries the substance known by *Leibniz* as "Phosphorus igneus", "Pyropus" (Greek: fiery-eyed), and "Phosphorus κατ' ἐξοχήν" [33] was given a whole variety of names, some of which referred to its properties, while others were intended to refer to the supposed discoverer. Thus *G. C. Kirchmaier* [34] calls it "*Kunckel*'s phosphorus", a name that rapidly found general acceptance and soon became the only name in common use, since in his publications *Kunckel* had claimed [35] as his own the discovery, or at least the rediscovery and the first planned preparation, while enjoying the support of his friend *Kirchmaier*, and later also that of *Homberg* (1692) [20], *J. H.*

[22] *G. W. Leibniz*: La phosphore de M. Krafft ou Liqueur et terre secche de sa composition qui jettent continuellement de grands éclats de lumiere. Le Journal des Scavans du Lundy 2. Aoust, 1677. Paris, p. 244.

[23] *J. S. T. Gehler*: Physikalisches Wörterbuch; neu bearbeitet von *Brandes, Gmelin, Horner, Muncke, Pfaff*, Vol. 7, 1. Abth. E. B. Schwickert, Leipzig 1833, p. 474 (*Gmelin*).

[24] *H. Kopp*: Geschichte der Chemie. 4 Bde. F. Vieweg & Sohn, Braunschweig 1843–1847. Vol. 2, p. 233; cf., however, Vol. 3, p. 327ff.

[25] Cf. ref. [18], p. 1191.

[26] Cf. ref. [19], p. 88.

[27] *W. Herz*: Grundzüge der Geschichte der Chemie. Richtlinien einer Entwicklungsgeschichte der allgemeinen Ansichten in der Chemie. F. Enke, Stuttgart 1916, p. 38.

[28] *E. v. Meyer*: Geschichte der Chemie von den ältesten Zeiten bis zur Gegenwart. 4th Edit. Veit u. Co., Leipzig 1914, p. 133.

[29] *H. Valentin*: Geschichte der Pharmazie und Chemie in Form von Zeittafeln. 3rd Edit. Wiss. Verlagsgesellschaft, Stuttgart 1946, p. 37.

[30] *E. Pilgrim*: Entdeckung der Elemente mit Biographien ihrer Entdecker. Mundus-Verlag, Stuttgart 1950, p. 78.

[31] *A. J. Ihde*: The development of modern chemistry. Harper and Row, New York 1966 (1964), p. 747.

[32] *E. Farber*, U.S. nat. Museum, Bull. *240*, 177 (1966) (not available to the present author).

[33] Cf. ref. [1], p. 92.

[34] *G. C. Kirchmaier*: Nocticula constans et per vices fulgurans, diutissime quaesita, nunc reperta. Wittenberg 1676, p. 12.

[35] *Kunckel*'s report [3] (Historia von dem Phosphoro, welchen einige Lumen constans genennet) is reprinted in parts in ref. [16], p. 13, as an English translation by *T. L. Davis*, J. chem. Educat. *4*, 1105–1110 (1927).

Cohausen[36], and *Hellot* (1737) – in spite of *Leibniz'* justified opposition – and most of the older versions of the discovery of phosphorus. *Leibniz* comments[37]:

"But it is all the more amazing that he [*i.e. Brand*] is reported dead at the time when *Krafft* and *Kunckel* were spreading the news of the discovery of phosphorus throughout the world by the spoken and written word, and that *Kunckel* should have reawakened the art that had been lost with the original discoverer, while it is beyond doubt that *Kunckel*, while visiting *Brand*, had been initiated in the art by the latter, and that *Brand* lived for a long time and complained about *Kunckel*... But when *Kunckel* had returned home and made not few mistakes in the manipulations (in enchiresi), he was for a long time unable to prepare the phosphorus and sent letters of complaint to *Brand*, which I have seen, and in which he lamented that he had not told him the secret sufficiently openly. However, *Brand*, who regretted that he had been so thoughtless as to divulge his secret, refused to show the erring *Kunckel* the way. In the meantime, *Kunckel* corrected his mistakes himself, whence arose the pretentiousness (praetensio praetextusque), to dare to pose as the discoverer wherever he went, about which *Brand* complained bitterly."

Fortunately, *Leibniz* did not return *Kunckel*'s letters to *Brand* to the latter so that the accuracy of *Leibniz'* information can be confirmed to this day, and likewise *Kunckel*'s untruthfulness when he claimed (1713)[3,35] to have given *Brand* no promise of secrecy. While still on the homeward journey *Kunckel* wrote the following lines to *Brand* from Magdeburg in March, 1676[38]:

"Salve! Insonders hochgeehrter Doctor, zuverlässiger, wehrter Freundt, ehr wird sich wohl entsinnen, was wir mit einander abgeredet, nehmlich dass ehr mihr das lumen in einem Glase wollte nachschicken, nu sehe der Herr zu, dass ehrs in ein fein Cristallglas kricht und sende es mit dem ersten, dass ichs seh, dan ich habe darauf was herrlichs ausgesonnen..." [*]

At Wittenberg he then attempted to prepare phosphorous according to the information given to him by *Brand*; apparently without success for on June 25, 1676 he wrote[39]:

"... Wie angenehm mir des Herrn Doctors Brieflein von 3. Juni gewesen, kann ich nicht genug schreiben. Sehe daraus dessen gute Zuneigung, ehr had dakegen sich zu versichern, wass ich ihm so theur zu geschworen, dass ichs ehrlich halten wil, lebe auch der Hoffnung, der Herr Doct. wirt mir sein Feur getreuhlig geben; die Entschuldigung, dass ehrs der Feder nicht zu trauen darf, davohr trage ehr keine Sorge; der Herr Doctor schreibe so, ehr nehme die bewusste Materie, so oder so vihl, setze dieses darzu und mache es so, wehr wil das verstehn... Ich bitte dem Herrn, ehr solle mihr als ein gutter Freunt trauen, gebe es keinen Menschen mehr und lass mihr sorgen; so verne ehr es mir communicirt, wil ich, so wahr ich wil teihl an Gottes Gnade haben, so mit ihm handeln, dass ehr und die Seinigen sollen mihr Dank wissen, aber ehr muss mihr ohn Massgebung folgen... Der bewussten Matterie habe ich ein ziemlich Teyl. Habe es 2 mahl destilliert, aber kein Feuer gekricht. Bitte der Herr lasse meine Mühe nicht umbsonst sein; so baldt ein Schif geht, wil ich ihm mit Weitzen Mehl versehn; so er verlangt dass zu haben, womit ehr den Corallen die Tinctur extrahieren kann und in eine Massa als Pillen gebrauchen kan, wil ich ihm senden, was ehr von chymischen Medicamenten verlangt. Schreibe ehr mihr, weihl ich ohn dem hier eine Collectio chymicorum halte; muss ich sie doch machen und stehn mir übern Halse. Wil mihr der Herr eine kleine Probe von seinem Feuer schicken, nehme ichs zu Dank an und ich erwartte des Herrn Antwort und Communication. Befehl ihm sambt seiner Liebsten und kleinen Dochter in den Schutz des Höchsten... P.S. Der Herr Doctor schreibe mihr, was ich ihm von dem Provit, den ich mache, geben sol, oder wenn ich mehr mache, als so und so vihl, wie ihm deucht, dass ehr mit diesen wil vergnüget sein und wan ich et wem bei einem Grossen Herrn kohme, da ein Stück Gelt vohr die Communication kriegen könnte, die dem Herrn anständig und ich möchte wegen Ablegenheit seinen Consens nicht kriegen können, was ehr haben wil, dass ichs frey meines Eydes und Gewissen ohnbeschedigt thun mach, nehmlich wenn ichs einen communicirt. So ichs diese Post kriege und so vil davon gemacht als mir deucht, so wil ich in Persohn nach Florentz uns beiden zum Nutz damit; aber der Herr seh sich vohr, sehe nu wenigs nicht an und gebe nicht mehr hiervon; schreibe mihr der Herr cito, ich will allen den nachkommen, denn in Deutschland verlohnt es der Mühe nicht." [**]

However, *Brand* does not seem to have been inclined to give *Kunckel* further information regarding the preparation, in spite of the latter's promises. He had already heard the essential facts – indeed, he expresses in no uncertain terms his concern that Brand might tell others just as much – and deviated from *Brand*'s procedure only in that he mixed the urine extract with sand prior to distillation[40]. He than met with success. Such a practice, however, would seem to have been common enough in those days, for *Robert Boyle* adopted it immediately[41] once he had heard from

[36] *J. H. Cohausen*: Lumen novum Phosphoris accensum. Amsterdam 1717, p. 163.

[37] Cf. ref. [1], p. 93.

[38] Cf. ref. [18], p. 1196.

[*] "Salve! Most honorable Doctor, trusted and esteemed friend, you will no doubt remember our agreement, namely that you would send me the "lumen" in a glass. Now see that you get it into a suitable crystal glass and dispatch it soon, so that I can see it, for I have thought of something wonderful to do with it..."

[39] Cf. ref. [18], p. 1196.

[**] "I cannot say enough how pleased I was to receive your letter of June 3. In it I perceive your good will and can assure you that I will honestly keep that which I have sworn to you. I hope that you will give me your fire; the excuse that you did not dare to write it down should cause you no uneasiness. You should write it thus: You take the known material, so much, add another substance, and proceed thus; who will understand that ...? I bid you to trust me as a good friend, give it to no other people, and let me arrange the matter. If you tell it to me, then I – as sure as I wish to partake of God's grace – will behave in a manner such that you and yours will be grateful to me – but you must follow me unconditionally ... I possess a considerable amount of the known material; I have distilled it twice, but not obtained any fire. I ask you so that my efforts may not have been in vain. As soon as a ship departs I shall send you wheat flour. If you wish to have that with which you extract the tincture from coral and can make pills of the substance, then I shall send you all the chemical medicine that you desire. Write and tell me since I have here a collectio chymicorum as it is; I have to look after it nevertheless and it is beyond that which is sufficient. If you send me a small amount of your fire I shall gladly accept it. I expect to hear your answer and communication. I commend you and your dearest one and little daughter to the care of the Almighty ...

P.S. You should inform me how much I should give you of the profit I shall make; or if I obtain more then a certain sum you should tell me how much you require in order to be satisfied, likewise if I show it to an important man and can receive as much money for its communication as he deems fit, that without your consent, if I tell it to anybody I should like to do so while no longer bound by my oath and without hurting my conscience. When I have received this information by the next post and have done as much as I think proper, then I shall journey to Florence myself to our mutual benefit. But you should be certain that you give none of it to anybody else. Write to me soon and I will do so anyhow, because in Germany there is no use whatsoever."

[40] Cf. ref. [16], p. 25ff.

[41] *R. Boyle*: The Aerial Noctiluca, or new Phaenomena and a Process of a Factitious self-shining Substance. London 1680.– The Works of the Honourable Robert Boyle. New edition. Vol. 4, London 1772, p. 379–404.

Krafft, "...that at least the principle matter of his phosphorus was something that belonged to the body of man" [42] – without proceeding to make any claim to the discovery or rediscovery (thus *e.g. P. Walden* [15] still for *Kunckel* and *Boyle*), although he was the first to actually examine phosphorus closely and to find, *inter alia*, that "dry phosphorus" only luminesces in contact with air, whereas his predecessors had all spoken of an "eternal" light or fire. Moreover, *Boyle*'s procedure was the first to be published [43].

Krafft, whose name was also occasionally given to phosphorus, never made any claim to the first discovery or to any rediscovery himself. He was simply faster and more clever than *Kunckel* (and, of course, than *Brand*), from whom he first learned of *Brand*'s phosphorus in early 1676: He was able to start negotiations with *Brand* before *Kunckel* and "as he openly admitted, to purchase the art from *Brand* for money" [44]. It is doubtful whether he ever succeeded in the preparation himself; he used the samples he received as exhibition pieces and journeyed through various countries demonstrating them, together with other "phosphori", at Royal Courts and before Scientific Societies (as *Kunckel* also suggested to *Brand*), and advertised the "phosphorus" extensively in journals [45]. (The demonstrations at the Berlin Court, whose description by *Elsholz* represents the first publication on the new phosphorus, and also first gives this name to the new substance [46], at the Hanoverian Court where *Leibniz* was Hofrat, and before the Royal Society at London have already been mentioned.) Nevertheless, it was through *Krafft* that phosphorus became widely known – and it is indeed most fortunate that *Kunckel* and he ever came to know of its discovery (see below).

Although *Krafft* appears to have made no mention of the discoverer at Berlin, he named *Brand* as the discoverer at both Hanover – cf. *Leibniz*' letter of recommendation to the Royal Society [47] – and London [48]. And since even Kunckel did not dare to deny *Brand* all credit for the discovery, the latter became almost undisputedly [49] recognized as the discoverer of phosphorus in the late 18th century, when, for topical reasons (see below), interest in the history of the discovery was revived.

[42] Cf. ref. [41], p. 382.

[43] Cf. ref. [16], p. 27.

[44] *G. E. Stahl*: Experimenta, Observationes, Animadversiones CCC Numero, Chymicae et Physicae. Berlin 1731, p. 392.

[45] Cf. *G. W. Leibniz*: Sämtliche Schriften und Briefe. Erste Reihe: Allgemeiner politischer und historischer Briefwechsel, Vol. 2. O. Reichl, Darmstadt 1927, p. 392.

[46] *J. S. Elsholz*: De phosphoris quatour observatio. Berlin 1676, p. 1–6.

[47] Cf. ref. [18], p. 1197.

[48] Cf. ref. [41], p. 382.

[49] *H. E. Fierz-David* represents an exception among modern authors. In his 'Die Entwicklungsgeschichte der Chemie'. 2nd Edit. Birkhäuser, Basel 1952, p. 147 (1945, p. 146), he states: "His [*i.e. Kunckel*'s!] most important contribution was that he first [?] prepared elemental [?] phosphorus by ignition of evaporated urine with charcoal [?]. He [?] called the substance phosphorus ..."

Earlier attempts [50] to trace the discovery of phosphorus to a date previous to *Brand* and 1669, and even back to antiquity have been finally refuted by *Partington* [51] and *Weeks* [52].

Little is known about the discoverer *Hennig* (*Heinrich, Hennig*) *Brand* [53]; not even approximate dates are recorded for his birth and death. According to *O. Sperling*, he attempted, in 1688/1689: "bei Schipbek in dem Berge mit etzlichen Soldaten der Stadt, so er bedungen, zu graben nach einem allda verborgenen grossen Schatze, wovon er Bericht hatte bekommen, und hatte dazu von dem Herzog von Holstein *Christian Albrecht*, der sich zu Hamburg aufhielt, öfters und inständig darum angehalten, Zulassung erhalten ... Fing deswegen an zu graben mit Wünschelrute und anderem Zubehör und Zusehern aus der Stadt bei Tausenden ... Derselbe Chymikus schreibt ihm [d.i. sich] zu, dass er der erster gewesen, der ex spiritu urinae den Phosphor, wie es die Chymiker nennen, wann der Spiritus geschüttelt, feurig scheint, zuwege gebracht ..." (September 1688) [54] "Es hatte ein Schmied einige Nachricht davon erhalten, dass vor Jahren ein Fuhrmann, der Sand führte, wie er am selben Ort gegraben, einen Beutel mit Dukaten gefunden, welches ihnen anzeigen machte, daß noch mehr vorhanden sein müsste, und gruben darauf fort, weil der bemeldete Chymikus und der Schmied in Gesellschaft mit einander getreten, da der dann der Chymikus *Brand*, der sich Doctor nennen liess, bisweilen mit seinem sammeten Rock die Zeche an den Wirth bürgen werden müssen, und auch von den Soldaten, die gegraben hatten, und ihre Bezahlung von ihm nicht erhalten können Schläge mit Scheltworten hat bekommen" [*].

[50] Cf. [16], p. 2–6; *G. Landgrebe*: Über das Licht. Marburg 1834.

[51] *J. R. Partington*: A history of Greek Fire and gunpowder. Heffer and Sons, Cambridge 1960.

[52] *M. E. Weeks*: Discovery of the elements. 7th Edit., J. chem. Educat., Easton, Pa. 1967.

[53] The most important references are [3] (p. [35]), [1], where [20] is essentially corrected, as well as the correspondence *Brand-Leibniz-Krafft-Kunckel* [18, 19]; the best summary is to be found in [16], p. 9–12 (to which the reader is referred for detailed references).

[54] *O. Sperling*: Hamburgische Chronik (manuscript Royal Library Copenhagen), Vol. VI, p. 329. Cited after *R. Benzian*: Henning Brand. Mitt. Verein für Hamburgische Geschichte *8*, 253 (1902/1904), p. 267ff.

[*] "... to dig for a great treasure of which he had heard near Schipbek in the mountain with some soldiers of the town who he had contracted, and for which he had obtained permission after frequent and urgent application, from the Duke of Holstein, *Christian Albrecht*, who stayed at Hamburg ... Began digging with the aid of a divining-rod and other equipment, and spectators from the town of Hamburg by the thousand ... The same chymist claims to be the first to have obtained ex spiritus urinae, phosphorus, as it is called by chemists, because the spirit appears fiery when shaken ..." "A certain smith had heard that many years ago, a certain carrier, who transported sand, had dug at the same spot and found a purse containing ducats, which made them think that more must be hidden, and continued digging, because the above chymist and the smith had become acquainted, and since the chymist *Brand*, who called himself doctor, had to surrender his velvet coat to the host as surety for the bill and was unable to pay the soldiers who had dug, he received blows and curses." (Spring 1689 [55]) – In 1710, *Leibniz* wrote [56]: "Indeed, as I have heard, he was still alive in the year 1692, when these [*i.e. Homberg*'s] stories were being circulated, and I do not know to this day whether he is dead." – A search in Hamburg archives has so far brought no further details to light.

It is not even known whether *Brand* was born at Hamburg; all we can be certain of is that he worked in this city between 1669 and 1692. The fact that he used low German in common speech, as *Kunckel* disparagingly reported, certainly suggests a North German origin [57]. As a young man *Brand* served as an officer who had worked his way up from humble beginnings. During the period given above he was married to an originally wealthy widow, who had a son by her first marriage and later bore *Brand* a daughter. He practised as a physician and dealt in chemical medicaments, most of which he probably made himself (cf. *Kunckel*'s letter cited above). Although he called himself doctor medicinae, and is also referred to as such by *Leibniz* and in the apparently friendly letters of *Kunckel*, it is doubtful whether *Brand* had been able to complete a course of study in medicine. In any case, his name is not to be found in the list of members of the Hamburg Collegium medicum [57]. Some doubt also surrounds where *Brand* had obtained his extensive "chemical" and metallurgical knowledge, to which *Leibniz* attests in high degree, and which – if we ignore *Brand*'s own statements – also *Krafft* and *Kunckel* were compelled to recognize.

From *Leibniz*' reports to the Duke of Brunswick-Lüneburg and from the correspondence between him, *Brand*, and *Krafft*, we come to know *Brand* as a readily excitable, but also easily soothed personality, as a person who was full of often adventurous plans and ideas, of which he often failed to realize the significance and value [57]. *Leibniz* considered him to be the right man to carry out the process of the "secretum" twenty times a week in the smelting works of the Harz mountains, and in a report to the Duke characterized him in the following way:

"Dr. *Brand* is unable to judge his own capabilities, or to assert himself. Not that he does not often indulge in fanciful and conceited talk, but, like all men, he has a character of his own. He is easily led, lacks a developed power of judgment, and leads a disorderly life, but he is quick to act and an extremely skilled worker ... I have often noticed that he makes a great bustle about trivialities but makes little fuss about things that deserve it. He is always looking for great secrets and fanciful things instead of realizing that he could live better from that which he has already accomplished."

These words seem to portray *Brand*'s character admirably; in any case, other reports – such as the futile treasure hunt involving tremendous effort but no money, so that after the failure of the venture the contracted soldiers had to make up for their trouble with blows and curses – and statements made by *Brand*, of which *Leibniz* could then have had no knowledge, harmonize with this picture. In general, it appears that *Brand* was always short of money – his wife's capital was soon spent on alchemical experiments; *Leibniz* promised to pay his debts to the City of Hamburg – and that in spite of his large income as physician, which still remains when deductions are made from the figures contained in his letters to *Leibniz* since they may represent an attempt to obtain more money for his household at Hamburg and as compensation for loss of income during his visit to the Duke at Hanover.

During an official journey to Hamburg, *Leibniz* had visited *Brand* and made an agreement, subsequently endorsed by the Duke, that the latter tell *Leibniz*, who was committed to secrecy, about the preparation of phosphorus and continually keep him informed regarding his chymical experiments. *Leibniz* then insisted that *Brand* immediately accompany him on the return journey to Hanover, since there was a very real danger that *Johann Joachim Becher* (1635–1682) would try to secure *Brand*'s information for a better price. In fact, *Becher* was most interested in *Brand*'s alleged "secretum" for the transmutation of silver to gold, which *Leibniz* also wished to reserve for his Duke, should it prove successful. By various intrigues he had been able to keep *Brand* unaware of *Becher*'s offer. It is therefore understandable that *Brand* felt cheated – for a second time after his discovery of "cold fire", whose value he had not recognized, had been commercialized by others – when he eventually heard of the offer, and from then on his relationship to *Leibniz* became cooler and cooler, particularly when, after the death of Duke *Johann Friedrich*, the Hanoverian Court failed to fulfil its part of the agreement and various other promises.

Meanwhile, at Hanover, *Brand* set about the preparations for the large-scale manufacture of phosphorus from human urine, to be provided by the local garrison (there are reports of some 100 tons, corresponding to about 13140 liters), and told *Leibniz* the secret of the process, as agreed. When the phosphorus had been made, *Leibniz* immediately sent a sample to *Christian Huygens* at Paris and wrote the following words to the Duke of Chevreuse in December 1778: "At last I have obtained the procedure; I am now the fourth to possess it."

Brand remained at Hanover for five weeks and on his return he complained about the slow and incomplete payment he had received. Nevertheless, he made a second visit in the latter half of the year 1679. However, the planned manufacture of large quantities of phosphorus, for which *Brand* had taken his stepson as assistant, does not appear to have taken place: *Brand* soon fell ill and spent two months recovering at Hanover. The death of the Duke on December 28, 1679, appears to have deprived him completely of any reward for his efforts, for in a letter of April 23, 1682, *Brand* demands the remaining money owing to him, presumably once more in vain. – The Court had run into financial difficulties, and *Brand* had suffered yet another disappointment.

3. The Material Discovered

In his 'Historia' [58] *Leibniz* reports on the motivation for the discovery of 'Phosphorus igneus': "During his studies *Brand* came across a procedure, published in a

[55] Cf. ref. [54], Vol. VI, p. 382.

[56] Cf. ref. [1], p. 93.

[57] Cf. *H. Schimank*: Zur Geschichte der exakten Naturwissenschaften in Hamburg. Naturwiss. Verein in Hamburg, Hamburg 1928, p. 63.

[58] Cf. ref. [1], p. 93.

printed work, for the preparation of a certain liquor from urine by means of which pieces of silver could be matured to gold. On following the same procedure he discovered his phosphorus." In a letter of April 11, 1682, he suggested that the said book was one of the works of *Franz Thomas Kessler*[59]. However, *Peters*[60], supposes it to have been 'Alchimia Nova' by *H. Binelli*, a German translation of which had appeared in 1603. Even though this question will probably never be answered unequivocally, the text of *Binelli*'s book makes it quite clear to what end *Brand*'s investigations were directed and what he believed he had found[61]:

"... daß die Alchimy jhren Vrsprung auß keinem Stein oder Metall haben könne. Sintemahl solche Sachen nicht gebähren oder jhres gleichen zielen ... es könne die Alchimy weder aus einem vnuernüfftigen Thier, noch auch auß jrgend einem Gewächse oder Kraut ... herkommen vnd entspringen, so wende dich zu der Empfängnung vnd Geschöpff des Menschen selbst, ... so wirst du befinden, daß der Mensch ein gebährender Anfang oder Vrsprung auch der Alchimistischen Materien vnd Steine sey: Denn er ist ein vegetalisch, rationalisch vnd mineralisch Thier vnnd aller Elementen theilhafftig, vnnd hat Mineras vnd viel Poros oder Schweißlöchlein in sich. Geschicht dir aber mit dieser Antwort nicht genug, so hör vnnd merke für das ander, was die alte Philosophi sagen, daß nehmlich der Mensch die kleine Welt sey: Ist er nun die kleine Welt, so muß er auch alles dasjenige in jhme haben, was die andere grosse Welt in jhr hat, wiewol ein jedes in geringer Mänge. ... frag in diesem dein eygen Gesicht, das wird dich berichten, daß sich mineralische Sachen in deß Menschen Leibe finden, vnnd daß der Mensch zweyerley Potestates oder Vermögen in jhm habe als erstlich einen Samen ... Die andere Krafft aber ist etwas geringer ... als da sind Harn, Schweiß, Koht vnd dergleichen ... Ist demnach der Mensch ein solcher Anfang vnd Geschöpff, aus welchem die Steine vnd Materien der Alchimy jhren Vrsprung her haben ... Wenn man den Harn ansihet, so bekompt derselbige nicht allein für sich selbst vnd von Natur die Härte vnd Natur eines Steins, sondern kan auch durch die Kunst dazu gebracht werden: Kan demnach dasjenige, aus welchem die Alchimy herkompt vnd entspringt, sehr wol seyn. Vnd damit du dessen, daß dem nemlich so sey, noch mehr versichert werdest, so erjnnere dich dessen, so die Philosophi fürgeben, daß nehmlich jhr Stein in der kleinen Welt entspringe .. Sprichstu aber, ... ich ... kan mich aber nicht genugsam verwundern, woher doch dem Harn solche große Kraft ... komme: darauff gib jch dir zur Antwort. Das eben der Harn diese Natur vnd Proprietet oder Eygenschafft hat, daß er zu einem Stein wird. Vnd zwar so sagen die Skribenten, es müsse ein solcher Harn, welchen man hierzu gebrauchen wil, einer reinen Natur vnd ohn allen Schweiß seyn, vnd derowegen von einem jungen gesunden Knaben, so mit den besten Speisen vnd gutem köstlichem Wein vnterhalten vnd ernehret worden vnd sich der Vnkeuschheit weder in der That noch auch mit den Gedanken jemals beflissen, genommen werden."[*] (The generative power must be preserved in its entirely!)

Concepts of the human microcosm as a miniature embodiment of the macrocosm are extremely old. Since late antiquity, *i.e.* from the very beginning, they played an important role in alchemical thought. The fact that they had again assumed a particularly important place in alchemical thought in the 16th and 17th centuries is shown by *Boyle*'s reaction to *Krafft*'s intimation that the starting material for 'cold fire' was of human origin (see Section 2): He immediately started with urine.

But is it not just this general intellectual situation of alchemy that throws light on *Brand*'s relationship to the art and on his chemical aptitude? Was not he, as a crass outsider, actually the only person to have successfully carried out the generally known and recommended (but probably only rarely actually performed) process of extraction from urine until he had indeed obtained a substance possessing wonderful properties? Or was his lack of prejudice concerning the properties of the 'secretum' obtained an additional factor? The alchemists expected to find a "black" substance, the unfermented 'prima materia'; and for the 'spagyric art', 'fire' was only an external conditio sine qua non for the chemical processes that was not permitted to come into direct contact with the starting materials and intermediates, which were sealed off 'hermetically'. Or, was it merely the desperate situation arising from his permanent financial embarrassment that compelled *Brand* to invest such an uncharacteristic measure of patience in the preparation of the desired agent for the transmutation of silver to gold, and to place such faith in the old text. It was probably the fortunate combination of all three factors that actually led to the discovery.

It thus also becomes understandable why *Brand* kept his discovery secret for such a long time. The 'phosphorus' – in neither the liquid nor the solid form – was not the 'secretum' itself, but merely an important component or starting material, which he occasionally showed only to close friends. In 1677 *Brand* was still convinced that he would soon possess the 'secretum', and even two such important men as *Leibniz* and *Becher*, whose preliminary work later formed the

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[59] Cf. ref. [45], Vol. 3. Koehler u. Amelang, Leipzig 1938, p. 529 (Letter to *Ch. Philippi*). *Kessler*'s works are listed by *F. Ferchl*: Chemisch-Pharmazeutisches Bio- und Bibliographikon. Published for the Gesellschaft für Geschichte der Pharmazie, Nemayo, Mittenwald 1937, p. 271.

[60] Cf. ref. [19], p. 88, note 6.

[61] *H. Binelli*: Alchimia Nova, das ist die güldne Kunst; verdeutscht von *P. Uffenbach*. Frankfurt a. M. 1603, p. 3ff.

[*] "... that alchemy cannot have its origin in any stone or metal. Since such things cannot give birth and produce their equal ... alchemy cannot arise ... from an irrational animal or from any plant or herb, therefore turn to that which man creates with his body, ... then you will recognize that man is a procreating genesis or origin also of alchemical material and stones; for he is a vegetal, rational, and mineralistic animal and can partake of all elements, and he has mines and many pores or small sweat holes in his body. If this answer should not satisfy you, then listen and note what the philosophers of old said, namely, that man is the microcosm: Now if he is the microcosm then he must contain everything that the macrocosm contains, but in smaller amounts. ... ask yourself, then you will see that minerals are to be found in all men, and that man possess two kinds of potestas or strength: the first is his sperm ... the other strength is somewhat weaker ... that is urine, sweat, feces, and suchlike ... Man is therefore such a beginning or such a creature, from which the stones and materials of alchemy can arise ... If one considers urine, not only does it turn spontaneously and by nature into the hardness and nature of a stone, but it can also be induced to do so by the art: therefore it can well be the source and the origin of alchemy. To provide further support for this concept, keep in mind that the philosophers are of the opinion that their stone originates in the microcosm ... If you should wonder whence urine has its great power, I offer the answer that urine is capable of being transformed to a stone. And indeed the scribes say that the urine used must be a suitable one, of a pure nature and containing no sweat, and therefore from a young, healthy boy, who has been nourished with the best food and good wine, and chaste in thought and deed."

basis of *G. E. Stahl*'s phlogiston theory, opened negotiations to obtain this agent for their respective masters.

It is therefore perfectly feasible that earlier alchemists had already found the 'cold fire' – a procedure given by *Paracelsus* (1493–1541), for example, appears to suggest that this was the case [62]. Even *Brand*'s discovery only became known by a fortunate combination of circumstances.

Brand himself never published any reports concerning his phosphorus, and none of his remaining letters give away any information regarding the method of preparation. However, he did tell *Leibniz* of the preparation as agreed, and the latter successfully carried it out together with a number of assistants: ... *Brand* "honestly informed me of his process; for, with my assistants, I have repeated in another laboratory all that he accomplished" [63]. It has already been mentioned that in December 1678 he boasted to the Duke of Chevreuse of being the fourth (after *Brand*, *Krafft*, and *Kunckel*) to possess the procedure for the preparation of phosphorus. It is therefore a reasonably safe assumption that the procedure which he sent to *Ehrenfried Walter Freiherr von Tschirnhaus* (1651–1708), who was then in Paris seeking admission to the Academy, in an undated letter of the year 1682 was the very same recipe that he had received from Brand. The letter begins with personal and mathematical details and continues [64]:

"Phosphori Process kommt hierbey. Solchen werde, so lange M. Hr. mir nicht den ausgang seiner sach melde, nicht communiciren, zumahlen sie mir noch nicht geschrieben, was sie mir vor curiosa experimenta dafür communiciren wollen. M. Hr. wird solche doch auch leicht erfahren, und werde ich sie also durch ihn bekommen, hat also M. Hr. vom phosphoro nach seinem belieben zu disponieren. Nur dieses muss bekennen, dass das phosphorum zu machen, eine ziemlich beschwehrliche arbeit, und muss man sonderlich bey der letzten arbeit zusehen, dass die retorte nicht springe. Des Mons. *Boyle* ist etwas kürzer, aber wie ich aus seiner Beschreibung sehe, so fehlet er ihr bisweilen, gibt auch keinen so starken phosphorum, und überdies so ist er nicht instructif, denn er weiset nicht analysin subjecti et ex qua ejus parte potissimum veniat phosphorus. Zweifelsohne ist M. *Boyle* darauff gefallen, weil ihm der phosphorus imperfecte communiciret worden. Schicke hiermit beyde processus, sowohl wie ich es gemacht, als wie M. *Boyle*.

Composito des Feuers oder pyropi. Habe genommen urin so eine zeitlang gestanden, etwa eine tonne (wiewohl ich zweifle, obsolche fermentation oder putrefaction nöthig sey, weil mein Diener in Copenhagen den phosphorum noch selbige woche, als er hinkommen, gemacht), kochet es ab bis es beginnet dick zu werden, wie ein dicker sirup, alsdann thut man diesen dicken urin in eine retorte, lässet das phlegma und volatile vollends wegrauchen, und wenn rothe tropfen zu kommen beginnen, leget man einen recipienten vor, und empfängt darinn das oleum urinae. Alsdann schlegt man die retorte in stücken, darinn findet man ein caput mortuum, dessen unter theil ist ein hartes salz, so hieher nicht dienet, das obere theil ist eine schwarze lückere materi, die hebt man auff. Das oleum urinae thut man wieder in eine retorte und ziehet alle feuchtigkeit stark davon ab, so findet man in der retorte eine schwarze lückere materi der ietzgedachten, so in voriger retorte gewesen ganz gleich. Thut sie zusammen und treibt das feuer daraus folgendermassen. Nim eine guthe steinerne retorte, so kein stübgen nicht hält, darin thue etwa 24 Loth von der schwarzen materi oder capite mortuo oleoso, lege einen ziemlichen gläsern recipienten vor, so wohl verlatirt, und treibs also in freyen feuer, doch erstlich gelinde bis die retorte wohl glüet, treibs wohl 16 stunden lang, die letzten 8 stunden aber gar stark. Es kommen bald weisse Nebel oder wolcken und sezet sich wie ein schlammig oel zu boden. Gehet auch wohl etwas von einer materi mit über, die sich ganz hart an das glas anleget, ist wie ein Börnstein, darinn bestehet die beste krafft. Im ... destilliren ist der recipient ganz hell, und leuchtet im finstern. Was übergangen, ist alles leuchtend, doch das siccum mehr als das humidum. Hieraus ersiehet man, dass das feuer stecke in dem capite mortuo oleoso ...

Ich weiss keinen process, der auff die vulgata Chymicorum principia, sal, sulphur und mercurium, besser quadrire, als die compositio dieses feuers oder pyropi, denn dieses feuer komt eigentlich nicht aus dem sale fixo, noch aus dem volatili oder Mercuriali, sondern aus dem medio oder oleo vel sulphure. Und deucht mich, dass dieser process kein geringes licht gebe ..." [*]

[62] *Paracelsus*: Sämtliche Werke. Nach der zehnbändigen Huserschen Gesamtausgabe zum erstenmal in neuzeitliches Deutsch übersetzt ... von *B. Aschner*, Vol. 3. G. Fischer, Jena 1930, p. 18; cf. *O. C. de C. Ellis*: A history of fire and flame. London 1932, p. 24.

[63] Cf. ref. [1], p. 96.

[64] *G. W. Leibniz*: Mathematische Schriften, Vol. 4. G. Olms, Hildesheim 1962 (Halle 1859), p. 496 and 498.

[*] "The process for the preparation of phosphorus is enclosed. I shall not communicate it until you have informed me how your matter has gone, particularly as they have not yet written to tell me what curious experiments they wish to exchange for the communication. You will, however, also have no difficulties in obtaining such experiments, and if I learn of them from you then you will have phosphorus at your disposal. It must, however, be said that the preparation of phosphorus is rather difficult and that towards the end one must be particularly careful that the retort does not crack. The procedure of Mr. *Boyle* is somewhat shorter, but as I see from his description it has sometimes been unsuccessful and, moreover, it has not produced a very strong phosphorus. In addition, his description is not instructive for he does not order analysin subjecti and he does not know from which part of it the best phosphorus originates. This is undoubtedly due to the fact that he has only been imperfectly told of the preparation of phosphorus. Herewith I send you both procedures, not only that which I have used myself but also that of Mr. *Boyle*.

Composition of the fire or pyropus. Take approximately a full ton of urine that has stood for some time (although I doubt that such fermentation or putrefaction is necessary, for my servant has prepared phosphorus within a week of his arrival in Copenhagen), boil it until it begins to thicken, like a thick syrup, then place this thick urine in a retort, allow it to phlegm and the volatile part to vaporize, and when red drops appear a receiver is placed in front of the retort and the oleum urinae is collected. The retort is then broken into pieces. One finds a caput mortuum in it, the lower part of which is a hard salt that cannot be used, the upper part is a black loose material which one keeps. The oleum urinae is again transferred into a retort and all moisture is vigorously removed, one then finds a black loose material in the retort which looks just like that in the previous retort. Both are united and the fire is driven out in the following way. Take a good stone retort that has been very well cleaned, fill it with about 24 Loth of the black material or caput mortuum oleosum, place in front of the retort a suitable glass receptacle that is well stoppered, and heat over an open fire, gently at first, until the retort glows; heat for a total of 16 hours, and fiercely for the last 8 hours. White smoke or clouds soon appear and a kind of muddy oil deposits at the bottom. Some material also distills over which strongly adheres to the glass, it is like amber and that is the best material. On ... distillation the receptacle is very bright and shines in the dark. All that has distilled over shines, the dry part more than the moist part. One can thus see that the fire is in the capum mortuum oleosum ...

I know of no process that better quadrates the general principles of the 'chymists' – sal, sulphur, mercurium – than the composition of this fire or pyropus, for this fire does not come from the sal fixum or from the volatile or mercuriale, but from the medium or oleum vel sulphur. And it seems to me that this process gives a good light ..."

Robert Hooke (1635–1703) later published a far more complicated procedure "Phosphorus Elementaris, by Dr. *Brandt* of Hamburgh" [65], in a form that could hardly have originated from *Brand*. It is also uncertain how *Hooke* could have learnt of the method from *Brand*. It is in fact one of the many procedures to appear in the early 17th century subsequently ascribed to the discoverer of phosphorus by *Hooke*.

It has already been mentioned that *Brand* called the substance he discovered in urine "cold fire" or just "my fire". He clearly thought that he was in possession of elemental 'fire', one of the four Aristotelean 'elements' (earth, water, air, and fire); an assumption confirmed by his use of the alchemical symbol for 'fire' (Δ) in his letters. The term employed by *Hooke* "phosphorus elementaris" (presumably: "bearer of elemental light"), which has a very different meaning from "elemental phosphorus" in the sense of the later 'chemical' elements of the 19th century, is also suggestive of a similar interpretation.

Other early names are: Phosphorus fulgurans (*Elshloz*, *Kunckel*), Ph. igneus (*Leibniz*, *Boerhaave*), Ph. mirabilis or Wunder-Licht (miraculous light) (*Kunckel*); Lumen constans (*Kunckel*, *Elsholz*), L. perpetuum (*Kirchmaier*); Lux condensata (*Sturm*), Ignis perpetuus (*Krafft*), feu corporel (*Leibniz* in a letter accompanying the first sample he sent to *Huygens* [66]), Noctiluca constans (*Kirchmaier*, *Cohausen*), Noctiluca aerea (*Boyle*), Pyropus (*Leibniz*), *etc.*

All these names show that *Brand*'s discovery was regarded as a kind of light or fire material, or at least a "bearer of light" or "of fire". Even after *Stahl*'s proposal of the phlogiston theory (1703), *Nicolas Lémery* (1645–1715) 'pensionnaire chimiste' of the Paris Academy since 1699, wrote the following lines in his 'Muthmassungen und Betrachtungen über die Feuer- oder Lichtmaterie' [67]:

"Die Feuermaterie ist das vorzüglichste und mächtigste Auflösungsmittel irdischer Körper. — Man muß zugeben, daß sie der wahrhafte Stoff der Wärme, des Lichts und selbst der Flüßigkeit oder die Ursach der Schmelzung der mehresten irdischen Körper sey, die ohne diese Materie immer vest bleiben würden. Sie ist aber nicht immer so häufig da, oder sie trifft nicht immer Körper an, die ihr so wenig Widerstand leisten, daß sie dieselbe zum Fließen brächte, ja, man bemerkt oft, daß sie, anstatt diese zu schmelzen oder sie in der Flüssigkeit zu erhalten, die sie ihnen anfänglich mitgeteilt hatte, sich an dieselben hängt, und darinn so eingewickelt wird, daß sie eingekerkert zurückbleibt, und nicht eher heraustritt, als bis eine äußere Ursache ihr zu Hülfe kommt, und die Zellen, worinn sie zurückgehalten wurde, öfnet.

Hierbei ist ein doppelter Umstand zu bemerken, daß sie nämlich 1) manchmal das Gewicht der Körper, worinn sie enthalten ist, merklich vermehrt [!]; und daß sie 2) während der ganzen Zeit ihrer Einkerkerung doch die eigenthümlichen Eigenschaften der Feuermaterie behält, die sie deutlich äussert, so bald sie frey wird ... Spießglaskönig, Bley, Zinn und selbst Quecksilber wiegen nach der Verwandlung in Kalk mehr, als im metallischen Zustande, ob gleich viel von ihnen bey der Operation verflüchtigt wird. Da nun die Feuermaterie sie in den verkalkten Zustand gebracht hat, soll man ihr nicht auch das vermehrte Gewicht zuschreiben? ... Unter allen Körpern, worinn die Feuermaterie am losesten eingeschlossen ist, sind die Phosphoren. Man braucht sie nur ans Licht zu stellen, da sie sogleich neue annehmen, die die erstere in Bewegung setzt. Es sind Lichtschwämme, die es eben so leicht von sich geben, als sie es annehmen ..." [*]

This view was destined to persist in a more or less similar form for a considerable time; even towards the end of the 18th century yellow phosphorus was still regarded merely as a particularly striking example of a whole series of "phosphorus", of "light (or fire) bearers" or "light imbibers", which differed from the others in that it did not have to be first exposed to light or fire in order to luminesce, as *Leibniz* put it.

As late as 1790 the following description appears in *Gehler*'s 'Physikalisches Wörterbuch' under the heading 'Phosphorus' [68]:

"According to its entymological meaning, the name phosphorus (light bearer) applies to any body that luminesces in the dark. However, the sun, the fixed stars, and burning or glowing bodies, whose luminescence is an everyday phenomenon, are excepted, and the name phosphorus applied only to the other substances that luminesce of themselves, whose light in the dark belongs rather to the rare and unexpected phenomena. Such substances are either natural or artificial phosphors. A number of the natural ones are considered under the heading 'luminous bodies'; the artificial phosphors therefore represent the main subject of this article".

The enumeration starts off in chronological order, beginning with Bologna phosphorus (BaS), whose discovery is incorrectly cited as having occurred in 1630 – it is first mentioned by *Julius Caesar la Galla* ('De Phaenomenis in Orbe Lunae'; Venice 1612), and a detailed description was given by *Fortuno Liceti* ("Litheophosphorus, sive de lapide Bononiensi'; Udine 1640) and *Athanasius Kircher* (Magnes, sive de arte magnetica ...'; Cologne 1643, as well as 'Ars Magna Lucis et Umbrae ...'; Rome 1656); the discovery occurred between 1602 and 1604, and is attributed to the Bolognese shoemaker *Vincenzo Cascioroli* [69]:

[*] "The fire material is the most powerful solvent for earthly substance – One has to admit that it is actually the substance of heat, of light, and even of liquid or the cause of the melting of most earthly substances, which, without this material, would always be solid. It is not, however, always present in such a degree, or it does not always find substance which offer so little resistance that they are made to flow; moreover, one often notices that, instead of melting these bodies or keeping them liquid as in the beginning, it attaches itself to them and becomes so intimately mixed with them that it remains imprisoned within them and cannot be freed until an external cause assists and opens the cell in which it is held back.

Two things are to be noted, namely that the fire material 1) sometimes increases considerably the weight of the bodies in which it is contained [!]; and 2) retains the properties of the fire material which it clearly exhibits when it is freed, for the duration of its imprisonment ... antimony, lead, tin, and even mercury, weigh more after calcination than in the metallic state, although large amounts of them are volatilized during the operation. Since the fire material transformed them to their calcined state, why should one not also attribute the increase in weight to it? ... The phosphors belong to the substances in which the fire material is most loosely bound. If they are exposed to light they immediately take up fresh fire material, which sets the confined fire material in motion. They are light sponges which release light just as readily as they absorb it ..."

[65] *Robert Hooke*: Philosophical Experiments and Observations of the late eminent Robert Hooke, publ. by *W. Derham*. London 1726, p. 178–180.

[66] Oeuvres complètes de Christiaan Huygens ... Tome VIII. M. Nijhoff, La Haye 1899, pp. 214–218; Letter No. 2192 of September 8, 1679.

[67] After the translation in ref. [6], p. 34–39. (Hist. de l'acad. royal des sciences, anné 1709. Amsterdam 1711).

[68] Cf. ref. [7], p. 475.

[69] *J. R. Partington*: A history of chemistry, Vol. 2. MacMillan and Co., London 1961, p. 334ff.

"It became luminous on exposure to both sunlight and candles, but not to the light of the moon or of another phosphor ... This discovery naturally led to the corpuscular concept of light, which not long afterwards became the basis of *Newton*'s theory of light. Here one saw, as it were, bodies, which attracted light and re-emitted it, light imbibers or light magnets (corpora lumen bibentia), which names have also been adopted" [70].

The second "phosphorus" to be dealt with by *Gehler* is *Balduin*'s phosphorus, which was first reported on by its discoverer in 1674 (see Section 1); he then goes on to discuss *Homberg*'s phosphorus ($CaCl_2$) and a series of other "artificial" phosphors, *i.e.* phosphorescing substances, before he comes to "*Kunckel*'s or urine-phosphorus".

The Bologna phosphorus and *Balduin*'s phosphorus (ignited calcium nitrate) indeed created great excitement in the scientific world and stimulated the search for other "phosphoruses". For example, *Homberg* had studied the former in Italy and as soon as he heard of *Balduin*'s discovery he payed the Saxon magistrate a visit at Grossenhain. In continuation of his journey he came to Berlin, where he met *Kunckel* who told him about another new phosphorus, *i.e. Brand*'s 'cold fire', and gave him a sample. *Kunckel* himself reports that a few weeks after his having become acquainted with *Balduin*'s discovery and been given a small sample, he was demonstrating the same during a visit to Hamburg when he heard that a Herr *Brand* of Hamburg had also discovered a luminous substance [71]. His informant was *Peter Hessel*, who was preacher at the Hamburg plague spital from 1670 to December 26, 1677, and apparently one of the few friends to whom *Brand* had shown his "fire" – fortunately, as we can now appreciate; for it is only due to facts that *Kunckel* had learnt of *Balduin*'s phosphorus from the discoverers publications and had been able to secure a small sample, that he demonstrated this at Hamburg, and that the versatile and literarily very active preacher, who had already seen *Brand*'s phosphorus, also happened to be present at the demonstration that *Brand*'s discovery ever came to *Kunckel*'s notice. He described what he had seen in a letter to his friend *Krafft* at Dresden and thus set in motion the course of events whose beginning are described above. *Brand* himself could never have dreamed of the significance of his discovery, or even of the possibility of a financial exploitation, so that we actually owe our knowledge of it to an unlikely combination of various chance circumstances – even though the discovery of the substance would certainly have followed later, and that in a less fortuitous and unconscious manner.

It has already been mentioned that "phosphorus" was originally prepared in one of two forms, either as a grayish or yellow solid or as "phosphorus liquidus" – *Elsholz* [46] reports *e.g.* that *Krafft* possessed samples of both kinds. Recent investigations on earlier reports and procedures have shown that the liquid form must have been a suspension of finely divided phosphorus in water (*Brand*, *Krafft*) or must have contained impurities. Such contamination, particularly with sulfur, would lead to a melting point below the normal temperature [72]. And the frequent contamination with sulfur, along with the ready combustibility (ascribed to the former principium sulphur), seems to have led to phosphorus being regarded as "a sulfur or a sulfurous substance" after the original idea of elemental light or fire had gradually been abandoned, or modified as in the above passage by *Lémery*, as a consequence of *Boyle*'s discovery that contact with air was an essential condition for luminescence of the solid material.

Homberg (1692), for example, like *Leibniz*, considered it to be the sulfurous principle of pre-phlogiston chemistry, when he said that phosphorus is the fattiest, *i.e.* the most combustible, part of urine, which is concentrated on a highly flammable earth.

Nevertheless, *Boyle* [73] had already recognized that the residue left by burning phosphorus possesses acid properties, so that it was only natural for *Stahl*, the founder of the phlogiston theory, to regard phosphorus as a compound of phlogiston and a concentrated acid. It is, however, remarkable that he was thinking, not of a specific acid, but of hydrochloric acid. Certain experiments by *Boyle*, which cannot be considered here, led him to this conclusion; he was so convinced of the correctness of his assumption that he, and his successors, considered any proof entirely superfluous. The deciding factor in the preparation of phosphorus was then thought to be the choice of the correct method of combining the phlogiston with the hydrochloric acid. Thus it can be read, *e.g.* in *Johann Juncker*'s widely read work 'Conspectus Chemicae' of 1730: "Phosphorus consists primarily of hydrochloric acid and phlogiston, which are bound most intimately by fire, and is therefore a kind of sulfur" [74]. The symbol $\overset{\triangle}{\ddagger}$, derived from the old symbol for the 'element' fire ($\triangle$), which *Brand* himself had used for phosphorus, found general acceptance (sulfur: $\overset{\triangle}{+}$).

It is clear that this theory made the preparation of phosphorus no easier. The only methods available were still the old, time-consuming, and inconvenient processes used by *Brand*, *Kunckel*, *Krafft*, and *Boyle*, which had undergone only slight modification. It was much simpler, although more expensive, to import phosphorus from England, where *Ambrose Godfrey Hanckwitz* (1660–1741), a pharmacist of Göthen in Anhalt who had emigrated to England and had become assistant to *Robert Boyle*, had set about producing phosphorus on a large scale. By closely guarding the secret of his preparation, which only became known sketchily in the 1730's, he had almost suc-

[70] Cf. ref. [7], p. 476.

[71] Cf. ref. [3], p. 660; also ref. [35].

[72] Cf. ref. [16], p. 29.

[73] *R. Boyle*: New Experiments and Observations, Made upon the Icy Noctiluca. London 1681/82: [41], p. 469–495.

[74] *G. J. Mielke* in *A. S. Marggraf*: Einige neue Methoden, den Phosphor im festen Zustande sowohl leichter als bisher aus dem Urin darzustellen als auch denselben bequem und rein aus brennbarer Materie (Phlogiston) und einem eigentümlichen, aus dem Urin abzuscheidenden Salze zu gewinnen. Translated from the Latin and French and edited by *G. Mielke*. W. Engelmann, Leipzig 1913, p. 45.

ceeded in establishing a monopoly for the production of phosphorus. The first records of shipments of phosphorus from London to Germany refer to the year 1685, and in the same year *Hanckwitz* advertised his product in London in the following way: "He sells Solid Phosphorus, wholesale, 50 s. an ounce, and retail, £ 3 sterling, the ounce." The prices remained at this level – in 1731 *Stahl* gives the price as 40 shillings the ounce in London and 32 Belgian guilders in Amsterdam –, and after the death of their father, *Hanckwitz*' sons were able to continue production for the same high profit [75].

It is thus also understandable that in 1736 the Paris Academy commissioned *Hellot*, *Du Fay*, *Geoffroy*, and *Du Hamel* to examine an offer of a more economical process for production of phosphorus which had been made by an unnamed foreigner, and that they subsequently bought the process. According to the report given by *Jean Hellot* (1685–1766) to the Academy on November 13, 1737, $3^1/_2$ pounds of calcined starting material gave 9 gros and a few grains of a phosphorus that was "at least as beautiful as that coming from England" [76]. The novelty of the process – and the only direct influence of the phlogiston theory on the preparation of phosphorus – was the addition of powdered charcoal *i.e.* "highly concentrated phlogiston", apart from sand or earthenware fragments (to ensure even heat distribution), to the starting material, putrified urine.

Then, a few years later, in 1743, *Andreas Sigismund Marggraf* (1709–1782) published a treatise in 'Miscellanea Berolinensia' which not only stripped phosphorus of its mystery, but also considerably simplified its preparation [77]. The author described what prompted him to undertake his experiments in the following lines [78]:

"Around the year 1734 I was fortunate enough to receive tuition by the famous and skilled *Henckel* [*Johann Friedrich Henckel*, 1679–1744] in Freiburg ... We frequently discussed phosphorus and its high price and exchanged our views on the matter, and on one such occasion he assured me that quite by chance, he had once produced phosphorus using only low heat," – the fierce heating, which had to be kept up for a considerable length of time had always caused difficulties – "while engaged in work on the mercurificatio [experiments to obtain 'mercurius' from metals]; he had already published this method in his 'Pyritologia' ['Pyritologia Oder Kiess-Historie'; Leipzig 1725]. I searched for the place and found on p. 1004, paragraph 14, the following words: 'Bleykalk mit Salmiak, Weinstein und altem Urin digeriert, endlich destilliert, giebt einen arsenikalischen Geruch, ja endlich einen schönen Phosphor' [*] ..."

Henckel provided him with further detailed information about the process, which was then studied systematically by *Marggraf* with the result that it became easier to prepare phosphorus, using less heat, and in greater yields when not only charcoal (as had become common practice since 1737), but also molten lead chloride [Hornblei] ($PbCl_2$ in the solid state), horn silver (AgCl), or cadmia fornacum (ZnO) was added to the concentrated urine. He studied which part of the urine actually gave rise to the phosphorus, or whether it might even have arisen from the substances added, particularly those containing chlorine, thus proving the conclusion reached by *Stahl* from his theory to be correct and phosphorus could be prepared without urine. During these studies he came across the "highly remarkable urine salt" ($NaNH_4HPO_4$), which had long been known under the name of sal microcosmicum (see above) and from which, in admixture with charcoal only, with charcoal and sand, or with charcoal and horn silver, could be prepared a "very beautiful and pure phosphorus". It should be only this salt that came into question for the preparation, as well as an "acid" obtained by ignition ($NaPO_3$), which is reduced to phosphorus by charcoal. Phosphorus could, however, be more readily obtained by reduction of the acid, upon which the urine salt is based, by charcoal.

According to this reasoning phosphorus was the compound of a specific acid, *i.e.* phosphoric acid, with phlogiston. As far as phosphorus was concerned, *Stahl*'s thesis had been disproved. Phosphorus, or rather phosphoric acid, had been recognized for the first time as a specific substance.

Carl Wilhelm Scheele (1742–1786) and his assistant *J. G. Gahn* (1745–1818) then discovered, in spring 1770 although it did not become known until 1774, the composition of "animal earth", *i.e.* of bone ash, and thereby found a new starting material for the preparation of phosphorus, before *Antoine Laurent Lavoisier* (1743–1794) opened, with his many experiments on the combustion of phosphorus and sulfur in 1772, "the crucial year", as it is called by *Henry Guerlac* in a recent presentation of *Lavoisier*'s experiments in this year.

On November 1, 1772, *Lavoisier* deposited a short, sealed note in the Academy, which was opened in May of the following year and published. The text runs thus [79]:

"il y a environs huit jours que j'ay decouvert que le Souphre en brulant loin de perdre de Son poids (en brulant) en acquieroit au contraire; Cest a dire que d'une livre de Souphre on pouvoit retirer beacoup plus dune livre dacide vitriolique, abstraction faitte de l'humidité de l'air. il en est de meme du phosphore Cette augmentation de Poids vient dune quantite prodigieuse d'air qui Se fixe pendant la combustion et qui Se Comnine avec les vapeurs.

Cette decouverte que j'ay Constaté par des experiences que je regarde Comme decisives m'a fait penser (ce) que Ce qui Sobservoit dans la Combustion du Souphre et du phosphore pouvoit bien avoir lieu a l'egard de tous les Corps qui acquier rent du poids par la Combustion et la Calcination et je me

[75] *M. Speter*, Chemiker-Ztg. *53*, 1005 (1929).

[76] Cf. ref. [16], p. 32.

[77] *A. S. Marggraf*: Nonnullae novae methodi Phosphorum solidum Tam ex urina facilius conficiendi, quam etiam eundem promtissime et purissime ex phlogisto et singulari quodam ex urina separato Sale componendi. Miscellanea Berolinensia *7*, 324 (1743). German version in ref. [74].

[78] Cf. ref. [77], paragraph 4; ref. [74], p. 4.

[*] "Massicot digested with sal ammoniac, tartar, and old urine, and eventually distilled, gives an arsenical odor, and finally a beautiful phosphorus."

[79] *H. Guerlac*: Lavoisier – The crucial year. The background and origin of his first experiments on combustion in 1772. Cornell University Press, Ithaca, New York 1961; p. 227ff. German version in ref. [81], p. 13.

Suis persuade que laugmentation de poids (de l) des chaux metalliques tenoit a la meme Cause. experience a Complettement Confirme mes Conjectures ... Cette decouverte me paroit une des plus interessantes qui ait ete faitte depuis *Sthal* [*Stahl*] et Comme il est difficile de ne pas laisser entrevoir a Ses amis dans la Conservation quelque chose qui puisse les mettre Sur la voye de la verité j'ay Cru devoir faire le present depost entre les mains de M. le Secretaire de lacademie (pour) en attendant que je rende mes experiences publiques [*]."

Two further notices dating from an earlier period have recently been discovered [80], which deal primarily with investigations on phosphorus, one written on October 10, and the other on October 20, 1772 ('Memoire Sur lacide du Phosphore et Sur Ses Combinaisons avec differentes Substances Salines terreuses et métalliques'). The paper 'On the combustion of *Kunckel*'s phosphorus and the nature of the acid formed by this combustion', which was read on April 16, 1777, possesses as great a significance as a step along the path to the further development of *Lavoisier*'s theory of combustion, as does the 'treatise on a particular process for the conversion of phosphorus into phosphoric acid without combustion' from the year 1780.

Yet in none of these reports does *Lavoisier* speak out against the phlogiston theory. However, he contends that the theory assumes unproven facts and expresses the hope that he will soon be able to provide experimental proof that combustion and calcination can be explained without the need for the assumption of a special basic substance such as phlogiston [81].

[*] "About eight days ago I discovered that sulfur does not lose weight on combustion but rather gains weight; that is to say, much more than a pound of sulfuric acid is obtained from one pound of sulfur, after deduction has been made for the humidity of the air. It is the same with phosphorus. This increase in weight is due to a considerable amount of air which is fixed during the combustion and combines with the vapors.

I concluded from these facts, which I have determined from experiments that appear decisive to me, that which is observed on combustion of sulfur and phosphorus might well take place with all bodies which gain in weight on combustion or calcination, and I have become convinced that the increase in weight on calcination of metals is due to the same cause. The experiment completely confirmed my supposition ... This discovery seems to be one of the most interesting since *Sthal* [*i.e. Stahl*]: I therefore believe to have acquired the priority of the same in that I place this in the hands of the Secretary of the Academy, where it should remain secret until I publish my experiments".

[80] Cf. ref. [79], p. 223–227.

[81] *M. Speter*: Lavoisier und seine Vorläufer. Eine historisch-kritische Studie. F. Enke, Stuttgart 1910, p. 12ff. (Special edition from: Sammlung chemischer und chemisch-technischer Vorträge, Vol. 15, Numbers 4–6.)

At this time, *Lavoisier*'s theory that a component of the air was responsible for all combustion and calcination had too many weaknesses, which he also recognized himself, for anyone other than he to be able to follow it. It seems, however, that it was precisely the combustion experiments with phosphorus and sulfur that were decisive for *Lavoisier*. Yet it was not until the discovery of the composition of water by *Henry Cavendish* (1731–1810), which came to *Lavoisier*'s notice in June 1783, that the theory received welcome confirmation, and was then, in 1789, brilliantly developed in 'Traité élémentaire de Chimie'. Rapidly accepted in France, the theory soon won general recognition by the chemists of Europe.

On the basis of this "antiphlogistic" theory, phosphorus was relegated to a simple, undecomposable substance, a chemical element. Thus, in 1795, *Gehler*, who as short a time ago as 1790 had been a convinced supporter of the phlogiston theory and had made just brief mention of *Lavoisier*'s work on phosphorus as a recent theory [82], had no alternative but to begin his remarks on phosphorus in a supplement to his dictionary with the words [83]:

"The name phosphorus has become reserved almost exclusively for *Kunckel*'s phosphorus or urine phosphorus, particularly since the antiphlogistic theory has come to regard it as a simple substance and has adopted a large number of derivations from its name in the nomenclature" ... It "has become an uncommonly important object in recent chemistry. The phenomenon of its combustion in atmosphere or dephlogistated air provides the antiphlogistic system its most important support, and proves with undisputable certainty that the basic part of the breath of life combines with the burning body on combustion ..."

Thus it took more than one hundred years for the material discovered by the Hamburg Chymist *Hennig Brand* to become the chemical element phosphorus. However, the credit for the discovery remains his; for while it is true that a science develops by continually wrestling with new interpretations from that which it observes, this is only made possible by the existence of a foundation established in history; and that stone provided by *Brand* was by no means unimportant. We can hardly reproach him for not realizing that his contribution would later assume a significant place in this foundation.

Received: July 4, 1969 [A 716 IE]
German version: Angew. Chem. *81*, 634 (1969)

[82] Cf. ref. [7], p. 483.

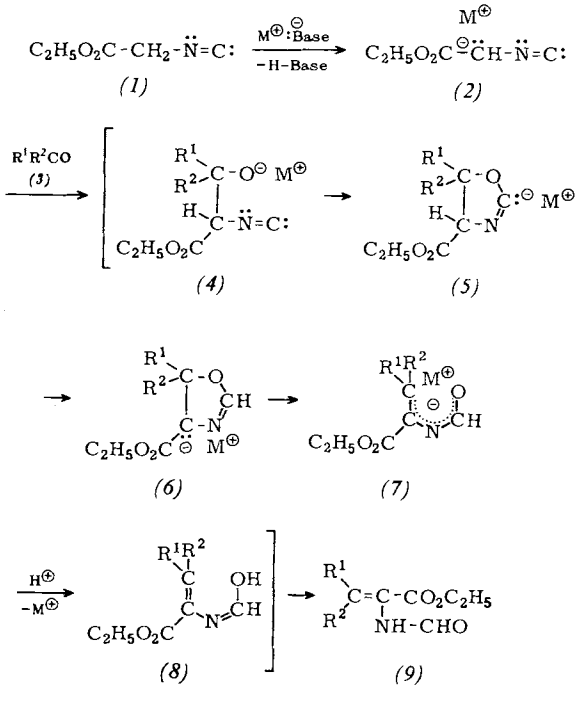
[83] Cf. ref. [7], Vol. 5, p. 708.

α-(Formylamino)acrylic Esters from α-Metalated Isocyanoacetic Esters and Carbonyl Compounds[1]

By *U. Schöllkopf, F. Gerhart,* and *R. Schröder*[*]

The conversion of carbonyl compounds *(3)* into β-substituted α-(acylamino)acrylic acids is preparatively important because these acids can undergo a variety of changes[2], *e.g.* to α-amino and α-keto acids. Previously the carbonyl compounds were condensed with acylglycines, and the resulting azlactones were hydrolyzed (Erlenmeyer synthesis); however, this procedure requires forcing conditions and is limited to carbonyl compounds that cannot undergo an aldol condensation[2].

We have now found that good yields of ethyl α-(formylamino)acrylate *(9)* are obtained if α-metalated ethyl isocyanoacetate *(2)* [prepared from ethyl isocyanoacetate *(1)*[3] and, *e.g.*, butyllithium or sodium hydride] is allowed to react with aromatic or aliphatic aldehydes or ketones *(3)* (cf. Table).



M = Li, Na

Oxazoline anions *(5)* are presumably formed as intermediates by way of the carbonyl adducts *(4)*, and pass into the anions *(6)* by intra- or intermolecular proton transfer from C-4 to C-2[4]. The ions *(6)* are converted by electrocyclic ring fission into the "pentadienyl anions"[5] *(7)*, which can be isolated in the form *(9)* after acid hydrolysis. A batch with benzaldehyde as carbonyl component (and butyllithium as base) was hydrolyzed without addition of acid — it then yielded *N*-formyl-β-phenylserine ethyl ester. Since compounds *(9)* are inert to dilute alkali, we assume that an intermediate *(8)* whose double bond is hydrated in an alkaline medium must be formed between *(7)* and *(9)*.

R^1	R^2	*(9)*	Yields (%)
C_6H_5	H	Ethyl β-(formylamino)-cinnamate	74 [a], 69 [b], 28 [c]
CH_3	H	Ethyl 2-(formylamino)-crotonate	13 [a]
$CH(CH_3)_2$	H	Ethyl 2-(formylamino)-4-methyl-2-pentenoate	58 [a]
C_6H_5	CH_3	Ethyl α-(formylamino)-β-methyl-cinnamate	81 [a]
C_6H_5	CH_3	*tert.*-Butyl α-(formylamino)-β-methyl-cinnamate	82 [a, d]
CH_3	CH_3	Ethyl 2-(formylamino)-3-methyl-2-butenoate	77 [a]
$-(CH_2)_5-$		Ethyl β-cyclohexylidene-α-formylaminoacetate	87 [a]
C_6H_5	C_6H_5	Ethyl α-(formylamino)-β-phenylcinnamate	81 [a]

[a] With butyllithium in THF. [b] With sodium hydride in THF. [c] With sodium ethoxide in ethanol (*N*-formyl-β-phenylserine ethyl ester isolated as main product after working up by acid).
[d] Prepared by *P. Markusch* from *tert*-butyl isocyanoacetate.

Ethyl β-(formylamino)cinnamate (9), $R^1 = C_6H_5$, $R^2 = H$:

a) With butyllithium: 0.04 mole of butyllithium (as *ca.* 16 ml. of a 2.5 N solution in pentane) is dropped in *ca.* 30 min, with vigorous stirring, into a solution of ethyl isocyanoacetate (4.52 g, 0.04 mole) in THF (30 ml) whilst the temperature is kept below —70 °C and care is taken that the drops fall directly into the reaction mixture. A solution of benzaldehyde (4.24 g, 0.04 mole) in THF (20 ml) is added to the suspension of ethyl isocyanolithioacetate at —60 °C, the whole is allowed to come to room temperature, the solvent is removed in a vacuum, the residue is treated with a mixture of glacial acetic acid (3.6 g, 0.06 mole) and water (50 ml), and the product is extracted with ether, dried over magnesium sulfate, and worked up in the usual way. This product is chromatographed on silica gel, from which ether removes ethyl β-(formylamino)-cinnamate (6.5 g, 74%; mixed isomers, b.p. 156—158 °C/0.1 torr).

b) With sodium hydride: A mixture of ethyl isocyanoacetate (4.52 g, 0.04 mole), benzaldehyde (4.2 g, 0.4 mole), and THF (30 ml) is added dropwise to a suspension of sodium hydride (0.96 g, 0.04 mole) in THF (50 ml) at room temperature with vigorous stirring. After 3 hours' further stirring, the solvent is removed in a vacuum and the mixture is worked up as in (a), the yield being 69% (6.05 g).

Received: May 27, 1969 [Z 25 IE]
German version: Angew. Chem. *81*, 701 (1969)

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[1] Part 3 of Syntheses by α-Metalated Isocyanides. — Part 2: *F. Gerhart* and *U. Schöllkopf*, Tetrahedron Letters *1968*, 6231.

[2] *H. E. Carter*, Org. Reactions *3*, 198 (1946).

[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] If there is no carbonyl group at position 4, the proton exchange does not take place; the anions of type *(5)* then fragment to olefins and metal cyanates; *U. Schöllkopf* and *F. Gerhart*, Angew. Chem. *80*, 842 (1968); Angew. Chem. internat. Edit. *7*, 10 (1968).

[5] Electrocyclic ring fission of anions has not yet been observed, but it has been shown by control experiments with oxazolines carrying an ethoxycarbonyl group at C-4 that anions of type (6) do suffer ring opening (*M. T. Reetz*, unpublished work).

Platinum(III) Bromide — a New Structural Type of AB_3 Compounds

By *G. Thiele* and *P. Woditsch*[*]

$PtBr_3$ *(1)* is formed on bromination of the metal in a closed system at 900 °C. In a temperature gradient of 900→300 °C compound *(1)* is transported to the colder zone where it

appears as blackish green needles having a metallic sheen. In the presence of an excess of bromine, bluish black needles of $PtBr_4$ *(2)* are also obtained; *(2)* forms rhombic crystals (a = 11.94, b = 14.47, c = 6.34 Å; space group Pbca-D_{2h}^{15}) of the PtI_4 type [1].

Compound *(1)* forms rhombohedral crystals of the space group $R\bar{3}$—C_{3i}^2. The lattice constants of the hexagonal unit cell are a = 22.32 ± 0.03, c = 9.024 ± 0.008 Å; Z = 36; $d_{X\text{-ray}}$ = 6.67 g cm^{-3}. The visually estimated intensities of 1033 reflections *hkl* from Weissenberg and precession photographs were considered in the structure determination; no correction was made for absorption. The structural model was calculated from three-dimensional Patterson syntheses and refinement of the atomic parameters with three-dimensional Fourier syntheses, as well as least-squares refinement with anisotropic temperature factors, to a reliability factor R = 0.096.

The atomic parameters are:

Pt^1:	0.007_0	0.093_6	0.158_1
Pt^3:	0.027_3	0.299_7	0.507_4
Br^{11}:	0.007_3	0.093_5	0.685_9
Br^{12}:	0.177_7	0.078_7	0.000_3
Br^{21}:	0.301_5	0.272_0	0.991_2
Br^{22}:	0.020_1	0.203_3	0.356_4
Br^{23}:	0.281_1	0.064_6	0.673_4
Br^{24}:	0.298_7	0.181_0	0.343_0

The structure of *(1)* contains Pt_6Br_{12} and $\frac{1}{\infty}[PtBr_2Br_{4/2}]$ units. The six Pt atoms of the Pt_6Br_{12} unit form an octahedron [Pt^1—Pt^1: 3.49 (4×) and 4.94 Å (1×)], the twelve Br atoms lying at the edges. In this arrangement, each Pt^1 has a square-planar environment (Pt^1—Br^{11} and Br^{12}: 2.447 ± 0.018 Å). This Pt_6Br_{12} group corresponds to that in the structures of $PtCl_2$ and $PtBr_2$ [2].

Pt^2 is surrounded octahedrally by Br[Pt—Br: 2.57, 2.52, 2.48, 2.47 (2×), and 2.44 Å]. Each octahedron is distorted and is linked to two others *via* common edges to form infinite chains, which run about the screw axes in $R\bar{3}$ along [001]. The two Br atoms that do not participate in linkage are *cis* to each other. This constructional pattern closely resembles that in the PtI_4 structural type [1].

The two structural units are bonded only loosely to each other. An additional Br from the $PtBr_6$ chain is situated above each $PtBr_4$ square plane [Pt^1—Br^{22}: 2.93 Å]; therefore there can only be weak electrostatic bonds in the crystals. Accordingly, the crystalline needles readily cleave into fibers along [001].

A structural principle with Pt^{II} and Pt^{IV} that can be unequivocally distinguished crystallographically has thus been detected by X-ray methods for the first time. Hitherto a structure $Pd^{II}Pd^{IV}F_6$ had been suspected on the basis of magnetic measurements on PdF_3 [3]. The absence of unpaired d electrons is understandable if dsp^2 and d^2sp^3 hybrid bonds are assumed on Pt^{II} and Pt^{IV}, respectively. Accordingly, the substance shows a weak, temperature-independent paramagnetism $\chi_m^{corr} = +280 \times 10^{-6}$ e.m.u.

Received: June 26, 1969 [Z 43 IE]
German version: Angew. Chem. *81*, 706 (1969)

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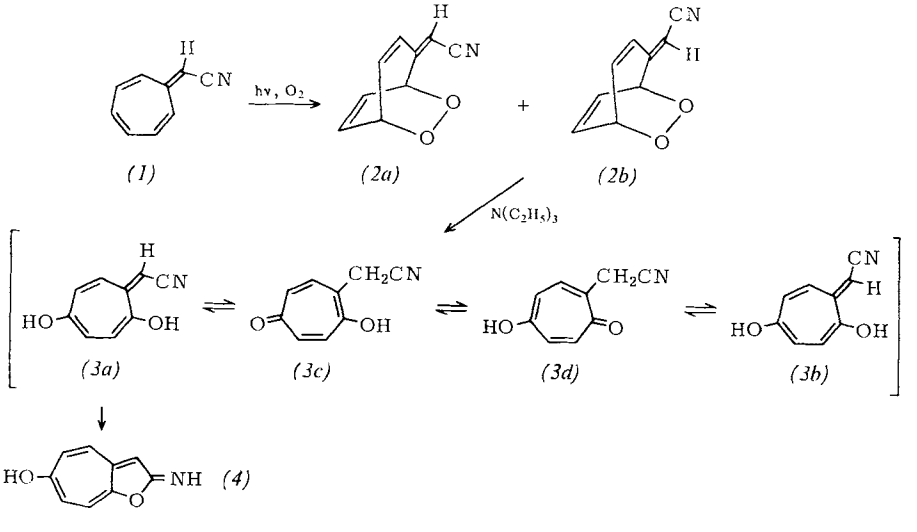
Photo-oxygenation of 8-Cyanoheptafulvene

By *M. Oda* and *Y. Kitahara* [*]

In the course of our attempts on photochemical (8+8)π dimerization of heptafulvenes, we have found that 8-cyanoheptafulvene *(1)* [1] is subject to photo-sensitized oxygenation in the presence of oxygen.

When the compound *(1)* was irradiated in acetone with a 100 W high-pressure mercury lamp through a water cooled Pyrex filter under oxygen, it slowly absorbed one mole of oxygen to give an epidioxide *(2)* as colorless crystals (m.p. 41—45 °C) which detonates at 106 °C in a capillary tube. In the presence of a sensitizer (Rose Bengal) the reaction goes to completion within two hours (85% yield). With a 300 W tungsten lamp almost the same result was obtained (80.5% yield). Although the epidioxide *(2)* shows one spot on silica-gel thin layer chromatography, the NMR spectrum reveals it to be a mixture of two isomers. The IR spectrum of the mixture *(2)* shows bands at 3050, 2960, 2230, 1634, 1620, 1580, 1364, 972, 955, 933, 917, 896, 838, and 700 cm^{-1} and the UV spectrum shows a band at 254 nm, indicating the presence of α,β,γ,δ-unsaturated cyanide and epidioxy groups. The ^{1}H-NMR spectrum ($CDCl_3$; TMS, internal) exhibits signals at 7.02—6.09 (complex multiplet, 4H), 5.62 (double quartet, J = 7.1, 2.7, and 1 Hz, 0.5 H), 5.33 (doublet?, 1 H) and 5.15—4.77 ppm (multiplet, 1.5 H), which are reasonably explained as *ca.* 1:1 mixture of isomeric epidioxides, *(2a)* and *(2b)*.

Treatment of the mixture *(2)* with triethylamine in methylene chloride [2] at room temperature for a few minutes afforded 6-hydroxy-1-oxaazulane-2-imine *(4)* [3] in 90% yield, thus providing further supporting evidence for the structure of *(2)*. *(4)*: yellow fine needles, m.p. 179—80 °C decomp., IR



ν_{max}(KBr) 3240, 3070, 1658, 1555, 1465, 1323, 1270, 1206, 872, 859, and 800 cm^{-1}; UV λ_{max}(EtOH) 232 nm (log ε = 4.23), 285 (3.62), 301 (3.69), 338 (3.95), and 414 (3.90). The intermediates of this reaction should be 1,4-dihydroxy-8-cyanoheptafulvenes, *(3a)* and *(3b)*, which probably isomerize to each other through the tropone structures, *(3c)* or *(3d)*, particularly under basic conditions. The compound *(4)* can be formed by intramolecular cyclization of *(3a)*.

Received: June 9, 1969 [Z 41 IE]
German version: Angew. Chem. *81*, 702 (1969)

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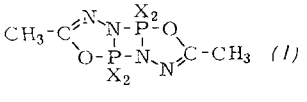
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Dimeric 1,3,4,2-Oxadiaza-P^V-phospholes, Ten-Membered Tricyclic Compounds Containing Pentacoordinated Phosphorus as a Bridgehead Atom[1]

By *J. Ebeling* and *A. Schmidpeter*[*]

Acetohydrazide reacts with trichlorophosphoranes to eliminate 3 mol. equiv. of HCl. The reaction products (see Table), having the composition $C_2H_3N_2OPX_2$, are colorless crystals, readily soluble even in nonpolar solvents, and sublimable in vacuum. They are thermally stable and resistant to oxidation, such behavior ruling out their formulation as acetylphosphinodiimines but being in accord with cyclic phosphazenes isomeric to them; moreover, their molecular weights are found by osmometry and mass spectrometry to correspond to twice that of the empirical formula. Of the various structural isomers consistent with the above data, the nuclear magnetic resonance spectra provide unequivocal evidence in favor of formula *(1)*[2]: The large positive ^{31}P shift can be attributed only to pentacoordinated phosphorus, and the multiplet structure of the ^1H-NMR signal when X = CH_3 and $N(CH_3)_2$ can only be due to a $H_nPP'H_n$ spin system with proximate phosphorus atoms.



(1)

Compound	*(1a)*	*(1b)*	*(1c)*
X	Cl	CH_3	$N(CH_3)_2$
Decomp. pt. (°C)	150	180	153
M.wt. (calc.)		264.2	380.4
(found [a])		264	380
$\delta^1H(CCH_3)$ (ppm) [b]	−2.12 [c]	−1.77	−1.85
J (Hz)	0.9		
$\delta^1H(X)$ (ppm) [b]		−1.68 [d]	−2.55 [d]
J (Hz)		14.4	13.5
$\delta^{31}P$ (ppm) [e]	+52.7	+42.5	+40.5

[a] Molecular ion in the mass spectrum; recorded by Dr. *H. Seidl*.

[b] Solution in CCl_4 with TMS as internal standard.

[c] Pseudotriplet; $|J_{POCCH} + J_{PNNCCH}|$ is given as coupling constant.

[d] Multiplet; $|J_{PCH} + J_{PNPCH}|$ is given as coupling constant for *(1b)*, and $|J_{PNCH} + J_{PNPNCH}|$ is given for *(1c)*.

[e] Solution in CCl_4 with 85% H_3PO_4 as external standard.

Compounds *(1)* should be regarded as products of phosphazene dimerization. Although dimerization of a phosphazene to the 1,3,2,4-diazadiphosphetidine ring is known in principle, the reaction has hitherto been limited to iminotrihalogenophosphoranes with strongly basic imino nitrogen carrying a not too bulky substituent[3]; phosphazines are known only as monomers. The dimerization of an oxadiaza-P^V-phosphole is therefore unexpected, at least when X = CH_3 and $N(CH_3)_2$, and would appear to be connected with the phosphorus becoming member of a small ring. For an oxadiazaphosphole an OPN angle of about 90° is required, which can be readily realized only with pentacoordinated phosphorus(v). Cyclophosphazenes having six or more members in the ring show no tendency to associate.

To satisfy the angle requirements, a phosphorus atom in *(1)* must participate in both the four-membered and the five-membered ring, with one axial and one equatorial bond of the trigonal bipyramid; the five-membered rings can be fused onto the longer (axial) or the shorter (equatorial) sides of the diazadiphosphetidine rectangle. If the two external rings are assumed to be in *trans* position, then two structures are possible for *(1)*, that with the electronegative oxygen in the axial position being the most likely[4]; it is confirmed for *(1b)* and *(1c)* by the equivalence of the methyl protons in the ^1H-NMR spectrum.

2,2,7,7-Tetrachloro-4,9-dimethyl-3,8-dioxa-1,5,6,10-tetraaza-2,7-diphospha-P^V-tricyclo[5.3.0.$0^{2,6}$]deca-4,9-diene (dimeric 2-dichloro-5-methyl-1,3,4,2-oxadiaza-P^V-phospole) (1a)

An intimate equimolar mixture of PCl_5 and acetohydrazide reacts exothermally with liberation of HCl and formation of a melt. Compound *(1a)* sublimes from the crude, glassy reaction product at 120 °C/0.1 torr in the form of needle-shaped crystals (yield 52%).

(1b) and (1c)

Trichlorophosphorane (0.1 mole) is added with stirring at 0 °C to a solution of acetohydrazide (0.1 mole) and triethylamine (0.3 mole) in benzene (120 ml). After the reaction mixture has been kept at 0 °C for 3 h and at 20 °C for 15 h, the triethylammonium chloride is filtered off and the filtrate is evaporated to dryness. *(1b)* can be sublimed at 130 °C/0.1 torr, and *(1c)* can be recrystallized from pentane (yield 80%).

Received: June 26, 1969 [Z 44 IE]
German version: Angew. Chem. *81*, 707 (1969)

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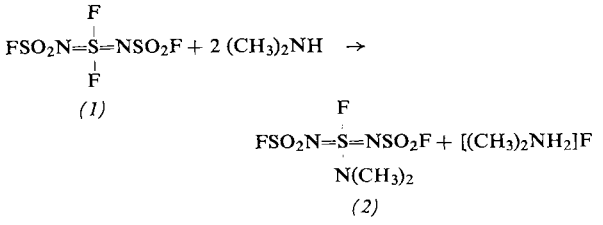
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Bis(dimethylamido)bis(*N*-fluorosulfonylimido)-sulfur, a Covalent Compound Containing the SN_4 Group[1]

By *H. W. Roesky* and *D. P. Babb*[*]

During investigations on fluorosulfonyl compounds we succeeded in preparing for the first time a covalent sulfur-nitrogen compound whose sulfur atom is surrounded by four nitrogen atoms.

Bis(*N*-fluorosulfonylimido)sulfur difluoride[2] *(1)* reacts with dimethylamine in diethyl ether to give dimethylamidobis-(*N*-fluorosulfonylimido)sulfur fluoride *(2)*.

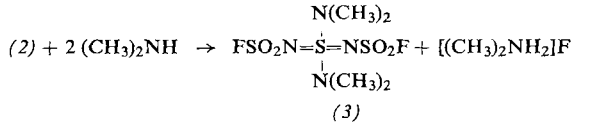


(1) *(2)*

Dimethylamine (6.8 g, 0.15 mole) is passed into a stirred solution of *(1)* (18.5 g, 0.07 mole) in diethyl ether (300 ml) at −78 °C during 1 h. The reaction mixture is then warmed to room temperature and the ethereal phase separated off. Removal of the ether under reduced pressure and subsequent distillation of the residue at oil-pump vacuum affords 6 g (20%) of *(2)*.

Compound *(2)* is a colorless liquid (b.p. 115 °C/0.01 torr) which was identified by elemental analysis and NMR spectroscopy. The ^{19}F-NMR spectrum recorded at room temperature shows a doublet due to the fluorine atoms of the FSO_2 groups, $\delta_{FSO_2} = -60.3$ ppm ($CFCl_3$ as external standard); $J_{FF} = 7.4$ Hz. The fluorine atom of the FSN_3 group gives rise to a multiplet of intensity ratio 1:6:17:32:46:52:46:32:17:6:1 by superposition of a triplet (FF coupling), which is split into three septets as a result of FH coupling. The intensity ratio $F_{SO_2}:F_{SN_3}$ is 2:1; $\delta_{FSN_3} = -58.4$ ppm. IR spectrum: ≈3300 w, ≈3400 w, 1410 s, 1240—1140 vs, 1100 s, 1045 m, 870—770 vs, 660 s cm^{-1}.

Compound *(2)* undergoes exothermic reaction with dimethylamine at room temperature in the absence of a solvent to give bis(dimethylamido)bis(*N*-fluorosulfonylimido)sulfur *(3)*.

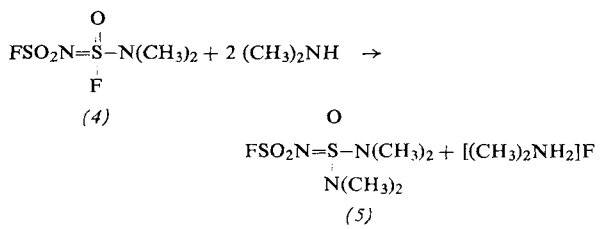


(3)

An excess of dimethylamine is passed very slowly — in order to avoid overheating — into compound *(2)* (4 g) in a 100-ml two-necked flask. The reaction product is extracted portionwise with 100 ml of ether and the extract purified, after removal of the ether, by sublimation at oil-pump vacuum. Yield: 1.5 g (34%).

Compound *(3)* is a white solid, m.p. 123 °C, which was characterized by elemental analysis and by its ^{1}H- and ^{19}F-NMR spectra (solution in CD_3CN). ^{19}F-NMR spectrum: one singlet, $\delta_F = -58.7$ ppm ($CFCl_3$ as external standard). ^{1}H-NMR spectrum: one singlet at $\delta_H = -2.90$ ppm (TMS as external standard). IR spectrum: ≈3420 w, ≈2950 w, 1460 m, 1392 vs, 1278 m, 1206 vs, 1100 vs, 1055 m, 962 vs, 860 s, 800 s, 765 s, 740 vs, 662 m, 603 s, 548 vs, 502 w, 460 w cm^{-1}.

Dimethylamido-*N*-fluorosulfonylimidosulfur oxide fluoride[3] *(4)* reacts with dimethylamine at room temperature, in a manner similar to *(2)*, to give bis(dimethylamido)-*N*-fluorosulfonylimidosulfur oxide *(5)*. We found that 18 g of *(4)* gives 8.3 g (41%) of *(5)*.



(4) *(5)*

Compound *(5)* is a colorless solid, m.p. 35 °C, b.p. 116 to 124 °C/0.01 torr. ^{1}H-NMR spectrum: one singlet, $\delta_H = -2.99$ ppm (TMS as external standard). ^{19}F-NMR: one singlet at $\delta_F = -58.5$ ppm ($CFCl_3$ as external standard). Elemental analysis confirmed the composition of the compound. IR spectrum: ≈2950 s, 1470 s, 1380 vs, 1270 vs, 1190 vs, 1090 vs, 1040 s, 960—940 vs, 825 vs, 765 vs, 734 vs, 678 vs, 602 s, 547 vs cm^{-1}.

Received: July 9, 1969 [Z 49 IE]
German version: Angew. Chem. *81*, 705 (1969)

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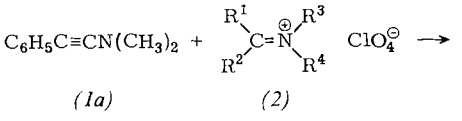
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Reactions of Ynamines with Iminium Salts[1]

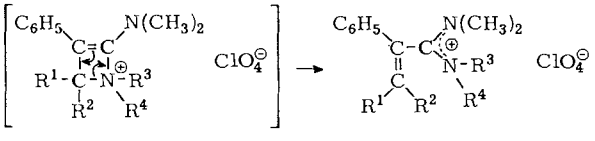
By *R. Fuks, G. S. D. King,* and *H. G. Viehe*[*]

Ynamines are highly reactive nucleophilic acetylenes[2], which readily undergo cycloadditions with carbonyl compounds[3], imines[3,4], and other isolated[5–9], conjugated, or cumulated multiple bond systems[4,9–12]. In this communication we describe the condensation of ynamines with iminium salts.

N,N-Dimethylphenylethynylamine *(1a)* reacts readily at room temperature in chloroform solution with aliphatic iminium salts *(2a)—(2e)* apparently *via* the cyclic intermediate *(3)* to give acrylamidinium perchlorates *(4a)—(4e)*; in the case of *(2c)—(2e)* this is noteworthy since it represents a C_2-ring expansion.



(1a) *(2)*



(3) *(4)*

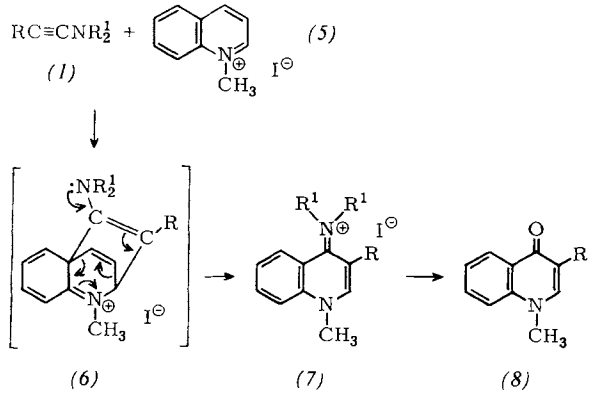
	(4) Yield (%)	M.p. (°C)
(a), $R^1 = R^2 = R^3 = R^4 = CH_3$	60	114
(b), $R^1 = R^2 = R^3 = CH_3$; $R^4 = C_6H_5$	97	208
(c), $R^1 = CH_3$; $R^2 = C_6H_5$; $R^3R^4 = -(CH_2)_4-$	72	172
(d), $R^1R^2 = -(CH_2)_5-$; $R^3R^4 = -(CH_2)_4-$	93	155
(e), $R^1 = R^3 = CH_3$; $R^2R^4 = -(CH_2)_3-$	83	116

The analytical and spectral data (UV, IR and NMR) confirm the proposed structure *(4)*. Hydrolysis of *(4a)* with 30% aqueous NaOH affords β,β,*N,N*-tetramethyl-α-phenylacrylamide in 84% yield. Melting point and mixed melting point (56 °C) are identical with that of the product obtained from *(1a)* and acetone[3].

Heteroaromatic iminium salts also condense easily with ynamines in chloroform at room temperature. Thus, with *N*-methylquinolinium iodide for example, compound *(1)* gives 4-amino-*N*-methylquinolinium iodide derivatives *(7)* possibly *via* intermediate *(6)*, which then loses an unidentified C_2-

unit. Upon hydrolysis in 10% aqueous NaOH compounds *(7)* give 3-substituted *N*-methyl-4-quinolones *(8)*.

The ynamines *(1a)* and *(1c)* react with *N*-methylisoquinolinium iodide derivatives *(9)* to give 2:1 adducts. In the case of *(1c)* and *(9)*, R^2 = H, the structure of the adduct was shown by X-ray analysis to be 2a,10-di-*tert*-butyl-2,9-bis-(dimethylamino)-1-methyl-2a,3,8,8a-tetrahydro-3,8-ethenonaphtho[2,3-*b*]-1-azetinium iodide *(11a)*. *(11a)* crystallizes in two monoclinic forms (C_{2h}^5) having 4 or 8 molecules in the unit cell. At the present stage the discrepancy factor is 0.22. The reaction leading to *(11)* might involve the intermediate *(10)*.



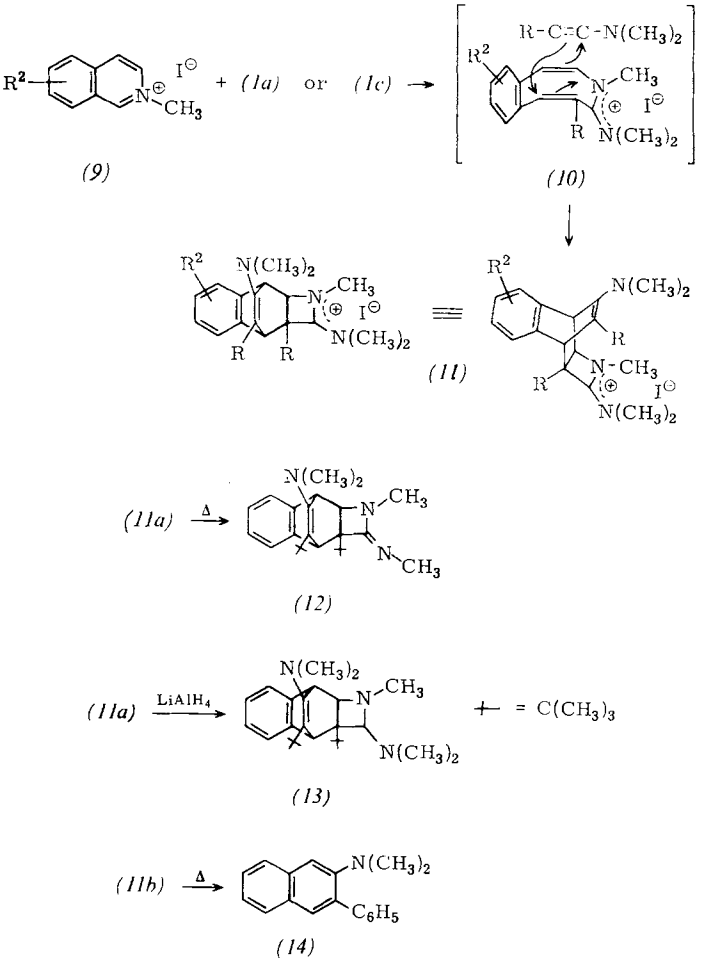
(1) *(5)* *(6)* *(7)* *(8)*

	(7)		*(8)*		
	Yield (%)	M.p. (°C)	Yield (%)	M.p. (°C)	
(a), R = C_6H_5; R^1 = CH_3	45	209	92	126	[13]
(b), R = C_6H_5; R^1 = C_2H_5	50	200	90	126	[13]
(c), R = $C(CH_3)_3$; R^1 = CH_3	75	283	95	132	

(11a) is remarkably stable; it remains unchanged on boiling for several hours in 10% aqueous NaOH or in 6 N HCl in spite of its enamine function. By pyrolysis at 240–270 °C it loses CH_3I with formation of *(12)* in 97% yield, which on treatment with CH_3I reverts to *(11a)*. The amidinium function can be reduced by $LiAlH_4$ to the aminal *(13)*. The analogous product *(11b)* decomposes at 200–240 °C to give 2-dimethylamino-3-phenylnaphthalene *(14)* in 68% yield.

General experimental procedure (in collaboration with *M. A. Hartemink*).

The solid iminium salt is added in small portions to a stirred and ice-cooled chloroform solution of the ynamine (15 ml for 2 mmoles, 10% excess of the stoichiometric quantity). The mixture is kept at room temperature for half an hour after which the solvent is distilled off. The residue is crystallized from chloroform, methanol, or mixed solvents such as



(9) *(10)* *(11)* *(11a)* *(12)* *(11a)* *(13)* *(11b)* *(14)*

Physical and spectroscopic data of compounds *(11a)*–*(14)*.

Compound	Yield (%)	M.p. (°C)	IR (KBr) (μ)	UV (CH_3OH) (nm) λ_{max} (ε × 10^{-3})	NMR (in $CDCl_3$) [a] (τ)
(11a), R = $C(CH_3)_3$; R^2 = H	94	266	5.89; 6.12	inf. 263 (1.5); 212 (31.0)	2.65 (m/1 H), 2.9 (m/3 H), 5.45 (d/1 H) [b], 5.76 (s/1 H), 5.76 (d/1H) [b], 6.34 (s/3 H), 6.45 (s/3 H) 6.57 (s/3 H), 7.62 (s/5 H), 8.83 (s/9 H), 9.17 (s/9 H).
(11b), R = C_6H_5; R^2 = H	53	181	5.84; 623	325 (3.2), 219 (48.6)	2.3–3.1 (m/14 H), 5.09 (d/1 H) [b], 5.24 (s/1 H), 5.58 (d/1 H) [b], 6.15 (s/3 H), 6.73 (s/3 H), 7.29 (s/6 H), 7.82 (s/3 H).
(11c), R = C_6H_5; R^2 = 5-OCH_3	26	255	5.81; 6.2	325 (5.6), 293 (5.5), 210 (46.0)	2.3–3.0 (m/12 H), 3.48 (dd/1 H), 5.08 (d/1 H) [b], 5.27 (s/1 H), 5.53 (d/1 H) [b], 6.11 (s/3 H), 6.24 (s/3 H), 6.68 (s/3 H), 7.24 (s/6 H), 7.78 (s/3 H).
(11d), R = C_6H_5; R^2 = 7-NO_2	57	220	5.83; 6.2	414 (1.2), 390 (1.3) inf. 300 (7.4)	1.8–2.9 (m/13 H), 4.28 (d/1 H) [b], 4.67 (s/1 H), 5.6 (d/1 H) [b], 6.27 (s/3 H), 6.8 (s/3 H), 7.22 (s/6 H), 7.78 (s/3 H).
(12) [c]	94	132	5.87; 6.1	inf. 262 (1.6), 205 (24.7)	2.9 (m/4 H), 5.87 (s/1 H), 6.05 (d/1 H) [b], 6.87 (d/1 H) [b], 6.98 (s/6 H), 7.68 (s/6 H), 8.82 (s/9 H), 9.23 (s/9 H).
(13)	80	180	6.11	inf. 264 (1.6)	3.05 (m/4 H), 6.1 (s/1 H), 6.22 (d/1 H) [b], 6.8 (s/1 H), 7.1 (d/1 H) [b], 7.63 (s/3 H), 7.74 (s/6 H), 7.98 (s/6 H), 8.88 (s/9 H), 9.41 (s/9 H).
(14)	68	106	6.14; 6.26	345 (2.2), 263 (43.4), 237 (30.0), 211 (39.6)	2.2–2.8 (m/11 H), 7.43 (s/6 H).

[a] We thank Mr. *R. Merényi* for interpreting the NMR spectra ($Si(CH_3)_4$ as internal standard). [b] $J \approx 4$ Hz.
[c] 22% of an isomeric component was present.

methanol-acetone-methyl acetate (or ether), and chloroform-acetone-methyl acetate (or ether).

Received: April 15, 1969 [Z 46 IE]
German version: Angew. Chem. *81*, 702 (1969)
Publication delayed at authors' request

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A Convenient Synthesis of Disulfides[1]

By *H. Alper* [*]

Pentacarbonyliron is a useful reagent for the preparation of *S*-alkyl(aryl)thiosulfonates $RSSO_2R$ from sulfonyl chlorides RSO_2Cl[2]. Reaction of sulfonyl chlorides *(1)* with hexacarbonylmolybdenum in anhydrous tetramethylurea (TMU) provides a facile method for obtaining a variety of disulfides *(2)*.

$$\underset{(1)}{RSO_2Cl} \xrightarrow{Mo(CO)_6 \text{ in TMU}} \underset{(2)}{RSSR}$$

The procedure involved is simple and rapid, giving disulfides in good yields. The metal carbonyl does not function as a catalyst and addition of boron trifluoride etherate does not improve the yield[2].

Sulfonyl Chloride	Yield of Disulfide (%)
Benzene	74
2-Naphthalene	68
p-Bromobenzene	55
p-Toluene	80
Methane	68
α-Toluene	60
n-Hexadecane	75

Hexacarbonyl-chromium and -tungsten proved to be relatively ineffective reagents for the reaction. For example, treatment of *p*-toluenesulfonyl chloride with hexacarbonylchromium under identical conditions to those described for $Mo(CO)_6$ (general procedure) gave recovered starting material. Di-*p*-tolyl disulfide was obtained in only 26% yield, along with 2% of the corresponding *S*-thiolsulfonate, even after heating at 85 °C for 12 hours.

General Procedure

A mixture of RSO_2Cl (5—35 mmol) and hexacarbonylmolybdenum, molar ratio 1:1.1 to 1.3 (use of a large excess of $Mo(CO)_6$ should be avoided as disulfides react with the metal carbonyl to form polymeric molybdenum sulfides[3]) in dry TMU (10—25 ml) was heated to 70 °C (oil bath temperature) with stirring under nitrogen for 2.0—2.5 hours. The suspended $Mo(CO)_6$ gradually dissolved. The reaction mixture was then heated to 100 °C for 10—15 minutes, cooled and filtered to remove any unreacted metal carbonyl. The filtrate was added to 20 volumes of water and the resulting precipitate (if the disulfide is a solid) was filtered, washed thoroughly with water, and sucked dry. Pure disulfide could then be obtained by recrystallization from a suitable solvent. Liquid disulfides, *e.g.* CH_3SSCH_3, were isolated by distillation of the reaction mixture.

Received: July 14, 1969 [Z 50 IE]
German version: Angew. Chem. *81*, 706 (1969)

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Bis(pentadienyl)dinickel

By *R. Rienäcker* and *H. Yoshiura* [*]

A suspension of anhydrous nickel(II) chloride in 1,4-pentadiene reacts with triethylaluminum at room temperature with evolution of non-stoichiometric amounts of ethylene and precipitation of bis(pentadienyl)dinickel *(1)* in the form of golden-yellow crystals (75.6% yield). Under similar conditions, suspensions of $NiCl_2$ in ether, benzene, or pentane are reduced to metallic nickel by $Al(C_2H_5)_3$.

The novel complex *(1)*, recrystallized from anhydrous pentane (1 g/l), is sparingly soluble in aprotic solvents and is extremely sensitive to air. Its composition is established by nickel analysis (calculated 46.55, found 46.0%), the mass spectrum [molecular ion *m/e* 250/252 and 254 ($Ni_2C_{10}H_{14}$), main fragments *m/e* 67 (C_5H_7) and 58/60 (Ni)], and X-ray structure analysis[1]. The IR spectrum provides no indication of free double bonds but contains a band that is typical for π-allyl compounds at 1480 cm^{-1} thus showing a certain analogy to the spectrum of bis(pentadienyl)chromium[2], which, however, contains only one metal atom bonded to two pentadienyl moeities. Protonolysis of *(1)* with 2-ethyl-1-hexanol affords small amounts of 1,3-pentadiene and C_{10} hydrocarbons in addition to 1-pentene, *cis*-2-pentene, and *trans*-2-pentene in the molar ratio 3:2:14.

Reaction of *(1)* with triphenylphosphine proceeds almost quantitatively to give 1,3,7,9-decatetraene and tetrakis(triphenylphosphine)nickel; the pentadienyl ligands are linked on displacement.

The reaction involved in formation of *(1)* is clearly of a complex nature: 1,4-Pentadiene loses hydrogen on conversion into pentadienyl; this hydrogen reacts with the excess of 1,4-pentadiene to give pentene. In the organoaluminum component, ethyl groups are replaced by C_5 groups with liberation of ethylene; these C_5 groups are found as pentene and pentane on hydrolysis of the mother liquor. The reaction presumably proceeds *via* nickel hydrides[3]. To summarize, we can formulate the following formation reaction:

$$2\,NiCl_2 + 5\,C_5H_8 + 4\,Al(C_2H_5)_3 \rightarrow \underset{(1)}{Ni_2(C_5H_7)_2} + 4\,AlCl(C_2H_5)_2 + 4\,C_2H_4 + 3\,C_5H_{10}$$

Received: July 14, 1969 [Z 51a IE]
German version: Angew. Chem. *81*, 708 (1969)

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Crystal Structure of Bis(pentadienyl)dinickel

By *C. Krüger* [*]

Bis(pentadienyl)dinickel [1] crystallizes as monoclinic prisms along { 001 } in space group $P2_1/n$ according to Weissenberg and precession photographs. The unit cell contains two centro-symmetric molecules, the calculated density being 1.804 g cm^{-3}.

The structure was determined with an automatic Hoppe-Siemens diffractometer ($Cu_{K\alpha}$ radiation, $\lambda = 1.5418$). Accurate cell constants were calculated by the method of least squares from 44 recorded reflections $\theta > 50°$: $a = 12.731 \pm 0.0004$, $b = 8.591 \pm 0.0003$, $c = 4.233 \pm 0.0004$ Å; $\beta = 90.525 \pm 0.005°$. The intensities of 879 reflections (hkl—$\bar{h}kl$) $\theta < 70°$ of a crystal measuring 0.13 mm × 0.37 mm × 0.69 mm were recorded by the 5-value method, a FORTRAN (IV) program (DIFFRA) having been developed for control of the diffractometer; three reflections were below the detection limit After corrections had been made for Lorentz, polarization, and absorption factors, the structure was determined by the Patterson heavy-atom method followed by least-squares refinement. The atomic positions and anisotropic temperature parameters given in the Table were found at a weighted R factor ($F_0^2/4W_0$) of 0.056 taking into account the hydrogen atoms found in a difference Fourier synthesis [2].

The most important interatomic distances and bond angles of the dimeric molecule symmetry C_{2h} are shown in Fig. 1 [2]; maximum errors ±0.006 Å and ±0.4°, respectively. A unit cell of the crystal is reproduced in Fig. 2.

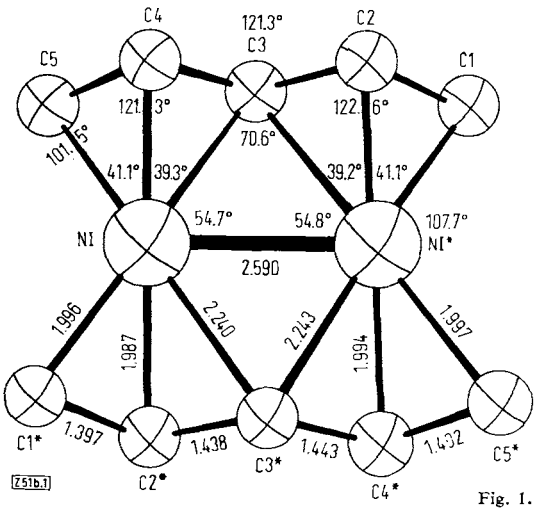


Fig. 1.

The best plane of the sp^2-hybridized carbon chain is described by the equation

$$6.034x + 4.723y - 2.930z - 2.298 = 0$$

C^3 protrudes from the plane C^1—C^2, C^4—C^5 by 0.23 Å. The terminal C—C bonds of the asymmetric π-allyl systems show more double bond character than the bonds C^2—C^3 and C^3—C^4. A typical three-center bond is possible between C^3 and the Ni atoms, which are separated by a bonding distance of 2.540 ± 0.001 Å; the experimental data are consistent with formulation *(1)*, the bonding shown being feasible *via* the geometrically favorable occupied molecular orbitals ψ_1, ψ_2, and ψ_3 of pentadienyl and the d orbitals of the nickel.

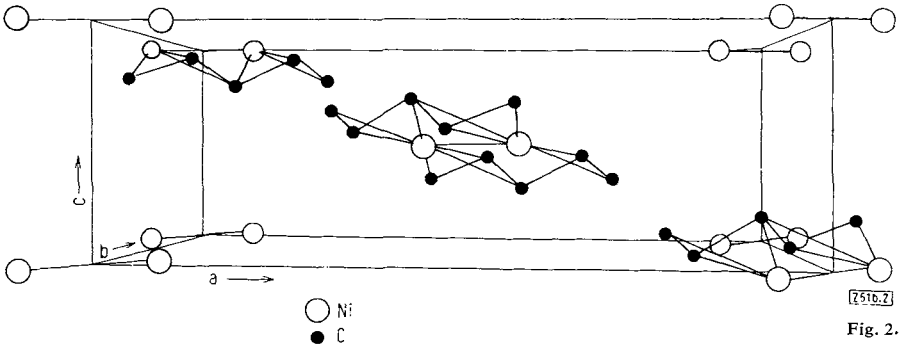
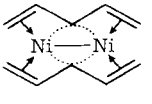


Fig. 2.

	(×10⁴)		
	x	y	z
Ni	4219	5966	4924
C^1	5756	1867	6774
C^2	4761	2311	5691
C^3	4184	3578	7059
C^4	3245	4179	5569
C^5	2782	5568	6592

	exp [−(h^2b_{11} + ··· 2 klb_{23})]					
	$b_{1,1}$	$b_{2,2}$	$b_{3,3}$	$b_{1,2}$	$b_{2,3}$	$b_{1,3}$
Ni	358	370	612	−21	1	25
C^1	367	291	704	− 8	77	− 9
C^2	325	271	549	−60	27	36
C^3	312	261	465	−92	38	21
C^4	237	337	527	−57	5	60
C^5	277	374	648	13	−28	129



(1)

Received: July 14, 1969 [Z 51b IE]
German version: Angew. Chem. *81*, 708 (1969)

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Crystal Structure of Methyltrimethylsiloxomercury

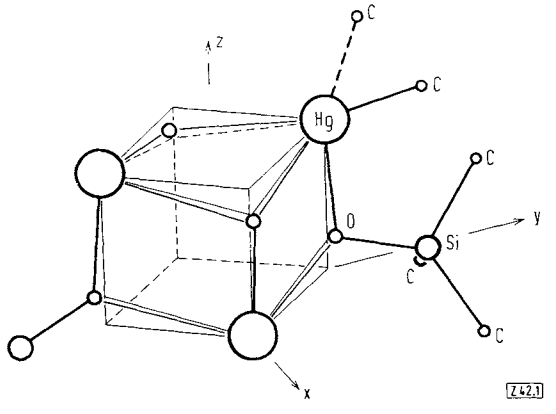
By *G. Dittmar* and *E. Hellner*[*]

$CH_3HgOSi(CH_3)_3$ *(1)* is monomeric in benzene[2] whereas the analogous compounds of zinc and cadmium are present as tetramers in this solvent[1]. A cubane structure has been proposed for $[CH_3MOSi(CH_3)_3]_4$, M = Zn, Cd. Crystal structure analysis also indicates that *(1)* has a cubane-like structure. All these compounds are sensitive to air, moisture, and X-rays.

Crystals of *(1)* were fused in glass capillaries and the intensities of 280 reflections were estimated visually from Weissenberg photographs; an absorption correction could not be carried out. The tetragonal unit cell, space group $P4_2/nmc$ with $a_0 = 13.190 \pm 0.002$, $b_0 = 13.190 \pm 0.002$, $c_0 = 9.798 \pm 0.005$ Å contains eight formula units. $d_{X\text{-ray}} = 2.37$, $d_{exp} = 2.21$ g cm^{-3}.

The structure was determined by the heavy atom method with the help of a Patterson synthesis, four Fourier syntheses, and eighteen refinements according to the method of least squares. An *R*-value of 0.250 was obtained on using individual anisotropic temperature factors with inclusion of unobserved intensities (0.209 for observed intensities alone).

The Hg atoms form a regular tetrahedron about the $\bar{4}$-axis with Hg—Hg distances of 3.71 Å; the O atoms form a distorted tetrahedron in opposing orientation, the Hg—O bond length being 2.11 Å. From the considerable anisotropic temperatures factors observed for the O atom in the Hg—O bond parallel to the *c*-axis it follows that the structure represents a transition from an assemblage of four individual molecules *(1)* about the $\bar{4}$-axis to the ideal cubane structure.



Z 42.1

Atomic coordinates:

Atom	Hg	Si	O	$C^{1,1}$	$C^{1,2}$	$1/2C^2$
x	0.2500	0.250	0.250	0.25	0.37 ± 1	0.38 ± 2
y	0.3899 ± 4	0.510 ± 3	0.389 ± 8	0.61 ± 2	0.54 ± 2	0.47 ± 3
z	0.3848 ± 8	0.110 ± 8	0.170 ± 24	0.25 ± 3	0.01 ± 1	0.46 ± 4

Crystal structure of methyltrimethylsiloxomercury.

Bond lengths and angles (Å)		(°)	
Hg—O	2.11 ± 0.2	O—Hg—C	112 ± 8
Hg—C	2.09 ± 0.4	Hg—O—Si	115 ± 6
Si—O	1.61 ± 0.1	C—Si—C	105 ± 7
Si—C	1.83 ± 0.4		
	1.86 ± 0.4		
Distances and angles between the molecules (Å)		**(°)**	
Hg—Hg	3.71 ± 0.007	Hg—Hg—Hg	60.0 ± 0.3
O—O	3.90 ± 0.20	O—O—O	76 ± 6
	3.14 ± 0.42	Hg—O—Hg	99 ± 6
Hg—O	2.75 ± 0.20	O—Hg—O	81 ± 6
			91 ± 3

The Si—O bond is directed towards the center of the Hg tetrahedron.

Two methyl groups are situated in the mirror plane of the space group parallel to *y*; these are linked to Hg or Si atoms. Weak reflections of the *hhl* group with $l = 2n-1$ indicate that the CH_3 group attached to Hg does not lie exactly in the plane of symmetry. A Fourier synthesis and intensity calculation on the subcell $P4_2/n$ gives two positions for these CH_3 groups, which are symmetric to the mirror plane and are statistically occupied.

Received: June 23, 1969 [Z 42 IE]
German version: Angew. Chem. *81*, 707 (1969)

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Complexing Behavior of Stannanide Ions: Tetrakis(trichlorostannanido)niccolate(0)[1]

By *Th. Kruck* and *B. Herber*[*]

Not only silanide ions $[SiR_3]^-$ (R = alkyl and aryl)[1] but also the homologous stannanide ions $[SnR_3]^-$ (R = aryl, halogen) have a strong tendency to form complexes with transition metals in low oxidation states. This can be illustrated by reaction of triphenylstannanide $[Sn(C_6H_5)_3]^-$ *(1)* and trichlorostannanide $[SnCl_3]^-$ *(2)* with metal carbonyls.

$Fe(CO)_5$ and $Ni(CO)_4$ react violently with the lithium salt[2] of *(1)* (molar ratio 1.5 : 1) in diethyl ether/tetrahydrofuran (THF) to give the monosubstituted carbonyl metalates *(3)* in almost quantitative yield according to the formulation:

$$M(CO)_n + Li[Sn(C_6H_5)_3] \xrightarrow{THF} [Li(THF)_x]^+[M(CO)_{n-1}Sn(C_6H_5)_3]^- + CO$$

(3)

They can be isolated as solvated lithium salts and in the form of complex salts $[As(C_6H_5)_4][Fe(CO)_4Sn(C_6H_5)_3]$ (yellowish green crystals, $\nu_{CO} = 2001$ (A_1), 1923 (A_1), 1897 (E_1), and 1877 (E_1) cm^{-1}; suspension in Nujol) and $[N(C_2H_5)_4][Ni(CO)_3Sn(C_6H_5)_3]$ (bronze colored leaflets, $\nu_{CO} = 2001$ (A_1) and 1962 (E) cm^{-1}; solution in dimethyl sulfoxide (DMSO)) that are stable towards heat and air.

Further CO substitution was not possible because of the considerable strengthening of the metal-CO bond on formation of the monosubstituted complex. Octacarbonyldicobalt reacts with the potassium salt of *(2)* (molar ratio 1 : 2) mainly *via* disproportionation of the metal carbonyl ($2\,Co^0 \rightarrow Co^I + Co^{-I}$) to give the red neutral complex *(4)* according to the equation:

$$Co_2(CO)_8 + K[SnCl_3] \xrightarrow[THF]{-40 \text{ to } 40\,^\circ C} CoI(CO)_4SnCl_3 + K[Co^{-I}(CO)_4]$$

(4)

Compound *(4)*, which is stable towards air, reacts with $[N(C_2H_5)_4][SnCl_3]$ in DMSO/THF (molar ratio 1 : 1) at 40 °C to give the olive-green crystalline complex $[N(C_2H_5)_4][Co^I(CO)_3(SnCl_3)_2]$ in *ca.* 35% yield.

Although the anionic ligands $[ElR_3]^-$ (El = Si, Sn; R = alkyl or aryl) are stronger donors compared to the isoelectronic neutral phosphines PR_3 and stibines SbR_3, $[SnCl_3]^-$ has a reduced donor character because of the electronegative Cl atoms. In the reaction with tetracarbonylnickel a distinct analogy is recognizable between PCl_3 and *(2)* so far as possibility of complex formation is concerned. Reaction of

tetracarbonylnickel with $K[SnCl_3]$ (molar ratio 1 : 4) over a period of two days and with UV irradiation leads to total loss of CO and formation of the isolable but impure potassium salt of tetrakis(trichlorostannanido)niccolate(0) *(5)*.

$$Ni(CO)_4 + 4\,K[SnCl_3] \xrightarrow[THF]{20\,^\circ C} K_4[Ni(SnCl_3)_4] \cdot x\,THF + 4CO$$
(5)

Compound *(5)* is the first homogeneous complex obtained that contains a ligand whose donor atom is an element of the fourth main group other than carbon.

The existence of the totally substituted complex anion was established by its conversion into the solvated acid *(6)* and into easily identifiable complex salts. On introducing hydrogen chloride into a THF solution of *(5)* the solution becomes hot, KCl separates out, and a bright yellow, pungent oil of low viscosity is formed. This oily compound contains acidic protons whose NMR signal appears at 8.75 ppm (referred to TMS)[3]. The characteristic Sn—Cl stretching vibrations of *(2)* appear in the IR spectrum at 295 (A_1) and 256 (E) cm^{-1}; no ν_{CO} bands appear[3]. Not THF, but its fission product with HCl, 4-chlorobutanol, functions as solvating agent for the protons; the isolated acid has the constitution $H_4[Ni(SnCl_3)_4] \cdot 4\,Cl(CH_2)_4OH$ *(6)* (this composition could also be established analytically). This compound, which is readily soluble in THF and in acetone, rapidly decomposes in air and on warming loses HCl; it is stable almost indefinitely under nitrogen. By reaction of a THF solution of *(5)* with aqueous solutions of bulky cations we have been able to prepare, *inter alia*, the complex salts $[As(C_6H_5)_4]_4[Ni(SnCl_3)_4]$ (beige crystals, decomposing at temperatures above 190 °C; ν_{SnCl} = 301 (A_1) and 242 (E) cm^{-1}) and $[Cr(C_6H_6)_2]_4[Ni(SnCl_3)_4]$ (orange crystals decomposing at temperatures above 190 °C) after reprecipitation from THF/pentane. Further proof for the composition of the acid *(6)* was afforded by reacting it in acetonitrile/THF with $[Cr(C_6H_6)_2]I$ — crystals (orange leaflets) were obtained, which, on the basis of elemental analysis and the IR spectrum, proved to be indentical with $[Cr(C_6H_6)_2]_4[Ni(SnCl_3)_4]$ prepared from the potassium salt *(5)*.

Received: July 1, 1969 [Z 45 IE]
German version: Angew. Chem. *81*, 704 (1969)

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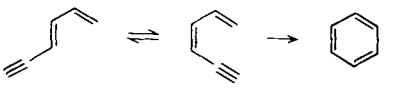
Preparation of Benzene by Pyrolysis of *cis*- and *trans*-1,3-Hexadien-5-yne

By *H. Hopf* and *H. Musso* [*]

Photoisomerizations of benzene, and a few of its derivatives, leading to polycyclic hydrocarbons have been known for some time[1]. Under certain conditions such photolyses can also lead to the formation of acyclic hydrocarbons. Thus, when benzene vapor is irradiated with light of wavelength 1849 Å it is first converted into fulvene and *cis*-1,3-hexadien-5-yne *(2)*; by a secondary reaction *(2)* is then converted into the *trans*-isomer *(1)*. With light of wavelength 2537 Å, a rapid *cis-trans* isomerization of *(1)* and *(2)* takes place in the gas phase, as well as a slow conversion of these compounds into benzene and fulvene[2].

Since excitation of unsaturated hydrocarbons may be achieved either photochemically or thermally[3]; we have investigated the pyrolysis of the hexadienynes *(1)* and *(2)*.

Gas-chromatographically pure samples of *(1)* and *(2)*[4] are stable in the gas phase (35—70 torr) up to temperatures of at least 224 ± 1 °C. At 274 ± 1 °C, however, both compounds undergo simultaneous *cis-trans* isomerization and are converted into benzene.



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

A mixture of 64 % *(1)*, 11 % *(2)*, and 25 % *(3)* as well as small amounts of polymeric material are obtained if *(1)* is heated for 90 min at 274 °C. Similarly, a mixture consisting of 9 % *(1)*, 55 % *(2)*, and 36 % *(3)* is obtained from *(2)* (determined chromatographically by triangulation: 50 m Golay column, polypropylene glycol, 30 °C; relative retention times *(1)* 1.00, *(2)* 0.91, and *(3)* 0.73).

Since, for steric reasons, it is unlikely that *(1)* is converted directly into *(3)*, it is assumed that an isomerization of *(1)* to *(2)* takes place first in the formation of *(3)* from *(1)*. On a preparative scale[5], compound *(3)* may be prepared in 50 % yield by pyrolyzing *(2)* (0.6 g) at 510 °C in a stream of nitrogen, the gas mixture being allowed to remain for 45 s in a tube filled with Raschig rings. Under these conditions *ca.* 20 % of a high-boiling mixture containing a least 15 components is also obtained; two of these components have been identified gas-chromatographically as styrene and naphthalene.

Further investigation ought to show — as is to be expected from the by-products — whether a radical reaction and the last step of the Berthelot benzene synthesis are involved here[6].

Received: June 13, 1969;
revised: July 11, 1969 [Z 48 IE]
German version: Angew. Chem. *81*, 704 (1969)

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[1] *H. G. Viehe*, Angew. Chem. *77*, 768 (1965); Angew. Chem. internat. Edit. *4*, 746 (1965); *D. Bryce-Smith*, Pure appl. Chem. *16*, 47 (1968); *D. M. Lemal* and *J. P. Lokensgard*, J. Amer. chem. Soc. *88*, 5934 (1966).

[2] *L. Kaplan*, *S. P. Walch*, and *K. E. Wilzbach*, J. Amer. chem. Soc. *90*, 5646 (1968).

[3] For a summary see *G. B. Gill*, Quart. Rev. (chem. Soc., London) *22*, 338 (1968).

[4] *F. Sondheimer*, *D. A. Ben-Efraim*, and *Y. Gaoni*, J. Amer. chem. Soc. *83*, 1682 (1961).

[5] B.p. and spectra agreed with those of authentic benzene.

[6] *M. Berthelot*, Liebigs Ann. Chem. *141*, 173 (1867).

The Physics of Liquids

Following the Faraday Society colloquium in April 1967 on the properties of liquids[1] and the International Center for Theoretical Physics course[2] on the theory of condensed matter in the autumn of 1967, The Institute of Physics and The Physical Society organized a conference on the physics of liquids, which took place in Norwich (England) on April 15—18, 1969. This series of events and the numerous recently published monographs[3] on liquids reflect the current strong interest in problems connected with the liquid state.

At present the development seems to be mainly in the direction of fluid dynamics, *i.e.* in investigations of the molecular motions within a fluid. This formed the subject of five out of seven plenary lectures at the conference. In this connection, the main interest centered on two themes:

1) Inelastic scattering experiments with slow neutrons.

2) Computer calculations (using the methods of molecular dynamics) on systems with specified intermolecular forces. In the discussion of the equilibrium properties of liquids, the main emphasis was experimentally on X-ray and neutron scattering, and theoretically on computer calculations (by Monte Carlo and molecular dynamic methods) and on a newly developed perturbation method[4] which considers the perturbing influence of an intermolecular potential on a model assembly of hard spheres (calculated by the Percus-Yevick method or by molecular dynamics).

The lecture by *B. Widom* of Cornell University, Ithaca, N. Y., USA, presently at Imperial College in London, dealt with generalization of the van der Waals equation of state. The thermodynamic consequences when small particles in a model system (*e.g.* point masses or rigid spheres) are embedded in a uniform negative potential were investigated. Previously[5] it had been found that the addition of a uniform negative potential to a computer-calculated system of hard spheres allows the melting process to be simulated. The uniform negative potential is expressed as a function of the density and temperature, from which changes of activity and energy density with respect to the model system are derived. A differential equation for the background potential can be derived from thermodynamic relationships, which establishes a connection between its dependence on density and its dependence on temperature.

The case in which the background potential is independent of temperature and proportional to the density was discussed more thoroughly. This leads to corrections for pressure and energy density corresponding to those of the van der Waals equation: the pressure and energy density of the model fluid should in each case be reduced by a term proportional to the square of the density. A considerable correction for compressibility with respect to the model fluid is also obtained. This, however, gives rise to a principal difficulty: since the background potential is supposed to be uniform, it exerts no force on the molecules. The molecular arrangement should therefore be identical with that of the model system. Since, however, the radial distribution function which describes the arrangement of the molecules is directly related to the compressibility by the so-called compressibility equation, the same molecular arrangements should lead to the same compressibility. *Widom* tried to solve this difficulty by taking into account the effect of fluctuations of the background potential for large molecular distances. Such fluctuations could have a considerable influence on the compressibility without disturbing either the molecular arrangement over smaller distances or the thermodynamic considerations.

It was pointed out in the discussion that the structure factors of many substances, as indicated by neutron and X-ray scattering, differ considerably from that of a model system consisting of hard spheres. It appears that the concept of a fluid as a system of hard spheres under a uniform potential is in many cases a gross simplification.

J. E. Enderby [Battelle Institute, Columbus, Ohio (USA)] spoke about structural investigations by neutron diffraction. While formerly the sources of error in these investigations were not fully understood, and the results were therefore often in error or their accuracy was overestimated, recent developments are marked by an improvement in the method and at the same time by a realistic estimate of the uncertainties. The results of neutron scattering experiments now agree satisfactorily with those gained from X-ray diffraction investigations.

After a discussion of the calculation of radial distribution functions and direct correlation functions from the structure factor $S(Q)$, *Enderby* described some results on systems which contain only one atomic species: the position of the first maximum of the structure factor for lead does not vary with temperature; the structure factor for zinc differs considerably from that of a model fluid consisting of hard spheres. If one can calculate the radial distribution function, and thence the structure factor, from a knowledge of pair interaction energies and statistical theory, it is also possible to draw conclusions about pair interaction energies using the experimentally determined structure factor and statistical theory. If the Percus-Yevick method is used as statistical theory, one obtains for metals a pseudo-pair potential which shows a shallow minimum at the nearest-neighbor distance and a broad positive peak for larger atomic distances. The usual oscillations of the pseudo-pair potential are not reproduced, possibly owing to failure of the Percus-Yevick method.

For systems containing two kinds of atoms, the total scattering cross-section is made up of structure factors related to the radial distribution functions for atoms of the same kind or of different kinds. By using different isotopes having different scattering length for neutrons, it is possible to analyze the total scattering cross section into these individual structure factors. Without such an analysis a misleading picture would be obtained for the molecular distribution function. Analyses of this kind are of particular importance in the investigation of liquid alloys, molecular fluids (carbon tetrachloride), and ionic melts.

The lectures by *P. Schofield*, Harwell (England), and *P. A. Egelstaff*, Harwell (England), dealt with the problems of inelastic neutron scattering.

[1] Discuss. Faraday Soc. *1967*, 43.

[2] Theory of Condensed Matter, Lectures Presented at an International Course, Trieste October 3, to December 16, 1967. International Atomic Energy Agency, Vienna 1968.

[3] a) *P. A. Egelstaff*: Introduction to the Liquid State. Academic Press, New York 1967; b) *S. A. Rice* and *P. Gray*: The Statistical Mechanics of Simple Liquids. Interscience, New York 1965; c) *H. N. V. Temperley, J. S. Rowlinson*, and *G. S. Rushbrooke*: Physics of Simple Liquids. North Holland Publ. Comp., Amsterdam 1968; d) *T. J. Hughel*: Liquids: Structure, Properties, Solid Interactions (Symposium, General Motors Research Laboratories). Elsevier, Amsterdam 1965; e) *G. H. A. Cole*: An Introduction to the Statistical Theory of Classical Simple Dense Fluids. Pergamon Press, Oxford 1967; f) *N. H. March*: Liquid Metals. Pergamon Press, Oxford 1968; g) *H. L. Frisch* and *Z. W. Salsburg*: Simple Dense Fluids. Academic Press, New York 1968.

[4] *J. A. Barker* and *D. Henderson*, J. chem. Physics *47*, 2856, 4714 (1967).

[5] *H. C. Longuet-Higgins* and *B. Widom*, Molecular Physics *8*, 549 (1964).

P. Schofield began his lecture with a review of the formalism used to describe fluid dynamics. The scattering function $S(Q, \omega)$ plays a central role, as it gives the relative frequency of the scattered particles which simultaneously transfer energy $\hbar\omega$ and momentum $\hbar Q$ to the fluid. It is necessary to distinguish between an incoherent scattering function $S_s(Q,\omega)$ and a coherent scattering function $S(Q, \omega)$. The former yields information about the individual movement of atoms and the latter about the correlated movement of many atoms. Starting from $S_s(Q, \omega)$ the velocity autocorrelation function $< v(0)v(t) >$ [*] and the frequency spectrum $\tilde{z}(\omega)$ [**] can be calculated.

The unified theoretical interpretation of the modes of motion of single particles and of the cooperative modes of motion is still an unsolved problem, and a number of models have therefore been developed. Some of the findings strongly resemble those for polycrystalline materials. The best model so far has proved to be one constructed on the basis of a viscoelastic continuum to which is added an adjustable attenuation function, which depends on momentum Q and energy transfer ω.

Egelstaff discussed the experimental results obtained for the coherent inelastic scattering function $S(Q, \omega)$ in relation to models in three ranges of momentum transfer: for small momentum transfers Q, at the maximum of the structure factor $S(Q)$, and for large momentum transfers. For small momentum transfers the characteristic quantity is the position of the subsidiary maxima in the scattered neutron energy distribution [$S(Q, \omega)$ against ω]. At the maximum of the structure factor a detailed investigation of the scattering function at constant energy transfer is of interest. The scattering function $S(Q, \omega)$ for $\omega = 0$ shows a sharper maximum *versus* Q than the structural factor $S(Q)$, while $S(Q, \omega)$ for large constant values of ω shows a minimum for the same values of Q. Finally, for large momentum transfers investigation of the half widths of the energy distribution is necessary. The structure factor, the scattering function for constant energy transfer, as well as the half width all show several maxima and minima as a function of the momentum transfer Q, but the extreme values of these functions do not occur at the same values of Q as one would expect on the basis of the theoretical models.

S. J. Cocking [Harwell (England) at present KFA Jülich] gave the results on inelastic scattering of slow neutrons in liquid lithium and liquid sodium [6]. The main point of the investigation lay in the incoherent scattering at small momentum transfers. From the incoherent scattering function $S_s(Q, \omega)$ the mean square of the distance over which the atoms move in time t was calculated, and from this the frequency spectrum of the liquid was derived. The diffusion model proposed by *Egelstaff* and *Schofield* was used to evaluate the results. The frequency spectrum of sodium thus calculated differs substantially from that given by earlier calculations, which are quoted in *Egelstaff*'s book [3a], and shows a broad maximum for small frequencies and a sharp maximum near the limiting frequency.

The lectures of *A. Rahman* [Institute for Theoretical Studies, Utrecht (Netherlands)] [7] and *L. Verlet* [Université de Paris, Laboratoire de Physique Theorique, Orsay (France)] were devoted to molecular-dynamics calculations. Most of these calculations were carried out on argon using a Lennard-Jones potential; other calculations were carried out with oscillating pseudo-pair potentials of metals or with a Coulomb potential for the electrons in a plasma. The number of particles used for these calculations was usually 864. Thus for argon the mean square of the distance traveled by an atom was calculated as a function of the time interval. The most interesting interval lies between 0.5×10^{-12} and 10×10^{-12} sec, in which time the transition from gas like to macroscopic behavior takes place. The second derivative of this quantity gives the velocity-autocorrelation function, which for high densities shows a weak maximum after the first fall, and then a second minimum before its value approximates to zero. The secondary maximum in the velocity-autocorrelation function only disappears at densities which roughly correspond to the critical density. Concepts in the theory of Brownian movement, such as friction constants, can also be checked by molecular dynamics calculations. Pair distribution functions and structure factors can be calculated directly. The extrapolation of the structure factor $S(Q)$ to $S(0)$ agrees to within 10—15% with the experimentally measured compressibilities. For the structure factor, curves for argon were obtained even in the critical region, which allows conclusions to be drawn on singularities in its compressibility. It is surprising that even in the region of the critical point macroscopic quantities can be well reproduced from calculations involving only 500—1000 particles. Coherent scattering functions could also be calculated as functions of the energy transfer down to a momentum transfer of 0.2 Å^{-1}. Smaller momentum transfers would require the use of more elaborate calculations.

Rahman also reported on a plasma calculation (1024 electrons in a cube with a side of 1500 Å; the Coulomb potential cut off at 500 Å). The pair distribution function and the scattering factor rose to a nearly flat plateau; despite the low particle density, a value near zero for the compressibility was reached by extrapolation.

Verlet investigated the influence of the different pseudo-pair potential functions on the structure factor and the velocity-autocorrelation function in metals. The oscillations of the pseudo-pair potentials had little influence on the above functions. On the other hand, the steepness of the repulsion potential at small atomic distances was important. A soft repulsion potential caused stronger oscillations in the velocity-autocorrelation function and a more rapid damping in the structure factor, as is characteristic for univalent metals.

It was also pointed out in a short paper that both for argon and for a Percus-Yevick calculation for hard spheres, the structure factor shows more oscillations than for rubidium.

J. G. Powles [Department of Physics, University of Kent (England)] talked about the possibility of utilizing light-scattering for problems of liquids. Since the interference effects of neighboring atoms are mostly destructive, the scattering intensity in liquids is very small and the need for optical purity is very acute. The scattered intensity is proportional to the mean square fluctuation of the dielectric constant. If this is taken as a function of pressure and entropy, it then depends on the square of the pressure fluctuation and the square of the entropy fluctuation, respectively. While the entropy fluctuation does not propagate, the pressure fluctuation does: its frequency is given by the product of the momentum transfer Q and the velocity of sound v_s. The scattered light therefore shows three lines, of which the middle one, the Rayleigh line, appears at the frequency of the incident radiation and is caused by the entropy fluctuation; the other two, the Brillouin lines, are displaced to both sides by the frequency Qv_s. One can also interpret this shift as a Doppler effect of the pressure fluctuations, which are moving with the velocity of sound. The width of the Rayleigh line is largely determined by the quotients of heat conductivity and heat capacity C_p, while the much greater width of the Brillouin lines is given by the sound absorption coefficient. The frequencies of the pressure fluctuations depend on the wavelength of the incident light, the angle of scattering, and the velocity of sound and are usually of the order of 10^9 Hz. The sound velocities (hypersound) obtained at these

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[*] If after a time t the particles move preferentially in the same direction, then the autocorrelation function is positive; if they move preferentially in the opposite direction, the function is negative; if after a time t there is no further 'memory', the function is zero.

[**] A distribution of the vibrational frequencies similar to that in solids also exists in liquids. The $z(0)$ value for this is finite and proportional to the diffusion coefficient.

[6] *S. J. Cocking*, J. physic. Chem., in press.

[7] *A. Rahman*, Proc. european physic. Soc., in press.

frequencies from the shift of the Brillouin lines do not on the whole differ much from those measured in the ultrasonic region (10^6 Hz). For CO_2 the hypersonic velocities for the vapor, liquid, and supercritical regions all lie somewhat higher than the ultrasonic velocities. At the critical point it also appears that the velocity of sound has a value differing from zero. The pressure fluctuations vary with C_v (the heat capacity at constant volume) and the entropy fluctuations with the difference $C_p - C_v$. The Rayleigh line should therefore disappear in water ($C_p \approx C_v$), but in the vicinity of the critical point, where C_p has a much stronger singularity than C_v, it should increase much more strongly than the Brillouin line. The divergence of C_p at the critical point was studied by measurements of the half width of the Rayleigh line. The Rayleigh line becomes very narrow in the vicinity of the critical point, and the measurements therefore require a direct electronic technique. At present only very few measurements of the half width of the Brillouin line are available, but they would be of considerable interest as complementary to the absorption measurements by ultrasonic methods.

The depolarization of the scattered light produced by reorientation (*e.g.* rotation) of anisotropic molecules is an interesting and as yet little explored phenomenon. By measuring the Doppler effect, light scattering might also be used for studying flow conditions. Thus, *Powles* reported a recording of the velocity-profile of a flowing liquid, using light scattering, and the investigation of the degree of turbulence as a function of the Reynolds number.

Views on the behavior of sound velocity in the hypersonic region were expressed by *J. P. Boon* [Université Libre de Bruxelles (Belgium)] and *P. Fleury* [Bell Telephone Laboratories, Holmdel, N. J. (USA)]. From this, a decrease in the velocity of sound at high frequency, an apparently negative dispersion, is to be expected on theoretical grounds. The above authors carried out measurements of the hypersonic velocity in liquid argon (between 85–100 °K) and liquid neon. The resulting values were a little lower than the ultrasonic measurements, but the difference was still within the range of experimental error of the investigations.

Of the other short lectures, a few more are selected because of their bearing on physicochemical problems.

P. Bratby and *N. H. March* [University of Sheffield (England)] attempted to obtain a theoretical interpretation of the fact that the ratio of the heat capacities C_p/C_v for liquid metals near the melting point lies between 1.2 and 1.3, while for argon it is 3. This seems to be connected with the fact that the repulsion branch of the pair potential rises much more steeply for argon, and the attraction branch falls away much more rapidly, than in the case of metals.

S. C. Smelser and *C. J. Pings* [California Institute of Technology, Pasadena, Calif. (USA)] reported on new X-ray scattering measurements on argon in the truly liquid region, at densities between 0.91 and 1.26 g/cm³. The pair distribution function for mean densities shows a shoulder between the first and second distinct maxima. If these results are used to calculate a pair potential by the Percus-Yevick method, one finds for the minimum of the pair-potential an improbably high dependence on density. It appears, therefore, that the Percus-Yevick theory fails at high densities.

The paper read by *D. W. G. White* [Department of Energy, Mines and Resources, Ottawa, Ontario (Canada)] gave an account of measurements of the surface tension of liquid metals (Sn, In, Pb, Zn, Cd) as a function of temperature. These determinations were carried out by the drop method in an atmosphere of hydrogen or helium, between the melting point and 550 °C, and were accurate to 1% (corresponding to ±5 erg/cm³). Of the metals investigated, only Sn shows a linear temperature dependence of the surface tension. For In and Pb, the temperature dependence is at first weakly negative and becomes more strongly negative at higher temperatures (for Pb a flattening sets in again at the highest temperatures); for Zn and Cd the temperature dependence above the melting point is at first actually positive. For Cd, the surface tension reached a maximum and then showed the usual decrease within the temperature interval investigated. The small (and sometimes even negative) value of the surface entropy near the melting point indicates a particularly ordered arrangement of the surface atoms.

C. A. Croxton and *R. P. Ferrier* [Cavendish Laboratory, University of Cambridge (England)] gave an account of electron diffraction measurements with relatively high-energy electrons, but the geometry of the setup was such that the electrons penetrated only to a depth of about six atoms. So far liquid lead, tin, and aluminum could be investigated, of which lead showed a series of subsidiary bands, but not tin or aluminum. This can be correlated with the measured values of the surface entropy. The same authors also presented a two-dimensional calculation of the surface structure for liquid argon by means of a molecular-dynamics method. The coupling to the interior of the liquid was simulated by arranging a number of atoms in a modulated statistical configuration along one side beyond the frame of the dynamical system. In this way the atoms within the framework arrange themselves into some well-ordered layers, in equilibrium with the sparsely populated gas phase.

The Monte Carlo calculations carried out by *K. Singer* [Chemistry Department, Holloway College, Egham, Surrey (England)] are selected from among the various contributions to the problem of liquid mixtures. Assuming the Lennard-Jones pair-potentials (characterized by the parameters ε_{ij}, σ_{ij}), the thermodynamic functions for equimolecular concentrations in a 108-particle system were calculated as follows: the parameters ε_{ii}, σ_{ii} of the pure component i were first transformed continuously into those of the other component j. The resultant changes in the thermodynamic quantities of interest were calculated. The two components which were made identical in this way were then mixed and the parameters were transformed to the set ε_{ii}, ε_{ij}, ε_{jj}, σ_{ii}, σ_{ij}, σ_{jj} valid for the mixture. The difference in the variations of the thermodynamic quantities measured along the changes in the parameter gives the excess thermodynamic functions. This calculation can be compared with theoretical models; it gave good agreement with the van der Waals model [8].

A really worthwhile investigation was carried out by *J. A. Chapman, F. J. Finnimore, P. J. Parpia,* and *B. L. Smith* [School of Mathematical and Physical Sciences, University of Sussex (England)], who investigated the relation between the density and the molar refraction of xenon (calculated by the Lorentz-Lorenz equation) over the whole range of density. They found that in the gas and liquid phase the molar refraction does not vary by more than ±1%, and that there were no anomalies at the critical point. The remaining slight density dependence varied systematically, the molar refraction increasing with the density at low densities, and decreasing at high densities. The temperature dependence is also slight; a small decrease of the refraction could be found with rising temperature. On transition to solid xenon, a small fall in the molar refraction was observed. This investigation justifies many earlier experimental investigations, especially near the critical point, in which the refractive index was measured instead of the density.

J. A. Brace and *J. V. Champion* [Department of Physics, Sir John Cass College, London (England)] gave a new explanation of the Kerr effect in liquids composed of nonpolar and optically isotropic molecules (*e.g.* CCl_4). According to this, the molecular distribution is disturbed by the electrical field in such a way that the internal field becomes optically anisotropic. Since this modification of the pair-distribution varies with the square of the field intensity, it gives rise to a pseudo-hyperpolarizability. The observed Kerr constants and their variation with temperature could be explained semi-quantitatively in this way.

Several short lectures dealt with the introduction of an "effective pair potential" which would take into account the

[8] *T. W. Leland, J. S. Rowlinson,* and *G. A. Sather,* Trans. Faraday Soc. *64*, 1447 (1968).

variations of the actual pair potential brought about by the presence of a triple dipole-interaction effect. It is important to note that the correction depends on the function which should be reproduced exactly. In several attempts, the correction was applied in such a way that the mean potential energy was correctly reproduced, in which case the analyses were carried out by Monte Carlo or perturbation calculations; others again correctly reproduced the radial distribution function and used a graphical method for this purpose. Both solutions result in an effective pair potential somewhat more positive than the two-body potential and showing a weak dependence on volume and temperature.

Finally, reference should be made to a preliminary Monte Carlo calculation on water, by *J. A. Barker* and *R. O. Watts* [University of Waterloo, Ontario (Canada)]. This was based on a charge distribution in the water molecule as given by *Rowlinson* and a Lennard-Jones potential and gave quite good agreement with the experimental results for energy, heat-capacity, and radial distribution. It is significant that, at least for a rough simulation of the properties of water, no specific mechanism of association had to be assumed.

F. Kohler [VB 207 IE]

German version: Angew. Chem. *81*, 710 (1969)

SELECTED ABSTRACTS

Preparation of synthetic graphite by low-temperature pyrolysis of methane has been accomplished by *S. D. Robertson*. Previously synthetic graphite could only be prepared by precipitation at 2000–2500 °C, recrystallization at 3000 °C/400 atm, and annealing at 3400 °C. *Robertson* pyrolyzed methane (600 torr) on the surface of iron, cobalt, or nickel foil at 650 or 750 °C. The crystalline structure of the product was established, *inter alia*, by electron diffraction and Moiré diagrams. / Nature (London) *221*, 1044 (1969) / —Kr.

[Rd 62 IE]

A new analytical method for the quantitative determination of tertiary nitriles has been found as a result of investigations on the reaction of nitriles with solvated electrons from various sources, *e.g.* Na/NH_3 and $Li/C_2H_5NH_2$. Reductive decyanidation of primary, secondary, tertiary aliphatic and of aromatic nitriles leads to the formation of inorganic cyanide, which can be titrated with $AgNO_3$ according to the method of *Liebig*. The loss of cyanide from tertiary nitriles is quantitative. They undergo exclusive reductive removal of CN with formation of the hydrocarbon, whereas primary and secondary nitriles are reduced to the amines. 1,4-Dicyanocyclohexane gives, *inter alia*, cyclohexane as well as 2- and 3-methylpentane. / *P. G. Arapakos, M. R. Scott*, and *F. E. Huber jun.*, J. Amer. chem. Soc. *91*, 2059 (1969) / —Ma.

[Rd 50 IE]

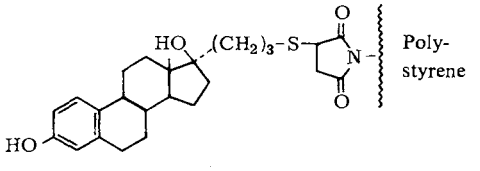
***E. coli* phenylalanyl tRNA synthetase "recognizes" its specific $tRNA^{Phe}$ by the 5′ loop.** On reduction with $NaBH_4$ or $NaBT_4$, $tRNA^{Phe}$ completely loses its ability to become charged with phenylanalyl. (Other tRNAs such as $tRNA^{Val}$ and $tRNA^{Met}$ show a 20% loss of activity.) As shown by *L. Shugart* and *M. P. Stulberg*, the activity decreases with the amount of hydrogen or tritium taken up. 80% of the tritium is incorporated into the odd bases 5,6-dihydrouridine and 4-thiouridine, and 20% is distributed over the tRNA molecule. Since the inactivation of $tRNA^{Phe}$ by heat also arises from the cleavage of 5,6-dihydrouridine and the partial loss of activity of other tRNAs on treatment with *N*-ethylmaleimide (reaction with 4-thiouridine) can be ascribed to attack at these bases, it seems reasonable to assign the functions of the recognition site to the loop in the proximity of the 5′ terminal of $tRNA^{Phe}$, which contains one molecule of 4-thiouridine and two molecules of 5,6-dihydrouridine. / J. biol. Chemistry *244*, 2806 (1969) / —He.

[Rd 68 IE]

LSD exhibits interactions with calf thymus DNA *in vitro*, which *T. E. Wagner* interprets, on the basis of CD findings, as intercalation into the DNA double strand. However, since it is unlikely that the resulting conformational changes lead to the chromosome breakages observed after administration of LSD, *Wagner* suggests that LSD instead neutralizes the phosphate ions of the DNA helix on intercalation, thus causing the dissociation of histones. The removal of these basic proteins, which are ascribed a protective function, could leave the DNA more open to attack. LSD-induced changes in the CD spectrum of DNA-poly-L-lysine complexes also support this hypothesis. / Nature (London) *222*, 1170 (1969) / —He.

[Rd 69 IE]

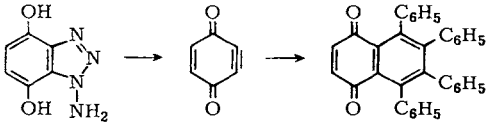
A new method for the isolation of the estrogen receptor from rat uterus is suggested by *B. Vonderhaar* and *G. C. Mueller*. Estradiol is bonded *via* a 17α side chain to a polystyrene resin. By working in batches, it is possible with the prepared resin, which contains 83 μmoles of estradiol per gram of dry product, to remove 93% of the estrogen receptor selectively from uterus homogenate. The resin remained stable and retained its selectivity over a period of two years. However,



difficulties are encountered during attempts to elute the receptor, a protein having a highly pronounced affinity for estradiol, in active form from the resin. / Biochim. biophysica Acta *176*, 626 (1969) / —He.

[Rd 70 IE]

The formation of dehydrobenzoquinone, 2-cyclohexen-5-yne-1,4-dione *(2)*, the simplest dehydroquinone, represents the subject matter of a report by *C. W. Rees* and *D. E. West*. On treatment with HNO_2, cyanic ester, H_2/Pd, HNO_2 + HCl, 2-nitro-3,6-dimethoxyaniline is converted into 1-amino-4,7-dimethoxybenzotriazole, which gives 1-amino-4,7-dihydroxybenzotriazole *(1)* (yield 65%) when demethylated with



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

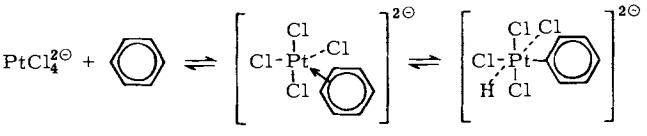
BBr_3 in CH_2Cl_2. Compound *(1)* is oxidized to 1-aminobenzotriazole-4,7-dione, an unstable orange-brown oil, by Ag_2O in THF + Na_2SO_4. Rapid dissolution in CH_2Cl_2 + 1 equivalent of tetracyclone and lead tetraacetate oxidation

gave a 40% yield of 5,6,7,8-tetraphenyl-1,4-naphthoquinone *(3)* (orange crystals, whose formation is most simply explained by cycloaddition of intermediate *(2)* to tetracyclone and decarbonylation). Oxidation of *(1)* by lead tetraacetate in the presence of tetracyclone afforded *(3)* in 60% yield. / Chem. Commun. *1969*, 647 / —Ma. [Rd 73 IE]

The adduct $BrF_3 \cdot SbF_5$ occurs as $[BrF_2]^+[SbF_6]^-$ according to an X-ray structure analysis carried out by *A. J. Edwards* and *G. R. Jones*. BrF_2SbF_6 crystallizes orthorhombically in the space group Pcca with a = 10.12, b = 5.81, and c = 10.95 Å ± 0.01 Å; Z = 4. The BrF_2^+ ion is bent (93.5 °), the BrF bond lengths having a value of 1.69 Å. The distorted SbF_6 octahedron has four short SbF distances of 1.83 Å (2×) and 1.84 Å (2×). The two remaining F atoms, which are *cis* to each other, are bridging atoms to two different BrF_2 ions (Sb—F, 1.91 Å; $BrF_2 \cdots F$, 2.29 Å; ∢Br ··· F—Sb, 153.5 °); the $F \cdots BrF_2 \cdots F$ unit is planar. Cations and anions combine in this way to form an infinite chain, for which a purely ionic formulation $[BrF_2]^+[SbF_6]^-$ is only of limited validity. / J. chem. Soc. (London) *A 1969*, 1467 / —HB. [Rd 76 IE]

$FXeOSO_2F$, $FeXeOClO_3$, $Xe(OSO_2F)_2$, and $Xe(OClO_3)_2$ have been prepared by *N. Bartlett et al.* by reaction of XeF_2 with stoichiometric amounts of either $HOSO_2F$ or $HOClO_3$ at −110 to −60 °C. All the compounds are colorless to pale yellow; the first three melt at 36.6, 16.5, and 43—45 °C, respectively. $Xe(OSO_2F)_2$ decomposes into Xe and $S_2O_6F_2$ at 20 °C; $Xe(OClO_3)_2$ decomposes in an undefined fashion into Xe, O_2, Cl_2O_7, and ClO_2 at −20 °C. $FXeOSO_2F$ and, presumably, the other compounds have covalent XeO bonds. On the basis of X-ray structure analysis the FXeO group in $FXeOSO_2F$ is almost linear, the Xe—F and Xe—O bond lengths being 1.94 and 2.16 Å resp. and the FXeO angle being 177.5 ± 0.4 °; the XeOS angle is 123.4 ± 0.6 °. In the Raman spectra the XeF stretching vibrations were detected at *ca.* 500 cm^{-1}, the XeO vibrations between 433 and 507 cm^{-1}. / Chem. Commun. *1969*, 703 / —HB. [Rd 77 IE]

The homogeneous catalyzed H—D-exchange in polycyclic aromatic compounds using acetic acid as solvent and tetrachloroplatinate(II) as catalyst has been investigated by *R. J. Hodges* and *J. L. Garnett*. The rates of exchange are found to be related to the highest bond order occurring in the molecule: A sharp maximum in the exchange rate is found at a bond order of about 1.77 (*e.g.* C-9 H and C-10 H bonds of phenanthrene). At smaller bond orders the formation of the π complex *(1)* is rate determining whereas at higher bond orders the formation of the σ complex *(2)* is rate determining.



(1) *(2)*

Polyphenyls exchange several H atoms during a catalytic cycle, condensed aromatic compounds exchange only one H atom. In *ortho*-condensed aromatic compounds, except those which contain condensed five-membered rings (*e.g.* acenaphthylene), the exchange is hindered. / J. physic. Chem. *73*, 1525 (1969) / —Hz. [Rd 78 IE]

BOOK REVIEWS

Grundlagen der photographischen Prozesse mit Silberhalogeniden (Principles of Photographic Processes Involving Silver Halides). Edited by *H. Frieser*, *G. Haase*, and *E. Klein*. Vol. 1: Physical and Chemical Properties of Silver Halides and of Silver; Vol. 2: The Photographic Emulsion and the Processing of Sensitive Materials; Vol. 3: Photographic Sensitivity. Akademische Verlagsgesellschaft, Frankfurt/Main, 1968. 1st Edit., 1500 pp., DM 390.—.

When the publications in a large field of research consist entirely of journal articles and monographs, it is time for existing knowledge to be gathered into one large work and presented without ballast.

The authors of the present three-volume work have succeeded in doing just this, *i.e.* in presenting more information by pruning. They have been able to demonstrate experimental results clearly, to emphasize the problems, and in part even to provide a retrospective view of the early stages of photography. It is surprising, particularly since the three volumes extend to a total of 1500 pages, to find that the book is very up-to-date, the literature being covered in part up to 1967. It contains almost 5000 references to the original literature or to other reviews. The Russian and Japanese literature, which is often treated very sketchily because of language difficulties, is given due recognition.

Volume 1, by *J. Eggers*, *G. Haase*, and *R. Matejec*, deals with the physical properties of silver halides and of metallic silver. The data on structure and bonding, mixed systems with other metal halides, defects, and crystal dislocations, as well as on the thermal, mechanical, electrical, and optical properties, are so comprehensive and up-to-date that they will often avoid the need for laborious searches in the literature, which is widely scattered in some cases. The chemical properties of silver and its compounds are given less space, but the treatment is just as detailed.

It is unfortunate that the work is sold only as a set, since the first volume in particular could be an important reference book to scientists who are concerned with silver, though not with photography.

Volume 2, by *J. Beersmans*, *H. Borginon*, *L. Busch*, *J. Eggers*, *R. Matejec*, *R. Meyer*, *E. Moisar*, and *M. N. Vrancken*, describes the preparation and chemical sensitization of photographic emulsions and their processing. Section 2 (of the complete work) describes, very briefly but impressively, gelatin and its properties. In the reviewer's opinion, more space might have been devoted to this important chapter. A few lines should perhaps also have been written about synthetic binders.

Chapter 3 presents an excellent account of the photographic emulsion and the complex subject of sensitization. The treatment is so skillful that even readers who do not work in this field should have no difficulty in understanding the material. No mention is made of the economically important rhodium effect, on which readily available literature exists.

Chapter 4 consists of three sections on the development of the photographic emulsion. The theory of development, which is based mainly on physical concepts, is followed by a section on the chemistry of the process. This section contains a very good survey of the most important developing agents known at present, and color development is also given the attention it warrants. A more detailed chapter on the Copyrapid process and on the related Polaroid process would have been preferred by the reviewer.

Chapter 5 deals with fixing, washing, and stabilization of the developed silver image. It is regrettable that so little is said

about the topical problem of the life of the silver in the image during storage.

Volume 3, by *W. F. Berg, F. Dörr, J. Eggers, G. Haase, R. Matejec, H. Metz, R. Meyer, E. Moisar,* and *F. Tomamichel,* presents, in Chapter 6, a review of spectral sensitization by dyes. After a description of the properties of sensitizing dyes and of spectrally sensitized emulsions, the two model views of sensitization, *i.e.* energy transfer and electron transfer, are discussed.

Chapter 7 gives an readily understandable description of the production of a blackening curve, and this is followed by a long chapter (8) on photographic effects. The two authors in this section have not only managed to present clearly the present state of knowledge on the bewildering multiplicity of photographic effects, but have also traced the literature back to the early stages of photography, and have thus made a valuable contribution to the history of scientific photography. The last chapter (9) is devoted to the latent image and its formation. The many stages in the formation of a latent image and the calculation models used for the understanding of the process are described in detail. From his own overall view, the author presents a survey that makes it easy for the reader to understand the relations involved.

This three-volume work will be useful to all who are concerned with the fundamentals of photography in theory or in practical research. *W. Bahnmüller* [NB 816 IE]

Physikalisch-chemische Kristallographie (Physico-chemical crystallography). By *K. Meyer.* VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1968. 1st Edit. 337 pp., 225 figures, 69 tables, bound DM 39.80.

Whereas crystal physics and crystal chemistry are normally treated quite independently in textbooks of crystallography, with seperate, systematically constructed chapters, the value of and the need for a complete, systematic discussion of the typically "physico-chemical" problems of crystallography, such as crystal formation and transformation, crystal habit and changes in habit and the many processes and reactions of and on crystal surfaces (epitaxy, topotaxy corrosion, *etc.*) are evidently not yet sufficiently recognized. This is surprising when one thinks of the importance attached by crystallographers and mineralogists to physico-chemical methods. This is shown in particular by the test methods used in these two fields.

K. Meyer's book probably provides the first systematic treatment, within the scope of a textbook, of the typically "physico-chemical" problems of crystalline materials, in which both the necessary physico-chemical (particularly thermodynamic) principles and their application to the range of crystallographic problems mentioned above are presented in clear, adequate, and neat definitions, formulations, and derivations. The treatment of the material is always carried through to the quantitative description and to the latest position, without the use of excessively demanding mathematics.

The book is fluent, well presented, and always technically adequate. It is unreservedly successful, and is strongly recommended to all crystallographers, mineralogists, chemists, physicists, and material scientists. Better paper would have been preferred for such a good book. The modest price is insufficient compensation from this point of view.

A. Neuhaus [NB 823 IE]

Die natürlichen und künstlichen Aromen. Zusammensetzung und Herstellung. (Natural and Synthetic Flavors. Composition and Preparation.) By *A. M. Burger.* Dr. Alfred Hüthig Verlag, Heidelberg 1968. 3rd Edit., 338 pp., 65 figures, plastic cover DM 48.—.

Behind this new, somewhat pretentious title is concealed the familiar "Buch der Aromen" (Book of Flavors) by the distiller and planter *Alfons M. Burger,* who died some time ago in Africa. Dr. *J. Hilger* of München has revised the manuscript, taking the latest knowledge into account. After the introduction and a short historical section, considerable space is devoted to the description of the various distillation processes and the apparatus required for them. Freeze-drying, spray-drying, extraction, and other industrial processes used in the commercial production of aroma complexes are also discussed at some length. This chapter should be made more concise in future editions, since sufficient first-class literature on these technological problems is already available.

This is followed by a section on the chemically definite aromatic essences, which is necessarily incomplete because of the very rapid progress that is currently being made in this field. Nevertheless, it provides a firm foundation for the newcomer. It would have been helpful to practical workers if the discussion of the individual aromatic essences had been accompanied by some information on their occurrence in natural products. A short chapter dealing with the different legal situations concerning the flavoring of foods and beverages in the principal countries would undoubtedly also have been welcome.

The most useful part to those who work in this field is a section of about 150 pages describing the production of spice oils, brandy flavors, citrus flavors, and fruit flavors. A simple formula is always given for the preparation of the corresponding synthetic flavor, though the legal permissibility of the components used has unfortunately not been considered. The user should therefore check the legal situation in every case.

After a short discussion of flavors of animal products (honey, butter, cheese), the book ends with a section on the flavoring of special products such as baker's produce, vinegar, confectionery and meat, as well as tobacco. An appendix provides information on solvents and solubilities. Whereas there are several very good English books, this volume closes a gap that has existed in the German literature on flavors. It should be welcomed by interested laymen and practical workers, and should always be available in the reference libraries of distillers. *E. Klein* [NB 824 IE]

Disk-Elektrophorese. Theorie und Praxis der diskontinuierlichen Polyacrylamidgel-Elektrophorese (Disc Electrophoresis. Theory and Practice of Discontinuous Electrophoresis on Polyacrylamide Gel). By *H. R. Maurer.* W. de Gruyter und Co., Berlin 1968. 1st Edit. xvi + 221 pp., 82 illustrations, 15 tables, plastic binding, DM 36.—.

Disc electrophoresis, which one connects with the names of *Ornstein* and *Davis,* is a variant of electrophoresis in polyacrylamide gel and differs from this in that discontinuities (discs) are set up with respect to pH and pore size within the separation medium. These cause concentration of the mixture to be separated, which collects as a sharp zone at the upper end of the column of gel and on subsequent separation leads to appearance of disc-like zones containing the individual components.

Technical details about the method — known for almost ten years — and modifications and applications are scattered through many different publications. It is thus especially welcome that the author, who has himself contributed several times to disc electrophoresis, has reviewed the material (602 references) and described the theory and practice of the method in an exemplary concise and precise manner. Fourteen gel systems, differing in pH, buffer composition, acrylamide concentration, *etc.,* have been summarized in tabular form; they should suffice for most problems of separation.

The book is well produced and of convenient form; since it is aimed at the practice of discontinuous polyacrylamide electrophoresis it should be consulted whenever knowledge is or should be sought about this technique needing only a minimum of technical equipment. The book is highly recommended. *B. Kickhöfen* [NB 818a IE]

Electrophoresis. Theory, Methods, and Applications. Edited by *M. Bier*. Academic Press, New York-London 1967. Vol. II. 1st edit., xviii + 553 pp., numerous illustrations and tables, bound, $ 21.00.

In 1959 appeared a book under the above title containing articles by various authors on specific aspects of free electrophoresis. After eight years it is followed by a second volume that is devoted more to the practical application of some of the methods that have meanwhile become established than to a theoretical treatment of electrokinetic phenomena. The only contribution closely connected to the first volume (an article by *J. Overbeek*) is that on electrophoretic mobility (*J. Overbeek* and *P. Wiersema*).

Especial attention will certainly be paid to the articles on gel techniques giving separation with high efficiency (*H. Bloemendal*) and on preparative electrophoresis (*K. Hannig*), since they are written with deep insight into the subjects. *H. Hochstrasser et al.* describe automatic electrophoresis in density gradients as realized in the 'Autophoresis' apparatus of Technicon Instruments Corp. The form of 'free zone electrophoresis' that occurs in a semifluid film stabilized by 0.1—0.2% of agar-agar, is treated by *N. Ressler*; since in this case separation occurs on a quartz plate the migrating zones can be followed directly by measuring the optical density at 200 nm ('Spectrophor', Bausch and Lomb).

It is open to question whether so much space should have been assigned to the results of electrophoretic analysis of gastrointestinal secretions (*G. Jerzy Glass*) and of lymph and cerespinal fluid (*F. Courtice*), each 60 pages. That one can write briefly with advantage was shown by *H. Grey* in his treatment of the electrophoretic behavior of antibodies and myeloma proteins and their fragments. A welcome should be extended to a review by *Barbara Bowman* of all the human serum proteins that occur in genetically controlled variants, since most of these proteins could only be discovered by electrophoretic methods.

P. Burtin and *P. Grabar* describe the nomenclature and identification of normal serum proteins; this article is valuable for those who have to carry out immunoelectrophoretic analyses and is a re-working of Chapter 5 of the book on Immunoelectrophoresis published by these authors in 1964. The article by *F. Šorm* and *B. Meloun* on the 'Primary Structure of Proteins' would have found a better place in a book on proteins since only the last quarter of it deals with electrophoresis (high-voltage electrophoresis of peptides); in this article the Reviewer regretted the absence of mention of *B. Hartley*'s diagonal technique. In summary: a book with a broad spectrum, somewhat related to an 'Advances' series; suitable and useful for libraries of chemical, biological, and medical research organizations.

B. Kickhöfen [NB 818b IE]

The Story of Fritz Haber. By *M. Goran*. University of Oklahoma Press, Norman, Oklahoma 1967. 1st Edit., xi, 212 pp., 4 illustrations, $ 4.95.

Morris Goran calls his book a story, an interesting, true-to-life story about an unusual and dramatic character[1]. The author, who teaches science at Roosevelt University and has written popular books on experimental chemistry, biology, and astronautics, has the gift peculiar to Anglo-Saxons of making scientific subjects simple and interesting. The life of *Fritz Haber* captured his imagination. The book is a simple but interesting tale, presented factually and without adulation, tending rather to a rough realism, though finally the author gets caught up in his subject.

We learn that young Fritz had a strict upbringing. His mother died when he was born and his father was forever telling his children that he had had to "work his fingers to the bone". At the age of 24 *Haber*, who had finished his studies and worked for a time in industry, went into the family business. His father insisted that the should have lessons to improve his handwriting. *Haber* did this, but even so did not see eye to eye with his father. After an unfavorable outcome to a business venture he had proposed, his father sent him away. "Go to university, business life does not suit you".

The book takes us through his life in great detail. The author has made a comprehensive study of his sources and obviously gathered extensive personal data. All the persons who played some part in *Haber*'s life are named and in many cases a character sketch is provided. A good, detailed index makes it easy to look up specific points. Not without interest for the German reader is the description of conditions and the way of life in a German university at the turn of the century from the pen of an American, who treats his subject objectively and without prejudice.

The critical point in *Haber*'s life — his activities in World War I and the organization of gas warfare — is dealt with in detail. The author presents a very factual defense of *Haber*. His patriotism is shown as a characteristic feature: *Goran* calls his patriotism "devotion", not "loyalty". In 1914 *Haber*, who was then 46, volunteered immediately, but was turned down. *Goran* remarks that almost all scientists before *Haber* and very many after him worked on the development of weapons, and in this connection he cites *Leonardo da Vinci* and *Galileo*. We learn that bombs filled with phosphorus and sulfur were used in the American Civil War, and that the Russians used chlorine at the beginning of World War I, but without success owing to the cold and to the weather conditions. In any case, gas was hardly a major weapon: less than 5% of all war casualties resulted from the use of gas; the casualty death rate for poison gas was 2.5%, and that for all other battle injuries 25%. Furthermore, it is difficult to make a moral distinction between gas and, say, submarine warfare. Nevertheless, even during the World War I there was a particular stigma attached to gas warfare, and we learn that *Haber*'s first wife was so distressed by her husband's war activities that in 1915 she committed suicide.

The chapter entitled "Understanding the man Haber" examines *Haber*'s habits, his views, his qualities, his way of life, and his sayings. We see here particularly clearly the biographer's art — our picture of *Haber* illuminated by a wealth of individual snips of information, details, and facts being left to speak for themselves. Here, as all through the book, we find enlightening anecdotes. For instance: *Haber*, who was no soldier, got annoyed because an officer of his company always wore spurs, though his activities were confined to office work. One day he said to him: "Captain, will you please get on your horse and ride into the next room to fetch those papers." *Haber*'s preferred reading is given as *Goethe*, the Bible — from which he loved to quote — and *Edgar Wallace*. He usually had a whodunit with him, and they helped him when he could not sleep. *Goran* thinks that they sharpened his wit, because he was always, like a detective, prying into the unknown. His enormous appetite for work, his activity, and his inner restlessness are attributed by *Goran* to a sense of insecurity resulting from childhood experiences, the loss of his mother, his initial failures, and his Jewish origin. I myself think that these rather manifestations of the normal inner tension of a strong, vital person who not only feels an urge to study and to achieve something, accompanied by ambition and a desire for recognition, but also experiences doubts and inner conflicts. *Goran* gives numerous examples of *Haber*'s sensitivity. — *Haber*'s last years and his bitter path into exile are given somewhat less space.

Despite the realistic and in ways matter-of-fact report, *Goran* sets the hero of his book on a pedestal. He considers him to be the greatest personality from the point of view of the synthesis of scientific research and industrial development. He refers to the way in which he develops an argument as a unique combination of clarity, originality, and conciseness, grounded on wit and irony. He was a romantic who thought about the unusual, applying an "uncommon common sense", a man who would have achieved eminence in any country, in

[1] Cf. Chemie in unserer Zeit *2*, 145 (1968).

England be might have been a Viceroy of India, in America a first-rate businessmann.

The book is an impressive document: The biographer, a man from another country, who did not know *Haber* personally, has diligently compiled the necessary material and has written a book which obscures and glosses over nothing, but which, after a cool examination of the facts, pays homage to a man wronged by his own country. *H. Sachsse* [NB 821 IE]

The Wave Mechanics of Atoms, Molecules, and Ions. By *C. J. H. Schutte.* Edward Arnold (Publishers), London 1967. XIII, 502 pp. numerous figures and tables, bound 84s.

This book is intended for students who wish to obtain a better understanding of the mathematical principles of the quantum-mechanical methods commonly used nowadays in physical chemistry. The book is divided into 16 chapters, the subject matter in each section being supplemented by several examples for practice.

The chapters deal in order with the fundamentals of quantum mechanics, the group theory and the MO methods of quantum chemistry. The applications of the theory in spectroscopy appear only in the third part of the book, with particular reference to the properties of the vibrational, rotational, and nuclear resonance excitation of molecules. An interesting but rather too short chapter for such a comprehensive book is devoted to the transition metal ions.

The book is adequately supplied with tables and figures, and is thus also a valuable reference book for students. The abundant literature references and references to original works are of great practical use to the reader.

Though the author, in his foreword, recommends the book to the practical chemist, it can scarcely be called a text book in the usual sense. The concise arrangement of the material makes familiarity with the manipulation of mathematical formulas a necessity, whereas this is not possessed by most practical chemists. On page 42, for example, the selection rules of the transition moments are discussed with the aid of direct products of irreducible representations without prior explanation of the symbols used. The book, which is crammed with facts, is therefore more useful as a collection of formulas or tables. Similarly, the problems for practice often involve considerable reasoning and numerical calculation, so that the average reader will be reluctant to spare the time required for their solution and discussion. It is nevertheless possible to obtain an insight into quantum-mechanical calculations by means of the solutions discussed in the Appendix. Though the book is well presented, some of the mathematical formulas contain printing errors, which are not always obvious owing to the author's often difficult arguments.

The author must be congratulated on producing a book that fills the gaps between the corresponding works on the precise methods of quantum chemistry and those on the experimental methods of physical chemistry. The fundamentals of quantum chemistry are treated in a readily understandable formal manner, and the results are illustrated by many practical examples. The book will probably be very useful to those who are familiar with the applications of quantum chemistry, and could provide a stimulus to further study.

P. A. Straub [NB 822 IE]

Principles of Organic Chemistry. By *R. A. Geissman.* Freeman and Co., San Francisco-London 1968. 3rd Edit., x+883pp., 98 illustrations, 70 tables, bound 70s.

This is the third edition of *Geissman*'s book, which is written as an introduction to organic chemistry within the framework of a one-year course. Departing from the classical division according to compounds customary in textbooks of organic chemistry, the author lays the main emphasis on reactions of functional groups. Properties and reactions of organic chemical compounds are presented as expressions of the characteristic behavior of the most important functional groups. It becomes apparent, however, that the content of organic chemistry cannot be divided quite systematically in this way; thus, in addition to the chapters corresponding to this division others are inserted dealing with, *e. g.*, absorption spectra of organic compounds, stereoisomerism, optical activity, ring formation, conformation, and molecular rearrangements. In the present, third, edition particular attention is paid to physical methods of characterizing organic compounds.

On the good side it can be noted that, while limiting strictly the amount of material, the author is yet able to bring the reader right up to the front of modern organic chemistry with a series of carefully chosen examples; the introductory chapter on the chemical bond and reaction kinetics is particularly successful. As a whole, the book is characterized by its clear and didactically successful presentation of its material. Its value is enhanced by the problems that are scattered in the text or collected at the end of each chapter.

Alongside the report of these successes some critical remarks may be permissible. It is hard to understand why radical mechanisms are not mentioned when polar reaction mechanisms are treated well and in detail; this leads to the omission of such elementary topics as the radical chain reactions in aliphatic substitution and autoxidation. Short-lived and stable radicals are not described. In the chapter on β-dicarbonyl compounds chelate formation is not mentioned in relation to enolization; complex formation is neglected in this connection and in connection with α-amino acids. It is surprising that the Ruggli-Ziegler dilution principle is not mentioned in treatment of macrocyclic compounds, nor is the special position of medium-sized rings. In the chapter on lactones the special behavior of γ-lactones is not noted. And the conformation of the ester group is not reported.

In spite of these isolated failings, the book as a whole is a success. In particular it will provide a stimulus for revision of the teaching of organic chemistry in German universities.

H. Stetter [NB 836 IE]

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 45075, Telex 461855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 10
OCTOBER 1969
PAGES 689–780

Vapor Pressure Isotope Effects

By A. Höpfner[*]

The vapor pressure isotope effect is a reflection of the thermodynamic relations in the condensed phase. It is possible to explain the observed effects on the basis of intermolecular vibrations, e.g. hydrogen bond vibrations, and the frequency shifts of the characteristic vibrations on condensation, though other effects must also be discussed. Information about the thermodynamics of liquids, e.g. about the degree of association or the expected positions of the lattice frequencies, can be obtained from the vapor pressure isotope effect.

1. Introduction

The thermodynamics of gases are based on the translational and rotational energies of the molecules and the energy levels of the internal degrees of freedom (vibrations and internal rotations). The intermolecular interactions are involved only as small correction terms (virial coefficients), which are perfectly understood in principle. If the lattice forces are known, the macroscopic thermodynamic functions of crystals can be satisfactorily represented by means of the thermodynamics of crystalline solids, the translational movement of the gas molecules in the crystal corresponding to harmonic or anharmonic vibrations about the lattice sites. Since a molecule remains in a lattice site for a very long time, Heisenberg's uncertainty principle predicts great certainty in the energy.

The interpretation of the properties of liquids, on the other hand, has not led to such satisfactory results. The "physical" theories, which are derived from the concept of the cell theory, are attempts to calculate the thermodynamic functions of liquids from predetermined intermolecular potentials. Against the conceptual clarity of these theories must be set the disadvantage that intermolecular potentials are known with sufficient accuracy only for simple molecules (*e.g.* inert gases). The phenomenological theories, such as *Eyring*'s theory of significant structures [1], do not depend on the intermolecular potentials; in these theories the liquid is described as a perturbed solid, the thermodynamics of which are assumed to be known. The perturbation is described in terms similar to those used for gases. The present article will show how the sign and magnitude of the vapor pressure isotope effect, as well as its dependence on temperature and concentration, can be used to deduce the thermodynamically relevant degrees of freedom in liquids.

2. Experimental Methods

Because of the logarithmic relation between free enthalpy of vaporization and vapor pressure (or more precisely fugacity)

$$\Delta_v G^\circ = -RT \ln p \qquad (1)$$

it is customary to use the ratio p_1/p_2 of the vapor pressures of two isotopic substances at a given temperature (or the logarithm of this ratio) to characterize the vapor pressure isotope effect (VPIE). If the masses differ (*e.g.* for C_2D_6/C_2H_6), the vapor pressure of the heavier substance is taken as the numerator and that of the lighter substance as the denominator. If the masses are equal (*e.g.* for CH_3CD_3/CH_2DCHD_2), the less symmetrical substance may be assigned to the

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[1] *H. Eyring* and *R. P. Marchi*, J. chem. Educat. *40*, 562 (1963); *T. S. Ree*, *T. Ree*, and *H. Eyring*, Angew. Chem. *77*, 993 (1965); Angew. Chem. internat. Edit. *4*, 923 (1965).

numerator and the more symmetrical to the denominator. Owing to the historical view that we are concerned only with pure mass effects, the vapor pressure isotope effect is referred to as normal when $p_1/p_2 < 1$, and as inverse when $p_1/p_2 > 1$. If the sign of $\ln(p_1/p_2)$ changes with the temperature, *i.e.* if p_1/p_2 passes through a value of 1, one speaks of the "cross-over" phenomenon.

In some cases the vapor pressure curves $p_1(T)$ and $p_2(T)$ were determined manometrically and used to find the ratio p_1/p_2. However, this method is sufficiently accurate only if the vapor pressure isotope effect is large, *i.e.* if the ratio p_1/p_2 is very different from 1. If the effect is small it may be masked by inaccurate temperature adjustment; the temperature dependence of the vapor pressure is so great that an error of 0.01 degree in the measurement of the temperature can lead to an error of about 0.1 % in the vapor pressure value.

A method in which the difference

$$\Delta p = p_1(T) - p_2(T)$$

is measured directly has consequently become accepted. The vessels containing the substances 1 and 2 are placed in the same temperature bath and connected to the two legs *e.g.* of a simple mercury manometer (Fig. 1), from which Δp can be read off directly. With

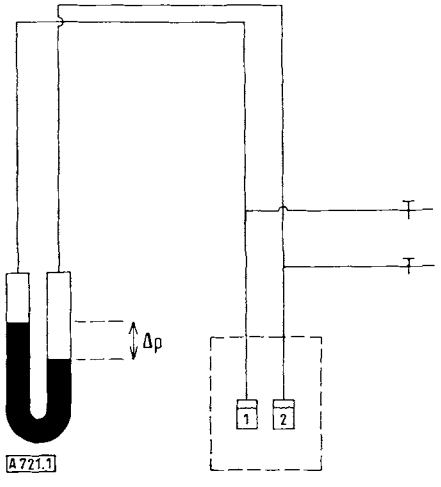


Fig. 1. Diagram of a vapor pressure difference apparatus with a shared temperature bath and a liquid manometer.

this arrangement, the accuracy with which Δp is obtained increases by a factor of ten, particularly since experience has shown that Δp does not depend so strongly on the temperature as the vapor pressures p_1 and p_2 themselves. The vapor pressure isotope effect is calculated from

$$\frac{p_1}{p_2} = 1 + \frac{\Delta p}{p_2} \qquad (2)$$

It is thus still necessary to determine the absolute pressure of one component, but the accuracy required is not very high.

Most of the published data on vapor pressure isotope effects have been determined by this method; if $\ln(p_1/p_2)$ is between 0.001 and 0.1 and p_1 is between 0.01 and 10 atmospheres, it is the most convenient method, provided that the substances can be obtained in the purity necessary for the vapor pressure measurements.

A third method is based on the measurement of the partition coefficient

$$\alpha = \frac{(N_1/N_2)_A}{(N_1/N_2)_B} \qquad (3)$$

for the partition of two isotopic forms between the two phases A and B. Except in extreme cases (see Section 6), mixtures of isotopes are ideal. Then, neglecting the deviation of the gas phase from ideality, we obtain

$$\alpha = p_1/p_2 \qquad (4)$$

and, if the effect is small,

$$\alpha - 1 = \ln (p_1/p_2) \qquad (5)$$

If the mixture of isotopes is slowly distilled, the α of eq. (3) is obtained by isotope analysis of the residue and the distillate. Very small effects (α-1 $\approx 10^{-4}$) can be determined if a column distillation is carried out instead of a single-stage distillation. The purity requirements are much less rigorous in this method than in the measurement of vapor pressures.

3. Experimental Findings

Figure 2 shows typical curves for the temperature dependence of the vapor pressure isotope effect.

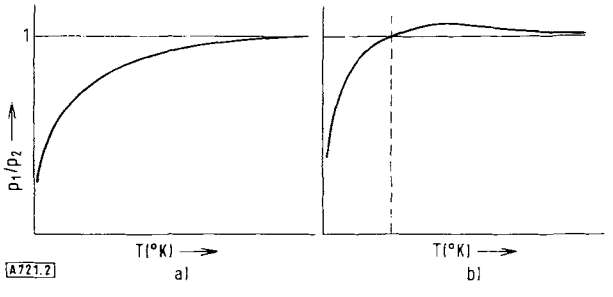


Fig. 2. Typical course of the vapor pressure ratio p_1/p_2, (a) without an inverse effect, (b) with an inverse effect at high temperatures.

A normal effect is always found at sufficiently low temperatures. The magnitude of this increases with falling temperature. Pronounced vapor pressure isotope effects are generally found at lower temperatures; thus the values for hydrogen and for helium are 0.34 and 0.31 respectively (cf. Table 1) at the boiling points of the lighter components. The effects are otherwise much smaller, and, as can be seen in Table 1, amount to only a few percent. Water and ammonia, on the other hand, exhibit strikingly large vapor pressure isotope effects. Vapor pressure ratios of 0.79

and 0.75 respectively are found for these two substances below the triple point.

No inverse effect ($\alpha > 1$) was found at very low temperatures. The cross-over for methane occurs only at about 75 °K; all known substances that exhibit inverse effects boil at higher temperatures than the boiling point of methane.

In every case where a cross-over is observed, $d\alpha/dT$ is positive, *i.e.* the vapor pressure isotope effect is normal below the cross-over temperature, and inverse above it. It cannot be established from the experimental observations whether all substances give a cross-over, at least at very high temperatures. This effect occurs at 220.7 °C for the pair D_2O/H_2O, and it can be inferred for alcohols, amines, and ammonia from the extrapolation of the $\alpha(T)$ curves. At least for helium and hydrogen, α is still well below 1 in the neighborhood of the critical points.

Normal and inverse effects differ markedly in their temperature dependences. Figure 3 shows the values

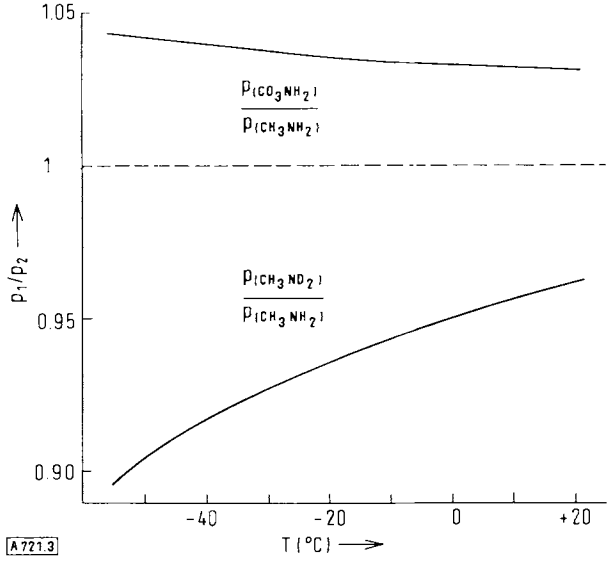


Fig. 3. Difference in the temperature dependences of the normal and inverse effects.

of p_1/p_2 for two pairs of differently deuterated methylamines, illustrating the strongly temperature-dependent normal effect resulting from substitution in the amino group and the weakly temperature-dependent inverse effect for substitution in the methyl group [18]. Whereas $d\alpha/dT$ is always positive for the normal vapor pressure isotope effect, both positive and negative values are found for substances giving an inverse effect. In the example of the ethanes, which is shown in Figure 4, the two cases with the maximum between them are clearly recognizable, despite the greater error at lower pressures [7].

If we regard the curve in Figure 2 as typical of the vapor pressure isotope effect, both the strong temperature dependence of the normal effect and the weak temperature dependence of the inverse effect become understandable. The values found for α and $d\alpha/dT$ depend only on the temperature range in which the measurements are carried out.

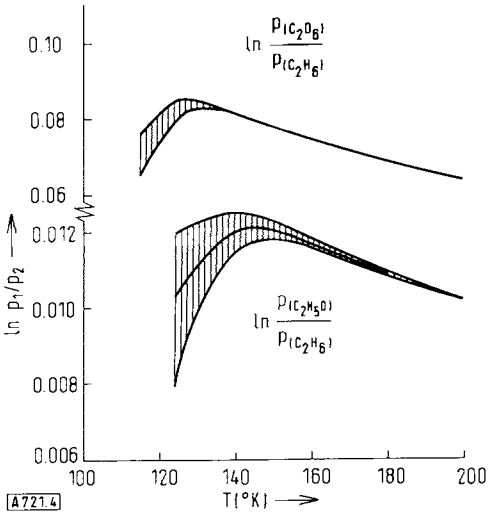


Fig. 4. Maxima in the inverse vapor pressure isotope effect of ethane.

The differences in the vapor pressures of isotopic substances pass through an extremum slightly below the cross-over temperature. The absolute value of Δp passes through a maximum at this point, but Δp itself is negative, so that the extremum is in fact a minimum. It occurs when the relative decrease in α near the cross-over temperature is no longer compensated by the exponential increase in the vapor pressure. This extremum, which has been observed at 171 °C for water (D_2O/H_2O) and at 12 °C for methylamine (CD_3ND_2/CH_3NH_2), should not be confused with the maximum of α, which is found in the region of the inverse effect, *i.e.* at much higher temperatures.

4. Interpretation of the Experimental Findings

The substances investigated at very low temperatures (He, H_2, Ne, N_2, *etc.*), for which a normal effect is found, fit readily into the framework of the theory. We shall first consider the vapor pressure isotope effects on replacement of hydrogen by deuterium in simple compounds whose vapor pressures can be accurately measured. A comparison of the literature data (cf. Table 1) shows that the inverse effect predominates for hydrocarbons and halogenohydrocarbons, except for methane derivatives, the effects of which are normal below 98 °K.

Conspicuous among the substances with normal vapor pressure isotope effects are water and ammonia, the molecules of which are known to be highly associated in the condensed state.

The normal effect of NO [20] must be mentioned here for historical reasons, though this is not a hydrogen compound. NO was the first substance for which an experimentally observed vapor pressure isotope effect was quantitatively traced to association in the condensed state [44].

The picture is rounded off by the data for alcohols and amines, which show that a normal effect occurs if the substance is associated in the condensed state and if the replacement of H by D has occurred in the group responsible for the association (hydroxyl or amino

Table 1. Vapor pressure isotope effects.

light component	B.p. (°K)	heavy component	p_1/p_2 at the b.p. of the lighter component	Ref.
^3He	3.19	^4He	0.3146	[2]
H_2	20.39	D_2	0.337	[3]
^{20}Ne	27.07	^{22}Ne	0.984	[3]
$^{14}N_2$	77.35	$^{15}N_2$	0.992	[4]
$^{16}O_2$	90.15	$^{18}O_2$	0.988	[5]
CH_4	111.7	CD_4	1.029	[6]
CH_4	111.7	CHD_3	1.018	[6]
CH_4	111.7	CH_2D_2	1.010	[6]
CH_4	111.7	CH_3D	1.003	[6]
C_2H_6	184.52	C_2D_6	1.069	[7]
C_2H_6	184.52	C_2H_5D	1.011	[7]
C_2H_4	167.80	C_2H_3D	1.007	[8]
C_2H_4	167.80	*trans*-$C_2H_2D_2$	1.016	[8]
$(CH_3)_4C$	282.7	$(CH_3)_3CCH_2D$	1.007	[9]
C_6H_{12}	353.89	C_6D_{12}	1.072	[10]
C_6H_6	353.25	C_6D_6	1.024	[10]
CH_3CCH	249.8	CH_3CCD	1.002 (cross-over at 226 °K)	[11]
CH_3CCH	249.8	CD_3CCH	1.037	[11]
CH_3CCH	249.8	CD_3CCD	1.039	[11]
CH_3Cl	249.3	CD_3Cl	1.034	[12]
CH_3Br	276.75	CD_3Br	1.032	[12]
CH_3I	315.95	CD_3I	1.049	[12]
HCl	188.1	DCl	0.993	[13]
HBr	206.30	DBr	0.9994	[14]
HCN	298.6	DCN	0.981	[15]
CH_3OH	337.95	CD_3OH	1.007	[16]
CH_3OH	337.95	CH_3OD	0.973	[16]
CH_3OH	337.95	CD_3OD	0.976	[16]
H_2O	373.15	D_2O	0.951 (cross-over at 221 °C)	[3]
$CH_3CHOHCH_3$	355.7	$CH_3CHODCH_3$	0.983	[17]
CH_3NH_2	266.89	CH_3ND_2	0.947	[18]
CH_3NH_2	266.89	CD_3NH_2	1.034	[18]
CH_3NH_2	266.89	CD_3ND_2	0.977	[18]
$C_2H_5NH_2$	287.98	$C_2H_5ND_2$	0.968	[18]
NH_3	239.95	ND_3	0.883	[19]
$^{14}N^{16}O$	121.49	$^{15}N^{16}O$	0.968	[20]
$^{14}N^{16}O$	121.49	$^{14}N^{18}O$	0.956	[20]
$^{14}N^{16}O$	121.49	$^{15}N^{18}O$	0.923	[20]

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[16] *J. Beersman* and *J. C. Jungers,* Bull. Soc. chim. Belgique *56*, 72 (1947).

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group). An inverse effect is observed, on the other hand, for unassociated substances or when isotopic substitution has taken place in an inert part of the molecule (as in the case CH_3NH_2/CD_3NH_2).

The existence of a connection between the normal vapor pressure isotope effect and association is also indicated by the strong temperature dependence of the normal effect, which corresponds to the variation of association with temperature. The vapor pressure isotope effect for water (D_2O/H_2O) becomes inverse at 220.7 °C; this could be explained by the decrease in hydrogen-bond association at this temperature, which allows other effects to predominate.

This view is in agreement with the fact that the normal effect of methylamine gives way to an inverse vapor pressure isotope effect on dilution with an inert solvent (*e.g. n*-hexane)[18] (cf. Fig. 5). The change occurs close to a mole fraction of $x_1 = 0.15$, and the inverse effect in this case would be more accurately described

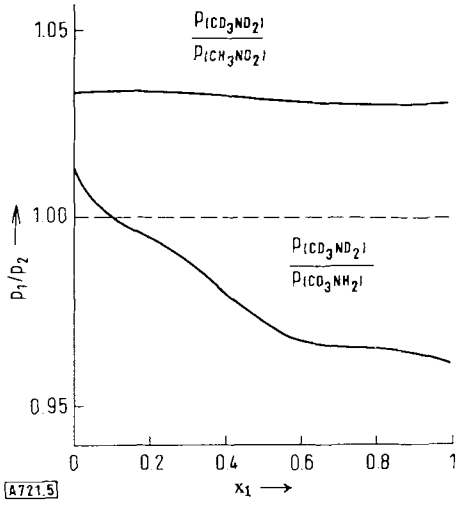


Fig. 5. Concentration dependence of the partial pressure isotope effect of substances that form hydrogen bonds.

as a partial pressure isotope effect. At the mole fraction mentioned, the associates have largely disappeared. The corresponding inverse effect (*e.g.* of the pair CD_3ND_2/CH_3ND_2), on the other hand, shows no concentration dependence. Similar observations have been reported for ammonia[19] and for methanol[21].

5. Theories of the Vapor Pressure Isotope Effect

The temperature dependence of the vapor pressure isotope effect (large effect at low temperatures, vanishing effect for $T \to \infty$) indicates that this is a

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typical quantum effect. Whereas *Fajans* [22] assumed in 1914 that the thermodynamic properties of the isotopes are exactly the same, *Lindemann* [23] in 1919 predicted a vapor pressure isotope effect for monatomic solids. According to *Lindemann*, it should be possible, by investigations on the vapor pressure isotope effect (and on the associated isotope effect of the mass action constants), to reach conclusions that could confirm the correctness of the predictions of the quantum theory, particularly in relation to the zero-point energy. According to *Stern*, whose unpublished formula is cited by *Keesom* and *van Dijk* [24], the vapor pressure isotope effect of a monatomic Debye solid should be given by

$$\ln \frac{p_1}{p_2} = -\frac{9}{8}\frac{\Theta}{T}\left(1-\frac{m_1}{m_2}\right)+\frac{3}{40}\left(\frac{\Theta}{T}\right)^2\left(1-\frac{m_1}{m_2}\right)+\cdots \qquad (6)$$

where the first term (with the coefficient 9/8) is omitted in the presence of the zero-point energy. It follows that the vapor pressure isotope effect is normal if the zero-point energy occurs, and is otherwise inverse. Since *Keesom* and *van Dijk*, in 1931, found a normal effect for the pair $^{20}Ne/^{22}Ne$, they regarded this as experimental proof of the zero-point energy.

The first quantum correction for the partition function of the harmonic oscillator

$$Z = Z_{cl}\left[1-\frac{1}{24}\left(\frac{h\nu}{kT}\right)^2\right] \qquad (7)$$

as was noted by *Herzfeld* and *Teller* [25] in 1937, leads to a normal vapor pressure isotope effect. *Herzfeld* and *Teller* made only qualitative attempts to explain the inverse effect, which had been observed *e.g.* in 1936 by *Bailey* and *Topley* [26] for benzene.

The rule of the geometric mean played a part in the earlier discussion of the vapor pressure isotope effect. If the molecular weights M_1, M_2, and M_3 of three isotopic substances form an arithmetic series, the corresponding vapor pressures p_1, p_2, and p_3 form a geometric series. Expansion of the ratios of the vapor pressure as functions of the relative mass ratios, which are assumed to be small, gives

$$\frac{p_2}{p_1} = 1 + a\frac{\Delta m}{m} + b\left(\frac{\Delta m}{m}\right)^2 + \cdots \qquad (8)$$

and

$$\frac{p_3}{p_1} = 1 + a\frac{\Delta m'}{m} + b\left(\frac{\Delta m'}{m}\right)^2 + \cdots \qquad (9)$$

where $m = M$, $\Delta m = M_2 - M_1$, and $\Delta m' = M_3 - M_1$. We obtain

$$p_2^2 = p_1^2\left(1 + 2a\frac{\Delta m}{m} + \cdots\right) \qquad (10)$$

and

$$p_1 p_3 = p_1^2\left(1 + a\frac{\Delta m'}{m} + \cdots\right) \qquad (11)$$

i.e. the values are equal, to a first approximation, for the case

$$\left(\frac{\Delta m'}{m}\right) = 2\left(\frac{\Delta m}{m}\right) \qquad (12)$$

In quantum-statistical notation, the same result is obtained if eq. (25) is considered only for translational degrees of freedom and if the characteristic vibration temperature is replaced by the masses in accordance with

$$\Theta_1^2/\Theta_2^2 = M_2/M_1 \qquad (13)$$

and the sinh expanded into a series. This rule is obeyed with surprising accuracy in the case of hydrogen ($H_2/HD/D_2$), since the rotational degrees of freedom for this system are unchanged on condensation. In general, however, the shape of the molecules has a greater effect than the mass.

5.1. Intermolecular Vibrations

A comprehensive theory of the vapor pressure isotope effect was published in 1961 by *Bigeleisen* [27]. On methodical grounds, we shall start here with the procedure reported by *Wolff* and *Höpfner* [28], which was originally developed only for the description of the vapor pressure isotope effect of substances that form hydrogen bonds.

If p_D and p_H are the vapor pressures of a deuterated (and hence heavier) and an undeuterated substance, and if the isotope effect for a thermodynamic function is denoted by Δ_i, then it follows from eq. (1) that

$$\Delta_i\Delta_v G^o = -RT\ln\frac{p_D}{p_H} \qquad (14)$$

G^o_{gas} and G_{cond} in $\Delta_v G^o = G^o_{gas} - G_{cond}$ must be calculated in accordance with the rules of statistical thermodynamics for each isotopic form.

We shall deal first with the external degrees of freedom. According to *Schäfer* [29], the three translational degrees of freedom for the gas state (deviations from the ideal gas laws will be ignored) at $p = 1$ atm are given by

$$G^o_{trans} = -RT\ln\left[\left(\frac{2\pi k}{N_L h^2}\right)^{\frac{3}{2}}\frac{1}{N_L}\right] - RT\ln g - \frac{3}{2}RT\ln M - \frac{5}{2}RT\ln T - RT\ln R \qquad (15)$$

For the investigation of the vapor pressure isotope effect, we are interested only in the term that changes on isotopic substitution

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[29] *Kl. Schäfer*: Statistische Theorie der Gase, Göttingen 1960.

$$\Delta_i G^{\circ}_{trans} = -\frac{3}{2} RT \ln \frac{M_D}{M_H} \quad (16)$$

or, if only one translational degree of freedom is considered,

$$\Delta_i G^{\circ}_{trans} = -\frac{1}{2} RT \ln \frac{M_D}{M_H} \quad (17)$$

Similarly, when there are three rotational degrees of freedom, if the temperature is not too low we have

$$G_{rot} = -RT \ln \left[\frac{16\pi^3 \sqrt{2\pi} k^{\frac{3}{2}}}{h^3} \right] + RT \ln s - \frac{3}{2} RT \ln \bar{I} - \frac{3}{2} RT \ln T \quad (18)$$

which leads to

$$\Delta_i G_{rot} = -\frac{3}{2} RT \ln \frac{\bar{I}_D}{\bar{I}_H} + RT \ln \frac{s_D}{s_H} \quad (19)$$

Thus the masses M, the moments of inertia I, and any change in the symmetry number s (*e.g.* between CH_4 and CH_3D) are important. The term $RT \ln(s_D/s_H)$ plays no part in the discussion of the vapor pressure isotope effect, since it is compensated for in the condensed state in all known cases by another term having exactly the same magnitude, which is due to the irregular position of the arbitrarily oriented molecules.

The characteristic vibrations of the molecule will be treated separately (see Section 5.3), since they remain constant to a first approximation on transition from the vapor to the condensate; their changes, must, however, be used for the interpretation in particular of the inverse vapor pressure isotope effect.

In the calculation of G_{cond}, it is necessary to use a liquid model whose parameters are commonly used in thermodynamics, so that the results can also be interpreted thermodynamically. Since only a few experimental investigations with solid condensates have been carried out, all discussions on the vapor pressure isotope effect must be concerned with the liquid state. *Eyring*'s theory of significant structures [1] can be used for the discussion of the vapor pressure isotope effect, since it regards the liquid state as a mixture of the other aggregation states (solid and gaseous), which are assumed to be known in principle, and can give the mixing ratio.

We therefore assume that the external degrees of freedom of the gas molecules in the liquid correspond to either gaslike degrees of freedom (this case is of no interest, since it leads to $\Delta_i \Delta_v G^0 = 0$), or to lattice vibrations. A distinction is made between vibrations or translational oscillations, which correspond to the translational movement in the gas, and librations, which may be regarded as hindered rotations. This distinction is possible because the librations usually have a higher wave number, and are changed to a greater degree than vibrations on isotopic substitution (replacement of H by D in this case). In water, for example, wave numbers of 180 cm^{-1} and 710 cm^{-1} are found for the vibrations and the librations respectively [30, 31]. The high wave numbers of the lattice vibrations in this case are caused by the strong hydrogen bonds in water. The corresponding wave numbers for methyl iodide, the crystals of which are held together only by dispersion and dipole forces, are 60 and 100 cm^{-1} [47].

Instead of the wave number ν, it is customary in thermodynamics to use the characteristic vibration temperature Θ, which can be calculated from ν by means of

$$\Theta = hc\nu/k \text{ where } hc/k = 1.4384 \text{ deg. cm} \quad (20)$$

For each degree of freedom of the condensed state that occurs as a vibration, we can put

$$G_{osc} = \frac{1}{2} R\Theta + RT \ln (1 - e^{-\Theta/T}) = RT \ln 2 \sinh \left(\frac{\Theta}{2T} \right) \quad (21)$$

In the case of vibrations with force constants f and molecular masses M, the frequency law

$$\nu = (1/2\pi) \sqrt{f/M} \quad (22)$$

leads, for two isotopic oscillators, to

$$\Theta_D/\Theta_H = \sqrt{M_H/M_D} \quad (23)$$

For librations, the mass is replaced by the moment of inertia.

$$\Theta_D/\Theta_H = \sqrt{I_H/I_D} \quad (24)$$

Determining the left hand side of eq. (14) using eq. (16) and eq. (23), (or eq. (20) and eq. (24)), we find that the contribution of one degree of freedom to the vapor pressure isotope effect is given by the factor

$$\frac{p_D}{p_H} = \frac{\Theta_H}{\Theta_D} \frac{\sinh \Theta_D/2T}{\sinh \Theta_H/2T} \quad (25)$$

The first factor (Θ_H/Θ_D) comes from the thermodynamics of the gas, while the second comes from the lattice vibrations of the condensed phase. For different conditions in one phase, therefore, only one factor would be affected.

Eq. (25) describes the behavior of the normal vapor pressure isotope effect; it also leads to the observed temperature dependence, with a large effect at low temperatures and a vanishing effect at high temperatures, since, owing to

$$\sinh x = x + \frac{x^3}{3!} + \frac{x^5}{5!} + \cdots \quad (26)$$

the second factor yields Θ_D/Θ_H for large T (and hence small x) and cancels the first factor.

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[30] *P. A. Giguère* and *K. B. Harvey*, Canad. J. Chem. *34*, 798 (1956).

[31] *D. F. Hornig, H. F. White*, and *F. P. Reding*, Spectrochim. Acta *12*, 338 (1958).

It must be emphasized that though $\Delta_i\Delta_v G^\circ$ vanishes at high temperatures, $\Delta_i G^\circ_{trans}$, $\Delta_i G_{rot}$, and $\Delta_i G_{osc}$ do not.

In Figure 6, numerical values for $\Theta_H/\Theta_D = 1.01$, 1.1, and $\sqrt{2}$ calculated from eq. (25) are represented by continuous curves.

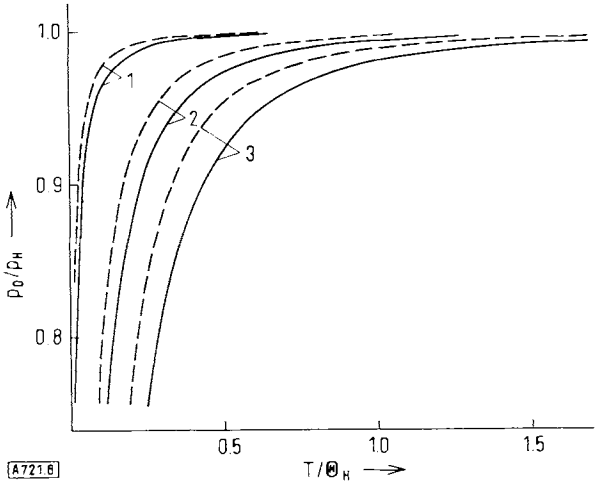


Fig. 6. Theoretical vapor pressure ratios calculated from eq. (25) —— and (30) - - -; 1: $\Theta_H/\Theta_D = 1.01$, 2: $\Theta_H/\Theta_D = 1.1$, 3: $\Theta_H/\Theta_D = \sqrt{2}$.

Table 2, the values in which were calculated from spectroscopic data reported by *Gray* and *Lord*[32], shows the usual values of the isotope effects for the mass and moments of inertia, and hence for $(\Theta_H/\Theta_D)^2$, of organic molecules.

Table 2. Relative masses and moments of inertia of the methylamines.

	CH_3NH_2	CH_3ND_2	CD_3NH_2	CD_3ND_2	Absolute value of CH_3NH_2
M	1	1.0645	1.0986	1.1613	31.056
I_a	1	1.3195	1.6539	1.9702	8.1363
I_b	1	1.1204	1.2260	1.3664	37.1207
I_c	1	1.1619	1.2161	1.3985	38.6802

The replacement of H by D in organic molecules is most strongly reflected in the moments of inertia, whereas the relative changes in the mass are small. Pronounced isotope shifts in the lattice vibrations are consequently found only in the librations (in water by *Giguère* and *Harvey*[30], in ice by *Hornig*, *White*, and *Reding*[31]), whereas the translational vibrations exhibit only a very small isotope effect.

5.2. Frequency Distribution of the Lattice Vibrations

Eq. (25) is based on the assumption that only one frequency can be assigned to each degree of freedom. This is generally not so. In the ideal case, the coupling of the lattice vibrations leads to a Debye frequency distribution, in which the frequency corresponding to the characteristic temperature Θ is now merely the maximum (limiting) frequency, and is accompanied by a continuous spectrum of lower frequencies. This leads even qualitatively to a decrease in the quantum effect calculated for eq. (25).

If we assume a simple Debye distribution, we obtain

$$G_{osc} = \frac{3}{8} R\Theta + RT \ln (1 - e^{-\Theta/T}) - \frac{1}{3} RT D_3\left(\frac{\Theta}{T}\right)$$
$$= -\frac{1}{8} R\Theta + RT \ln \left[2 \sinh \frac{\Theta}{2T}\right] - \frac{1}{3} RT D_3\left(\frac{\Theta}{T}\right) \quad (27)$$

with the Debye function

$$D_3(x) = \frac{3}{x^3} \int_0^x \frac{\xi^3}{e^\xi - 1} d\xi \quad (28)$$

There are two expansions for the numerical evaluation of $D_3(x)$

$$D_3(x) = \sum_{n=0}^{\infty} \frac{3B_n}{(n+3)n!} x^n = \frac{\pi^4}{5x^3} - \sum_{n=1}^{\infty} \left[3 + \frac{9}{nx} + \frac{18}{(nx)^2} + \frac{18}{(nx)^3}\right] \frac{e^{-nx}}{n} \quad (29)$$

with the Bernoulli numbers

$$B_n = 1, -\frac{1}{2}, \frac{1}{6}, 0, -\frac{1}{30}, 0, \frac{1}{42}, 0, -\frac{1}{30}, 0, \frac{5}{66}, 0, -\frac{691}{2730}, 0, \frac{7}{6}, 0 \ldots$$

The first series is suitable for high temperatures ($x < 2$), while the second expansion is used for low temperatures, at which it soon leads to the T^3 law.

If we calculate $\Delta_i\Delta_v G^0$ as above, but using eq. (27) instead of eq. (21), we obtain the following expression for the vapor pressure isotope effect:

$$\frac{p_D}{p_H} = \frac{\Theta_H}{\Theta_D} \cdot \frac{\sinh \Theta_D/2T}{\sinh \Theta_H/2T} \cdot \exp\left[-\frac{1}{8}\left(\frac{\Theta_D}{T} - \frac{\Theta_H}{T}\right) - \frac{1}{3}\left(D_3\left(\frac{\Theta_D}{T}\right) - D_3\left(\frac{\Theta_H}{T}\right)\right)\right] \quad (30)$$

The values calculated from this formula are shown by broken lines in Figure 6. The effect is smaller by about 1/3 in relation to eq. (25).

5.3. Influence of the Intramolecular Vibrations

It has been assumed so far that the frequencies of the intramolecular vibrations remain unchanged on condensation. This is not quite true. Small displacements to longer wavelengths are usually observed, and these also influence the vapor pressure isotope effect.

If the characteristic vibration temperatures of a given degree of freedom are Θ_H and Θ_D in the gas and Θ'_H and Θ'_D in the condensed state, it follows directly from eq. (21) that

$$\Delta_i\Delta_v G_{osc} = RT \ln \frac{\sinh \Theta_D/2T \sinh \Theta'_H/2T}{\sinh \Theta_H/2T \sinh \Theta'_D/2T} \quad (31)$$

The characteristic vibrations of most molecules have Θ values of more than 2000 °C, so that since $\sinh x =$

[32] *A. P. Gray* and *R. C. Lord*, J. chem. Physics *26*, 690 (1957); *H. Wolff* and *E. Wolff*, Ber. Bunsenges. physik. Chem. *69*, 467 (1965).

$^1/_2(e^x - e^{-x})$ becomes $^1/_2 e^x$ for large x, eq. (31) can be replaced in these cases by

$$\Delta_i \Delta_v G_{osc} = \frac{R}{2} (\Theta_D - \Theta'_D) - (\Theta_H - \Theta'_H) \quad (32)$$

and hence

$$\frac{p_D}{p_H} = \exp \frac{(\Theta_H - \Theta'_H) - (\Theta_D - \Theta'_D)}{2T} \quad (33)$$

According to *Buckingham*[33], the ratio $(\Theta - \Theta')/\Theta$ is independent of the nuclear mass to within 1 % (rigorously for diatomic molecules at least). Application of this rule in eq. (33) leads to a positive exponent and to an inverse vapor pressure isotope effect, if it is assumed that $\Theta_H > \Theta_D$.

Mention should be made here of the infrared effect discussed by *Baertschi* and *Kuhn*[34], in which the vapor pressure isotope effect of CCl_4 ($^{12}CCl_4/^{13}CCl_4$ and $C^{35}Cl_4/C^{37}Cl_4$) is attributed to the dispersion forces between the molecules. The question of the frequency distribution on condensation has been discussed by *Ulbrich*[35], though not in relation to the vapor pressure isotope effects.

Apart from the difficulty of giving exact frequencies for liquid bands, it must be noted that the spectroscopically observed bands at strongly anharmonic potentials correspond not to the thermodynamically relevant frequencies, but to the differences between the ground terms and the overtones, which may be considerably displaced from the ideal harmonic position.

For the practical evaluation of measurements of the vapor pressure isotope effect, the experimental values are often expressed by means of the relation

$$\ln p_D/p_H = -A/T^2 + B/T \quad (34)$$

The term in T^{-2} can be identified with the effect of the lattice vibrations in accordance with eq. (25) or (30), and the term in T^{-1} with the effect due to the displacements of the characteristic vibrations of the molecules [eq. (33)]. Good examples of this method are found in *van Hook*'s work on ethanes[7] and in *Bigeleisen*'s work on [D_2]-ethylenes[8].

[33] *A. D. Buckingham*, Trans. Faraday Soc. *56*, 753 (1960).

[34] *P. Baertschi* and *W. Kuhn*, Helv. chim. Acta *40*, 1084 (1957).

[35] *R. Ulbrich*, Z. Naturforsch. *23a*, 1323 (1968).

5.4. Numerical Examples

Wolff[28,36] has given examples in which vapor pressure isotope effects were calculated from spectroscopic data with the aid of equations (25) and (33) and compared with the experimental values.

In the case of water, an effect of 0.99 was found at 0 °C for three translational degrees of freedom, 0.53 for three rotational degrees of freedom, and 1.57 for the intramolecular vibrations in accordance with eq. (33), *i.e.* a total of 0.82, which is in good agreement with the experimental value of 0.80.

The translational degrees of freedom make practically no contribution here and in other cases, partly because M_D/M_H is much smaller than I_D/I_H, and partly because the Θ values of the translational vibrations are so small that the corresponding degrees of freedom are fully excited at the temperature in question and make no further contribution.

The vapor pressure isotope effects of methanol, HCl, HBr, and H_2S have also been calculated from spectroscopic data[36] (cf. Table 3). These calculations present difficulties, since the spectra of the solid or even of the liquid state are known with sufficient accuracy in only a few cases. Liquids in particular give broad IR and Raman bands, the maxima of which are rarely sharp.

Table 3. Calculated and measured vapor pressure isotope effects [28, 36].

Isotopic pairs	t (°C)	Translational degrees of freedom	Rotational degrees of freedom	Intramolecular degrees of freedom	p_D/p_H calc.	p_D/p_H exp.
D_2O/H_2O	100	0.99	0.68	1.39	0.94	0.95
	0	0.99	0.53	1.57	0.82	0.80
	− 15	0.99	0.46	1.73	0.79	0.79
CH_3OD/CH_3OH	80	1.00	0.68	1.37	0.93	0.98
	50	1.00	0.64	1.41	0.90	0.97
	20	1.00	0.58	1.46	0.85	0.95
D_2S/H_2S	−120	1.00	0.797	1.190	0.948	0.935
	− 90	1.00	0.857	1.157	0.992	0.982
DCl/HCl	−120.5	1.00	0.81	1.23	1.00	0.98
	−115.55	1.00	0.82	1.22	1.01	09.5
DBr/HBr	−123	1.00	0.837	1.200	1.005	0.993
	− 88	1.00	0.887	1.159	1.028	0.993

5.5. The Anharmonicity of the Lattice Vibrations

The effects described so far yield quantitative information about the vapor pressure isotope effect. They require a knowledge of the positions of the lattice vibrations and of the frequency displacement on condensation. The present state of spectroscopic techniques is such that these data can be obtained in principle, though often only with difficulty.

It was formerly necessary to assume that, contrary to reality, the vibrations were always harmonic. If a condensed substance has a measurable vapor pressure, the probability of a molecule's leaving the force field of its neighbors to pass into the gas phase must be high. This involves its emerging from the region of harmonic forces, for which, by definition, the restoring force is proportional to the displacement from the equilibrium position.

[36] *H. Wolff*, *E. Wolff*, and *H.-E. Höppel*, Ber. Bunsenges. physik. Chem. *72*, 644 (1968).

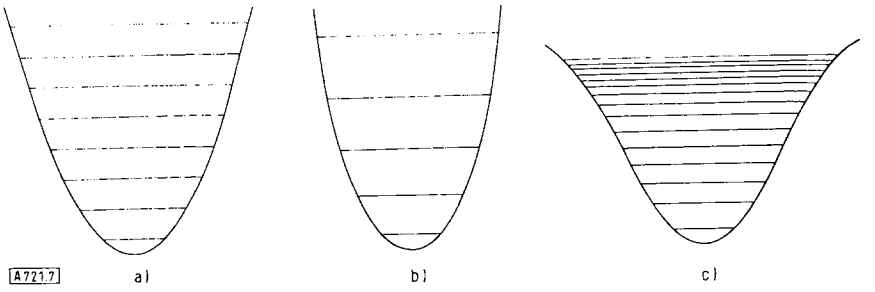


Fig. 7. Influence of anharmonicities on the partition function of the oscillators; (a) Z^*_{cl}, (b) $Z^*_{anh} < Z^*_{cl}$, (c) $Z^*_{anh} > Z^*_{cl}$.

A harmonic potential leading to a series of equidistant energy steps is shown in Figure 7a. Let the corresponding partition function be Z^*_{harm}.

At large displacements of a translational vibration, it must be expected that the repelling forces from the neighboring molecules will become more noticeable because of the high repulsion exponents, so that the potential will rise more steeply than the harmonic potential. According to the quantum theory of the anharmonic oscillator (see *e.g. Pöschel* and *Teller*[37]), therefore, the energy levels will be farther apart, with the result that the partition function Z^*_{trans} will be smaller than for the harmonic case (Fig. 7b).

The librations, on the other hand, will always change into more or less free rotations at large displacements, so that it is necessary to assume a periodic potential, the troughs of which are separated by potential barriers. The result is the case indicated in Figure 7c, in which the potential curve is shallower than in the harmonic case. The states are closer together, and give a greater partition function. These anharmonicities have a greater effect for lighter molecules, since the amplitudes of their vibrational movement are greater. From the relation between the partition function and the free enthalpy

$$G = -RT \ln Z^* \qquad (35)$$

this leads to a contribution $\Delta_i G_{anh} < 0$ for translational vibrations in the solid state and to $\Delta_i G_{anh} > 0$ for the librations, whence we find a normal effect in the former case and an inverse effect in the latter. This effect will appear in particular when the degrees of freedom in question are fully excited, *i.e.* when eq. (25) no longer has any effect.

The prospects of a quantitative treatment of this effect are poor as long as no data on the anharmonicities of lattice vibrations are available.

5.6. The Size of the Molecule

The C–H bond may be expected to be longer than the C–D bond, even if the force constants are assumed to be identical. The corresponding stretching vibrations are not yet excited at normal temperatures, so that the state is that of the zero-point vibration. The energy of the zero-point vibration of deuterium is situated lower in the potential trough because of the greater mass, and in view of the asymmetry of the trough, the time-average position of the deuterium nucleus is closer to

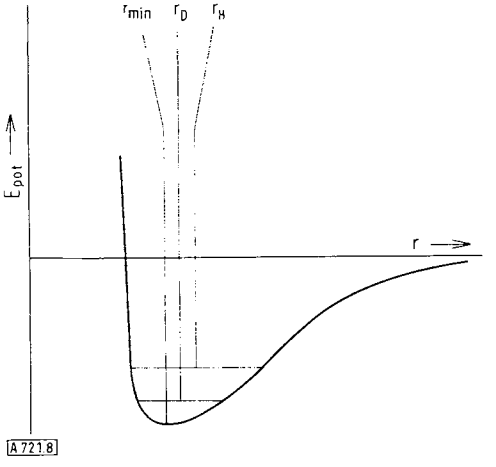


Fig. 8. Because of the anharmonicity of the bonding forces, the average bond length is smaller for the heavier atoms (r_{min} = potential minimum, r_D = position of D at lowest state r_H = position of H at lowest state.

the carbon than that of the hydrogen nucleus. Macroscopically, therefore, deuterated molecules should be smaller than the corresponding undeuterated molecules, and this should be reflected in a negative isotope effect for the molar volume $\Delta_i V < 0$.

Dorfmüller and *Bigeleisen*[38] have carried out measurements on liquid ethylene, which gave an effect of about 1 %. The experimental determination of $\Delta_i V$ is fundamentally difficult, since the molecular weight of the substance, and hence the isotopic composition of the sample, must be known very accurately for the calculation of the molar volume from the densities. Difference measurements, such as were used for the vapor pressure, are not possible in this case.

The denser packing of the heavier molecules leads to an increase in the force constants f or d [in eq. (22)] in relation to those of the lighter substance. An extra factor

$$f_D/f_H > 1 \text{ or } d_D/d_H > 1$$

thus appears on the right-hand sides of equations (23) and (24). In eq. (25) this gives $p_D/p_H > 1$ even at high temperatures, where the vapor pressure isotope effect should have disappeared long ago on condition that $f_D = f_H$.

[37] *G. Pöschl* and *E. Teller*, Z. Physik *83*, 143 (1933).

[38] *Th. Dorfmüller* and *J. Bigeleisen*, Lecture at the "Bunsen-Tagung" in Cologne, May 1967.

6. Isotopic Mixtures

Isotopic mixtures are mixtures of mutually isotopic components, *e.g.* D_2O/H_2O, $^4He/^3He$, HD/H_2, *etc.* The problem is the usual one for mixtures, *i.e.* to what extent can the properties of the mixtures be explained on the basis of the properties of the components?

Very few cases are known at present in which isotopic mixtures deviate from ideal behavior. The free enthalpy of mixing can nearly always be calculated from the mole fractions in accordance with

$$\Delta_m G = RT\,(x_1 \ln x_1 + x_2 \ln x_2) \tag{36}$$

If the corresponding gas phase is also ideal, the vapor pressure over the mixture is described by the well known Raoult line. Deviations from ideal behavior must be expected at very low temperatures for "quantum liquids", when the free enthalpy of a monatomic ideal gas

$$G = RT \ln \left[\frac{N_L}{V_M} \left(\frac{h^2}{2\pi mkT} \right)^{\frac{3}{2}} \right] \tag{37}$$

requires the addition of terms of the form

$$\pm\, RT \frac{N_L}{V_M} \times \left(\frac{h^2}{2\pi mkT} \right)^{\frac{3}{2}} \times \left(\frac{1}{2} \right)^{\frac{3}{2}}$$

and higher terms [29].

Positive deviations from Raoult's law have been found at 20 °K in the system D_2/H_2 [45], and deviations of this type are so strong for $^3He/^4He$ that a miscibility gap occurs below 1 °K [39].

It is generally considered that the deviations observed for helium and hydrogen are due, not to intermolecular forces, but merely to the quantum-statistical condensation effects [40].

The chemist, on the other hand, is interested in cases where deviations from ideal behavior occur even at normal temperatures. Investigations so far have been confined to the system D_2O/H_2O, for which a heat of mixing of 7.5 cal/mole has been found at 25 °C [41], and whose boiling behavior has also been studied. The observed deviations from ideality are again positive, and lead to the occurrence of an azeotrope near the cross-over point at 221 °C [42]. The observations can be explained on the basis of a ternary mixture of D_2O, HDO, and H_2O, the components of which are assumed to exhibit ideal mixing behavior. The variables of the system are thus the equilibrium constant of the reaction

$$D_2O + H_2O \rightleftharpoons 2\ HDO \tag{38}$$

and the vapor pressure of HDO [43].

[39] *N. E. Phillips*, Annu. Rev. physical Chem. *19*, 559 (1968).
[40] *F. L. Byrns* and *R. M. Mazo*, J. chem. Physics *47*, 2007 (1967).
[41] *A. Narten*, J. chem. Physics *41*, 1318 (1964).
[42] *K. Zieborak*, Z. physik. Chem. *231*, 248 (1966).
[43] *R. E. Weston*, J. chem. Physics *42*, 2635 (1965).

7. Vapor Pressure Differences Between Equivalent Isomers

Investigations on equivalent isomers, such as the three $[D_2]$-ethylenes [8] or the eight ethanes from C_2H_6 to C_2D_6 [7], which include three pairs of isomers, have led to conclusions regarding the forces acting in the liquid state. Thus *van Hook* [7] showed in the case of the ethanes that the vapor pressure isotope effect of equivalent isomers (higher vapor pressures were found for the more asymmetric isomer) is essentially attributable to a frequency shift of the torsional vibrations toward shorter wavelengths on condensation, which must itself be temperature-dependent (or rather density-dependent).

In the case of the $[D_2]$-ethylenes, the *trans* form has a higher vapor pressure than the *cis* form and the $[1,1\text{-}D_2]$-form. Representation of the experimental values by means of eq. (34) showed that the vapor pressure differences in the $[D_2]$-ethylenes are due to the term A, *i.e.* they result from an effect corresponding to eq. (25). Comparison with the moments of inertia of the ethylenes (Table 4) shows that the effect can be explained by hindered rotation about the axis lying in the direction of the C=C bond with the moment of inertia I_A. This moment of inertia is much smaller for *trans*-$[D_2]$-ethylene than for *cis*-$[D_2]$-ethylene or $[1,1\text{-}D_2]$-ethylene.

Table 4. Parameters of eq. (34) and moments of inertia of $[D_2]$-ethylenes.

	A	B	$I_A \times 10^{40}$	$I_B \times 10^{40}$	$I_C \times 10^{40}$
trans-CHD=CHD	716.0	6.865	8.06	33.70	41.72
cis-CHD=CHD	742.2	6.916	8.45	33.09	41.48
$CD_2{=}CH_2$	748.3	6.995	8.64	32.69	41.33
$CH_2{=}CH_2$	0	0	5.76	28.00	33.75

8. Closing Remarks

The investigations on the vapor pressure isotope effect provide clues for many branches of physical chemistry. The measurements on substances that form hydrogen bonds make it necessary for the spectroscopist to measure the hydrogen bond or lattice vibrations used for the interpretation of the effect in eq. (25) in the far IR region in the solid and liquid states.

It should be noted in this connection that vapor pressure measurements show much more clearly than spectroscopic studies that deuterium bonds are about 5 % stronger than hydrogen bonds [18,21].

The intermolecular forces are generally responsible for the frequency shift of the characteristic vibrations of the molecules on condensation, but in addition to the red shift in the stretching vibration, it is necessary also to assume a blue shift *e.g.* in the torsional vibration of ethane.

Our knowledge of the liquid state will be improved by numerous studies on the vapor pressure isotope

effect on both sides of the triple point, since it will then be possible to follow the various effects beyond the melting point.

The vapor pressure isotope effects of the quantum liquids helium and hydrogen occupy a special position, since the usual method of applying quantum corrections to the classical formulas does not work in these cases. The theory of the quantum effects in liquid hydrogen has been developed by *Bigeleisen* [46] on the basis of the vapor pressures of H_2, D_2, T_2, HD, HT, and DT, the ratios of the partition functions of the liquids being calculated from the vapor pressure isotope effects. The concept of the free rotation of the molecules in liquid hydrogen has thus been confirmed, since the observed effects can be explained in full on the basis of the translational degrees of freedom of the hydrogen molecules [*].

Received: December 3, 1968 [A 721 IE]
German version: Angew. Chem. *81*, 770 (1969)
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[45] *R. B. Newman* and *L. C. Jackson*, Trans. Faraday Soc. *54*, 1481 (1958).

[46] *J. Bigeleisen*, J. chem. Physics *39*, 769 (1963).

[*] Recent results of *Wolff* [48], who used improved spectroscopic data in order to calculate vapor pressure isotope effects, of *van Hook* [49], who expandes the theory to the adsorption equilibrium, and of *Lal* and *Swinton* [50] who determined enthalpies of mixing of isotopic mixtures (benzene/[D_6]-benzene and cyclohexane/[D_{12}]-cyclohexane) should be mentioned here.

[47] *M. Ito*, J. chem. Physics *41*, 1255 (1964).

[48] *H. Wolff* and *E. Wolff*, Ber. Bunsenges. physik. Chem. *73*, 393 (1969); *H. Wolff*, Ber. Bunsenges. physik. Chem. *73*, 399 (1969).

[49] *W. A. van Hook*, J. physic. Chem. *71*, 3270 (1967).

[50] *M. Lal* and *F. L. Swinton*, Physica *40*, 446 (1968).

Sorption Promotors in Biopharmaceutics

By W. A. Ritschel[*]

The absorption of drugs depends on the physico-chemical properties of the constituent substances. Drugs that are absorbed only with difficulty or only slowly, or even not at all, can be made to penetrate into the skin and the mucous membrane (penetration) or to pass through them (permeation) with the aid of "sorption promotors". The search for substances of this type and the elucidation of their principles of action form part of the field of biopharmaceutics.

1. Introduction

A drug is only very rarely used therapeutically in the form of the pure substance. The pure drug or a mixture of drugs is generally combined with adjuvants, to form a drug product. These adjuvants may include solvents, emulsifying agents, preservatives, antioxidants, coloring agents, flavoring agents, buffer mixtures, fillers, lubricants, binders, disintegrators, *etc.*, depending on whether the preparation is to be in the form of a solution, tablets, capsules, suppositories, or ointments. The various types of preparation help to ensure the fastest possible action on the target organ and to ensure that the active principle is in fact absorbed in cases where certain forms cannot be used.

2. General Observations on the Absorption of Drugs

Before a drug can act, it must reach the target organ. This organ may be the surface of the skin or of the mucous membrane and the deeper layers of the skin (*local* action), or it may be one of the internal organs or body fluids (*systemic* action). If the drug acts only on the surface of the skin we speak of *adsorption*, while if it passes into deeper-lying layers of the skin we speak of *penetration*. Absorption occurs if the drug passes through the skin barrier (*permeation*) to reach the layers containing the blood vessels, so that it also enters into the metabolism. Penetration and absorption are designated by the collective term "*sorption*". The uptake of a drug from the mouth and the gastrointestinal tract, the active principle being distributed in the body by the blood and lymph, is also absorption. Whether a drug is adsorbed, penetrates, or is absorbed depends on its physico-chemical properties (solubility in water, partition coefficient between lipid and water) and on the adjuvants present in the preparation (type of base, pH value, choice of adjuvants, *etc.*).

The absorption of a drug from a preparation consists essentially of four steps, which do not take place strictly in succession, but partly overlap. These steps are: release of the drug from the preparation, diffusion of the drug to the absorbing organ, penetration and

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permeation, and distribution in the transport medium (blood and lymph).

Only after it has been absorbed can the drug react with the receptor of the target organ and exert its action.

2.1. Release of the Active Principle and Diffusion

A therapeutic action can occur only if the drug is released in sufficient quantities from the preparation. This process depends largely on the preparation of the drug. Unsuitable adjuvants that interact with the drug by dispersion forces, directional forces, induction forces, hydrogen bonding, or complexing can strongly retard, or even prevent, the release of the drug, quite apart from the possibility of a change in the action of the drug due to chemical reaction. Similar results can, however, also be produced by physical effects, such as an increase in viscosity due to unsuitable adjuvants or unsuitable particle sizes, which would hinder dissolution or the disintegration, *e.g.* of tablets.

A drug can be released from a tablet or capsule only if the tablet or capsule disintegrates rapidly. Disaggregation into granular particles is not enough but must be followed by further disintegration into powder particles. The rate of dissolution of the drug in the gastrointestinal tract will obviously increase with the rate at which the preparation can be broken down into the smallest possible particles. Since the rate of dissolution depends on the surface area, micronized, *i.e.* extremely finely divided, drugs are absorbed particularly rapidly. The dissolved drug then migrates by diffusion to the "boundary organ" or lipoid barrier, *i.e.* to the skin or the mucous membrane.

2.2. Penetration, Permeation, and Distribution in the Transport Medium

To exert its action, the drug must reach the cells of the target organ. Since these cells are surrounded by an aqueous tissue fluid, the drugs must be at least partly water-soluble. They must, however, first penetrate into or through layers of cells in order to reach the tissue fluid, and this means that they must be soluble in the lipids that largely constitute the cell membranes. Absorption thus involves a partition process at membranes having mainly lipid properties. The hydrogen ion concentration influences the water-solubility and lipid solubility of weakly basic and weakly acidic substances, which is what most drugs are.

Molecules can be transported through the membrane either by diffusion or by convection (see Fig. 1)[1].

The diffusion of the dissolved molecules depends on the concentration difference between the outside (c_a) and the inside (c_i) of the membrane. The transport current (q) is proportional to the partition coefficient (f) of the molecular species between the membrane material and the solvent. It is

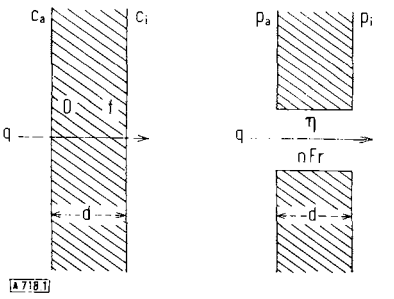


Fig. 1. Transport of dissolved molecules through a membrane by diffusion (left) and by convection (right) [1]; for explanation see text

also proportional to the area of the membrane (F) and the diffusion coefficient (D), and inversely proportional to the thickness of the membrane (d) [see eq. (1)]:

$$q = \frac{D F f}{d} \times (c_a - c_i) \qquad (1)$$

Whereas diffusion involves the transport of the dissolved molecules without displacement of the solvent the transport of dissolved molecules by convection is accompanied by displacement of the solvent, the extent and direction of the transport being determined by the hydrostatic pressure difference between the outside (p_a) and the inside (p_i) of the membrane. If the transport is assumed to take place by laminar flow through round, fairly wide pores of equal size, the transport current (q) is proportional to the cross-sectional area (F) of the individual pores, the number of pores (n), and the square of the radius (r) of the pores, and inversely proportional to the length of the pores, which is equal to the thickness of the membrane (d). The specific resistance of the solution to displacement by convection is given by the viscosity η [see eq. (2)]:

$$q = \frac{1}{\eta} \times \frac{n r^2 F}{d} \times (p_a - p_i) \qquad (2)$$

The membranes can be divided into four types, according to their permeability [1]:

Type I: The membrane consists of a material that is impermeable to molecules. Both diffusion and convection can, however, take place through water-filled pores.

Type II: The membrane consists of a closed, pore-free layer. In this case only diffusion is possible, and that only if the molecules are soluble in the material of the membrane.

Type III: The membrane consists of a material that corresponds to type II but it also contains pores, so that substances can diffuse through the membrane material, and can be transported through the pores both by diffusion and by convection.

Type IV: The membrane consists of a material that is impermeable to molecules. Penetration of the membrane is, however, possible by active transport, *i.e.* with the aid of a "carrier". According to this carrier hypothesis, it is assumed that a cell substance is present on the outside of the membrane and holds the molecule to be transported. The resulting complex diffuses to the inside, where the transported molecule is "released" and whence the carrier diffuses back to the outside. The molecules are bonded to a specific carrier in the same manner as to a receptor.

2.3. Absorption in the Gastrointestinal Tract

Most drugs are weakly acidic or weakly basic substances. The quantity absorbed per unit time and the absorption site depend mainly on the pH value at which the drug is present in the dissociated or in the undissociated form. The ionization constant K_a is expressed by

[1] *L. Dettli* and *P. Spring*, 23rd. Int. Kongress der Pharmazeutischen Wissenschaften, Münster 1963. Kongressbericht, Govi-Verlag, Frankfurt 1964, p. 85.

the pK_a value[2] in analogy with the hydrogen ion concentration.

The degree of dissociation of weak acids increases with the pH value, whereas that of bases decreases. The solubility in water increases with increasing dissociation, and the solubility in lipids increases with the concentration of the undissociated form. Weak acids are therefore more readily absorbed at the low pH value of the stomach, since dissociation is suppressed and most of the substance is in the undissociated form (cf. Fig. 2). Weak bases, on the other hand, are more readily absorbed in the alkaline medium of the intestine.

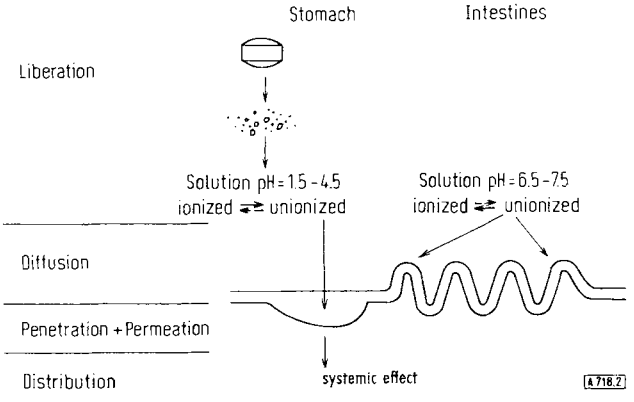


Fig. 2. Absorption of a weakly acidic drug from a tablet in the gastrointestinal tract [3].

The absorption of weakly acidic drugs from the intestine despite the lower content of the undissociated form in the alkaline medium is explained by the very large area of the intestinal tube.

The rate of absorption of the undissociated component of a substance increases with increasing lipid-solubility. The ratio of the solubilities in water and lipids is expressed by the partition coefficient of a drug between an organic solvent (*e.g.* hexane, heptane, chloroform, dodecanol) and an aqueous phase (buffer solution).

Brodie et al.[4–8] deduced rules for the absorption of drugs from the gastrointestinal tract on the basis of their pH hypothesis. These rules were summarized by *Münzel*[9] as follows:

"The gastrointestinal membrane behaves as a lipid barrier. This barrier allows mainly the undissociated form of acids and bases to pass.

The epithelium of the jejunum has a pH of 5.3, which is substantially independent of the pH of the contents of the intestine.

Most drugs are absorbed by passive diffusion.

The absorption rate depends qualitatively and semiquantitatively on the O/W partition coefficient (where O = heptane or chloroform). The more lipophilic the drug the faster, in general, the absorption.

The lowest pK_a value of an acid that still allows fast absorption is about 3.

The highest pK_a value of a base that still allows fast absorption is about 7.8.

In the steady state (equilibrium state) of flow experiments with a basic drug, the concentration of the drug is *higher* in the intestinal lumen than in the plasma; the ratio of these concentrations increases with increasing basicity of the drug until a certain limit is reached.

In the steady state in flow experiments with an acidic drug, the concentration of the drug is *lower* in the intestinal lumen than in the plasma; the ratio of these concentrations decreases with increasing acidity of the drug.

In general, acidic drugs are absorbed from the stomach, whereas basic drugs are not".

2.4. Absorption Through the Skin

The conditions for cutaneous absorption are essentially the same as for gastrointestinal absorption. Additional factors in this case, however, are the condition of the skin (intact or injured), its moisture content, the concentration of the drug in the locally applied preparation, the composition of the base, the area of the skin treated, the thickness of the skin (between 0.5 and 2.0 mm[10, 11]), and the skin type (seborrhoic, sebostatic).

The possibilities of cutaneous and gastrointestinal absorption are summarized in Fig. 3.

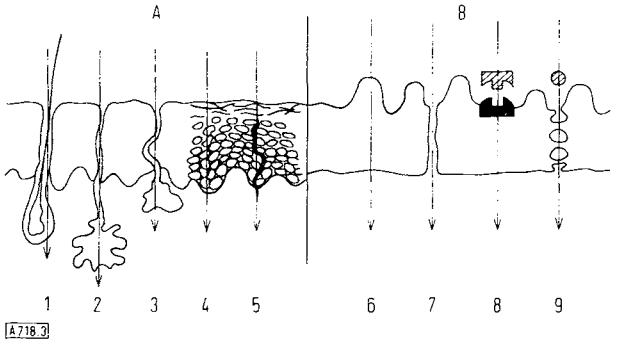


Fig. 3. Possibilities of cutaneous (A) and gastrointestinal (B) absorption of a drug (for explanations of 1 to 9, see text).

In cutaneous absorption (A), the drug can penetrate the skin in the following ways to reach the subcutaneous tissue layers containing the vessels: 1 = through the wall of the hair follicles (follicular absorption); 2 = through the sweat glands (glandular absorption); 3 = through the sebaceous glands (glandular absorption); 4 = through the cells of the horny layer (diffusion); 5 = between the cells of the horny layer (convection). Gastrointestinal absorption (B) can occur in the following ways: 6 = through the membrane (diffusion); 7 = through water-filled pores in the membrane (convection); 8 = by active transport (carrier hypothesis); 9 = by corpuscular absorption to form vacuoles (pinocytosis; persorption).

[2] *K. Münzel*: Der Einfluss der Formgebung auf die Wirkung eines Arzneimittels in Fortschritte der Arzneimittelforschung. Birkhäuser, Basel 1966, Vol. 10, p. 246ff.

[3] *W. A. Ritschel*, Dtsch. Apotheker-Ztg. *107*, 1835 (1967).

[4] *P. A. Shore, B. B. Brodie*, and *C. A. Hogben*, J. Pharmacol. exp. Therapeut. *119*, 361 (1957).

[5] *L. S. Schanker, P. A. Shore, B. B. Brodie*, and *C. A. M. Hogben*, J. Pharmacol. exp. Therapeut. *120*, 528 (1957).

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[7] *C. A. M. Hogben, D. J. Tocco, B. B. Brodie*, and *L. S. Schanker*, J. Pharmacol. exp. Therapeut. *125*, 275 (1959).

[8] *L. S. Schanker*, J. Pharmacol. exp. Therapeut. *126*, 283 (1959).

[9] *K. Münzel* [2], p. 252.

[10] *M. Barr*, J. pharmac. Sci. *51*, 395 (1962).

[11] *W. A. Ritschel*, Dtsch. Apotheker-Ztg. *108*, 1029 (1968).

3. Modification of Absorption

The absorption of drugs can be influenced, *e.g.* by chemical modification of the drug (to obtain a favorable lipid/water partition coefficient), by modification of the size of the molecule, by adjustment of the pH to a suitable value, by micronization (to increase the rate of dissolution), by suitable choice of the point of application and the form in which the drug is applied, and by the use of sorption promotors.

Sorption promotors are substances that have no therapeutic properties of their own, but which can improve the penetration of the drugs from the preparation into the skin, or their permeation through the skin, or can facilitate absorption of the drugs by the mucous membrane. With the aid of these agents the drugs pass through the skin or mucous membrane barrier into the blood and lymph streams, and so participate in the metabolism [12]. Since agents of this type are necessary in most cases to allow or to increase the introduction of drugs into the blood stream, the process involved is not merely penetration into the layers of the skin, but permeation through the skin. It would in fact be justifiable to speak of penetration and permeation promotors. This distinction, however, is very difficult to make. Whereas, *e.g.* the solvent dimethyl sulfoxide actually permeates, the surface active agents and complexing agents act mainly on the membranes; esters of fatty acids merely cause mixing of the carrier with the skin fats, and so do not permeate.

Of the various names commonly used in the German literature for these substances (Gleitschienen, Resorptionsförderer), some are appropriate, while others are less so [13, 14]. The English terms "penetration carrier" and "sorption promotor" are satisfactory in this respect.

4. Survey of Sorption Promotors

4.1. Organic Solvents

The percutaneous absorption of a dissolved drug is strongly influenced by the solvent [13]. For example, fat solvents can assist the absorption both of water-soluble and of oil-soluble substances [15]. The improvement in the absorption of oil-soluble substances is due to the partial leaching of the lipids present in the epidermal membrane by the solvent [16]. The increased absorption of oil-soluble substances in the presence of fat solvents is due to the dissolution of the sebum and the resulting improvement of the conditions for wetting and for transepidermal and transfollicular penetration [17]. It is important that the solvent should not remain on the surface of the skin, retaining with it the substance that is to be absorbed, as is the case, *e.g.* with phenol dissolved in glycerin or vegetable oil [15].

Since many drugs penetrate into the skin more readily from water than from organic solvents alone, it has been suggested that the organic solvent in which a water-soluble drug is dissolved must have a high affinity for water. Thus both the miscibility and the solution properties of the solvent are responsible for the transport of a water-soluble drug through the skin with the aid of organic solvents [18].

In certain circumstances organic solvents can increase the absorption to such an extent that toxic effects occur [19]. It is also known, on the other hand, that degreasing of the surface of the skin with ether before application of a preparation can reduce absorption [20], as has been found, *e.g.* for methyl salicylate. A list of organic solvents that have been referred to in the literature as sorption promotors is given in Table 1.

Table 1. Organic solvents used as sorption promotors.

Acetone	Cyclohexanone
Ethanol	Dimethylacetamide
Ethyl ether	Dimethylformamide
Ethylene glycol	Dimethyl sulfoxide
Benzene	Polyethylene glycol
Chloroform	Propylene glycol
Cyclohexane	Tetrahydrofurfuryl alcohol

Despite numerous investigations on the effects of organic solvents on absorption, it is difficult at present to deduce any general rule. The application of drugs in lipophilic solvents probably leads to a marked change in the penetration resistance of the skin barrier. This in turn probably influences the activity coefficient and the diffusion constant of the penetrating drug in the skin barrier [21].

In penetration experiments with solutions of physostigmine in alcohols and in esters, the quantity absorbed was found to depend on the length of the aliphatic chain [22].

Investigations on the absorption of pentobarbital into erythrocytes showed greater absorption from ethanol than from aqueous solution. It is assumed that ethanol can alter the distribution of weak acids between the cells and the intracellular space [23].

The percutaneous absorption of aminophenazone with organic solvents as carriers has been studied in animal and human experiments. Aminophenazone is absorbed by 40—60% of the body surface from a mixture of 20% of ethylene glycol, 30% of cyclohexane, 10% of cyclohexanone, and 40% of hexanol, but not when the components are used singly [24].

[12] *H. v. Czetsch-Lindenwald* and *H. P. Fiedler*: Hilfsstoffe für Pharmazie und angrenzende Gebiete, Editio Cantor, Aulendorf 1963, p. 138.

[13] *F. Meyer* and *L. Kerk*, Naunyn-Schmiedebergs Arch. exp. Pathol. Pharmakol. *235*, 267 (1959).

[14] *W. A. Ritschel*, Die Tablette. Editio Cantor, Aulendorf 1966, p. 136.

[15] *J. W. Hadgraft*, J. mond. Pharmac. (La Haye) *3*, 309 (1967).

[16] *S. Rothman* in *A. Bethe*: Handbuch der normalen und pathologischen Physiologie. Springer, Berlin 1929, Vol. 4, p. 107.

[17] *S. Rothman*: Physiology and Biochemistry of the Skin. University of Chicago Press, Chicago 1954.

[18] *R. T. Tregear*: Physical Function of the Skin, Academic Press, London 1966.

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[21] *T. Higuchi*, J. cosmet. Chem. *11*, 85 (1960).

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[23] *E. Greiser* and *K. Soehring*, Arzneimittel-Forsch. *17*, 207 (1967).

[24] *W. Klinger*, Pharmazie *16*, 510 (1961).

In comparative experiments on the absorption of fluocinolone acetonide from an O/W emulsion, a W/O emulsion, a hydrocarbon base, a polyethylene glycol base, and alcohol, the greatest quantity was absorbed with alcohol [25].

With monohydric alcohols as solvents, the maximum absorption rate is obtained with compounds containing 6 to 8 C atoms [13]. The percutaneous absorption can be increased to such a degree with the aid of carrier mixtures of this type that even cardiac glycosides can be given percutaneously [26,27].

Percutaneous absorption of sex hormones can be brought about by fat solvents. 17β-Estradiol, which is poorly absorbed from vegetable oil and only moderately well from water, exhibits a very high absorption from benzene solution [28].

Hydrocortisone and hydrocortisone acetate have no vasoconstrictive action in O/W emulsion, W/O emulsion, hydrocarbon base, or polyethylene glycol. On addition of tetrahydrofurfuryl alcohol and dimethylacetamide, however, they exhibit vasoconstriction comparable with that caused by the much stronger betamethasone 17-valerate and fluocinolone acetonide [29].

The results on the suitability of *lipophobic* solvents as penetrant carriers are contradictory. Propylene glycol, for example, is found to be effective in some cases, but retards the absorption of many drugs.

When combined with surface active agents, propylene glycol was found to be a suitable sorption promotor for water-soluble drugs that are absorbed transfollicularly [30]. The absorption of fluocinolone acetonide was found to be increased by the addition of propylene glycol to the base [31]. Similar experiments with hydrocortisone as the drug gave no positive result; this could, however, be due to the different solubility properties of hydrocortisone and fluocinolone acetonide, or to other factors connected with the formulation [32]. A 1% solution of 5-fluorouracil in propylene glycol is equivalent, in its clinical effectiveness against skin cancer, to a 5% preparation in the form of an ointment [33].

For a given drug in a given form of preparation, the effectiveness of each sorption promotor varies with its concentration. The effect of the sorption promotor propylene glycol at various concentrations was studied with a 0.025% fluocinolone acetonide gel having a polyethylene glycol base. The test was carried out *in vitro* with isopropyl myristate as the receptor phase. The optimum result was obtained at an addition of about 20% [34].

In the investigation of the release of the active principle and the absorption of the antihistamine diphenhydramine hydrochloride from various plastic gel bases on histamine hives, absorption was much better from polyethylene glycol than from O/W emulsion, W/O emulsion, and hydrocarbon bases [11].

The sorption-promoting action of aqueous ethanol has been studied, *inter alia*, for theophylline. An aqueous-alcoholic solution gives the same blood level in 15 minutes as is obtained only after two hours with tablets which disintegrate immediately [35]. The peroral absorption of an aqueous-alcoholic theophylline solution is roughly equivalent to the parenteral absorption after intramuscular injection [36].

One of the most extensively studied penetrants is dimethyl sulfoxide (DMSO). Following a report from the University of Oregon [37] in December 1963 that DMSO can transport a number of well known drugs through the skin and tissues of laboratory animals, investigations were started throughout the world to examine this substance as an active principle and as an adjuvant. Its toxicity on peroral, subcutaneous, and intravenous application is extremely low. Local application leads to irritation of the skin and mucous membrane but this rapidly disappears [38].

DMSO is miscible in all proportions with water, lower alcohols, aldehydes, ketones, ethers, esters, halogenated hydrocarbons, and heterocyclic and aromatic compounds. The higher homologs are mostly readily soluble [39]. Carbohydrates also dissolve readily in DMSO [40]. DMSO is a better solvent for inorganic salts than most organic solvents. In particular, it dissolves chlorides, nitrates, and salts of organic acids. Salts dissolved in DMSO are dissociated [41,42]. In the presence of ethanol, DMSO forms complexes with many organic compounds [49].

On cutaneous application, DMSO passes rapidly through the horny layer of epidermis (stratum corneum) in man and in animals [43–45]. As has been shown by histological analyses, this process does not change the structure of the skin [46]. Further penetration through the skin layers to the vessels is so fast that only a few minutes after cutaneous application of 70 to 90% DMSO solutions, a characteristic "sulfur odor" due to the formation of dimethyl sulfide occurs in the breath. DMSO can carry many drugs with it as it passes through the skin and membrane, and can thus act as a penetration carrier. The drugs are stored in the deeper layers of the stratum corneum, in some cases as deposits that can be detected for several days. Substances having molecular weights of 3000 or more cannot, however, be transported into deeper layers by DMSO. On the other hand, increased oxygen diffusion in ischemic myocardial tissue has been observed with DMSO on application of drugs that improve the oxygen supply [47]. DMSO is thus suitable above all for

[25] *E. Brode*, Arzneimittel-Forsch. *18*, 580 (1968).

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[32] *R. J. Feldman* and *H. I. Maibach*, Arch. Dermatology *94*, 649 (1966).

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[36] *M. Jørgensen* and *P. Møller*, Acta pharmacol. toxicol. (Köbenhavn) *18*, 129 (1961).

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[38] *S. Sommer* and *G. Tauberger*, Arzneimittel-Forsch. *14*, 1050 (1964).

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[40] *G. G. Gallo* and *A. Vigevani*, Tetrahedron Letters *1964*, 2839.

[41] *P. G. Sears, G. R. Lester*, and *L. R. Dawson*, J. physic. Chem. *60*, 1433 (1956).

[42] *J. E. Prue* and *P. J. Sherrington*, Trans. Faraday Soc. *57*, 1795 (1961).

[43] *S. W. Jacob* and *D. C. Wood*, Arzneimittel-Forsch. *17*, 1553 (1967).

[44] *F. Perman* and *H. F. Wolfe*, J. Allergy *38*, 299 (1966).

[45] *M. B. Sulzberger, T. A. Cortese, L. Fishman, H. S. Wiley*, and *P. S. Peyakowich*, Ann. New York Acad. Sci. *141*, 437 (1967).

[46] *A. L. Scherbel, L. J. McCormack*, and *M. J. Poppo*, Cleveland clin. Quart. *23*, 47 (1965).

[47] *J. W. Firmey, H. C. Urschel, G. A. Balla, G. J. Race, B. E. Jay, H. P. Pingree, H. L. Dormann*, and *J. T. Mallams*, Ann. New York Acad. Sci. *141*, 231 (1967).

the fast transport of low molecular weight substances into deeper skin layers, and hence into surrounding structures or into the blood stream to exercise systemic effects. It is active as a sorption promotor even at low concentrations (about 10%)[48].

The reasons for the increased penetration of membranes by the dissolved drugs is not yet known[49]. It is assumed that the penetration- and permeation-promoting action is due to the fact that DMSO is a weak base and forms complexes with various substances. The affinity of DMSO for water must also be considered as a possible factor in the promotion of penetration. The ability of DMSO to form chelates, for example, could lead to the breakdown of hydration sheaths on the cell membranes, so increasing the permeability of the membrane.

The rate-determining factor for percutaneous penetration is the stratum corneum. This thick, horny, coherent, plastic-like membrane, which consists of about 15 layers of close-packed, hornified, dead cells[50], has an extremely high resistance to the penetration of most substances, including water.

Many investigations have been carried out on the promotion of sorption by DMSO. In the case of salicylic acid it was shown that pretreatment of the skin with DMSO leads to a considerable increase in skin permeability. Aqueous salicylic acid solutions containing 20% of DMSO, on the other hand, gave poorer penetration of salicylic acid than simple aqueous solutions[51] Addition of 15% of DMSO to W/O and O/W bases, however, considerably increased the percutaneous absorption of salicylic acid (cf. Fig. 4).

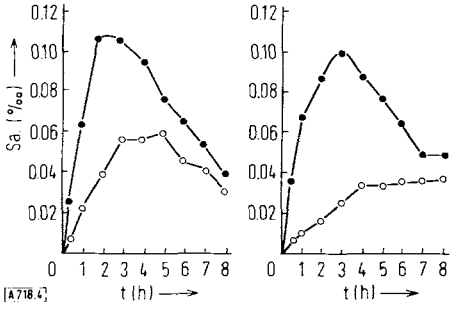


Fig. 4. Influence of DMSO on percutaneous absorption.
Left: 10% salicylic acid in an O/W cream.
Right: 10% salicylic acid in a W/O base.
• = salicylic acid (Sa) absorbed on addition of 15% of DMSO,
o = control [52].

DMSO has no effect on absorption in the application of sodium salicylate in the same bases. Practically no effect was observed on the absorption from polyethylene glycol bases[52]. The penetration of sodium salicylate, sulfadiazine sodium, Evans Blue, and heparin sodium from solutions containing 15% of DMSO, on the other hand, was considerably greater than from aqueous comparison solutions[49].

The absorption of the antiperspirant hexopyrronium bromide from 20% aqueous DMSO solution was 25 times, that of the vasoconstrictor naphazoline hydrochloride from 50% aqueous DMSO solution 50 times, and that of the corticosteroid fluocinolone acetonide from 25% aqueous DMSO solution 5 times as high as the absorption from the reference solutions[53]. These increases refer, not to the quantities per unit time, but to the total quantities that penetrated.

Whereas the penetration of the antibiotic demethylchlortetracycline hydrochloride (Declomycin) from aqueous solution takes more than three hours, penetration occurs in 20 minutes from 90%, 55 minutes from 70%, and 120 minutes from 50% DMSO solutions[54].

Figure 5 shows an interesting comparison of the effects of various solvents on the penetration of the skin by fluocinolone acetonide[25].

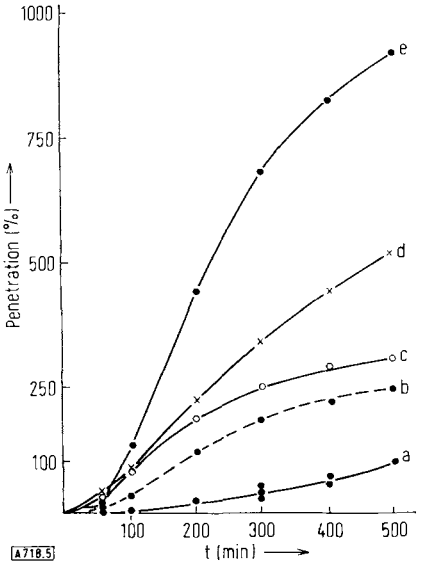


Fig. 5. Comparison of the percutaneous absorption of fluocinolone acetonide from various solvents [25]: a) Ethanol; b) tetrahydrofurfuryl alcohol; c) dimethylacetamide; d) propylene glycol; e) dimethyl sulfoxide.

Other investigations showed that DMSO has a sorption-promoting effect on the following drugs: testosterone propionate[55,61], hydrocortisone[56,57,61], triamcinolone acetonide[56], fluocinolone acetonide[57], cortisone acetate[58], 17β-estradiol[58], antitumorigenic substances such as "Cytoxan"[59] and 5-fluorouracil[60], methylene blue[41], iodine[41], iron pigments[41], hexachlorophene[62], physostigmine[63], phenylbutazone[63], local anesthetics[64], antibiotics[65], and quaternary ammonium compounds[66].

4.2. Fatty Alcohols and Esters of Fatty Acids

Many fatty alcohols and esters of fatty acids are used in dermatology as ointment bases. The most suitable base for any particular application depends on the

[48] *A. Kappert*, Schweiz. med. Wschr. *98*, 1829 (1968).

[49] *S. W. Jacob*, *M. Bischel*, and *R. J. Herschler*, Current Therap. Res. *6*, 193 (1964).

[50] *A. M. Kligman* in *W. Montagna*, and *W. C. Lobitz*: The Epidermis. Academic Press, New York 1964.

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[58] *T. I. Djan* and *D. L. Grunberg*, Ann. New York Acad. Sci. *141*, 406 (1967).

[59] *C. L. Maddock*, *M. N. Green*, and *B. L. Brown*, Cancer Res. *7*, 46 (1966).

[60] *K. W. Kitzmiller*, cited in *S. W. Jacob* and *D. C. Wood*, Arzneimittel-Forsch. *17*, 1086 (1967).

[61] *H. I. Maibach* and *R. J. Feldman*, Ann. New York Acad. Sci. *141*, 423 (1967).

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chemical and physical properties of the drug, the site of application, the depth to which the drug is to penetrate into the skin, and the condition of the skin.

The purpose of the ointment base is to bring the incorporated drug into the closest possible contact with the surface of the skin and to release it at the point of contact. The transfer of the drug depends on its solubility in the base and its partition coefficient between the base and the receptor phase, as well as on other factors.

As has been mentioned several times, the drug must be lipid-soluble as well as water-soluble. A drug will penetrate into the skin more readily if it is incorporated into lipids that can blend with the skin fats [67]. Attempts to produce greases having an affinity for skin have therefore been in progress for many years, but investigations on the effects of these greases on absorption have so far been relatively unsatisfactory. The improvement in the absorption of drugs with these substances involves gastrointestinal as well as percutaneous absorption. It is known, for example, that the absorption of drugs having low solubilities in water from suspensions in an aqueous vehicle is improved by the emulsification of a digestible oil in the preparation [68]. An example of this behavior is the good absorption of N^1-acetylated sulfisoxazole from an emulsion in which fatty oil acts as a sorption promotor [69]. The peroral absorption of griseofulvin can also be greatly increased by simultaneous administration of fats [70]. Some of the fatty alcohols and fatty acid esters in common use as sorption promotors are listed in Table 2.

Table 2. Fatty alcohols and esters of fatty acids used as sorption promotors.

Trade name	Composition
Cetiol®	Oleyl oleate
Cetiol V®	Decyl oleate
Cetiol A®	Hexyl laurate
Eutanol G®	2-Octyldodecanol
PCI products	Alkyl-branched fatty acid esters having low solidification point
Miglyol®	Mixture of triglycerides of saturated vegetable fatty acids of chain length C_8—C_{12}
Cremogen IP®	Mixture of esters of aliphatic dicarboxylic acids
Other liquid fatty acid esters	Isopropyl myristate
	Isopropyl palmitate
	Diisopropyl adipate

The mode of action of the fatty alcohol and fatty acid ester sorption promotors is not yet known. This action is assumed to be due to the good solvent properties of these substances for various drugs and above all to their miscibility with skin oils. Good spreading is also essential for close contact between the base and the skin [71]. Figure 6 shows the spreading capacity of several lipids and their influence on the permeability of the resulting lipid films to water vapor, *i.e.* on the loss of water through the skin. The sealing action of a lipid decreases with increasing spreadability.

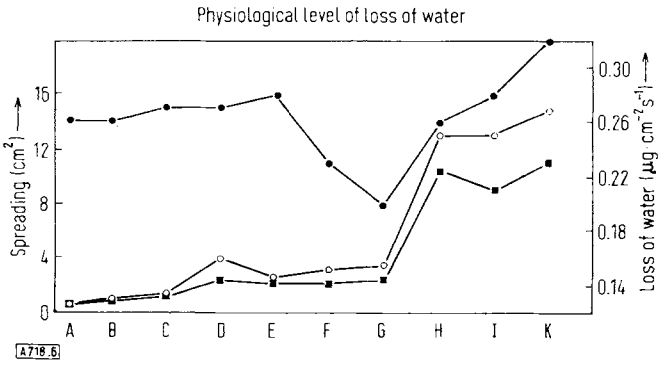


Fig. 6. Spreading capacities (■ : after 10 min, o: after 20 min, left-hand ordinate) of several lipids and their influence on the loss of water through the skin (•, right-hand ordinate). The bases plotted on the abscissa are A = partial ester, 60% C_8—C_{12}, 40% C_{18} = Witten 378 partial ester; B = castor oil, partly crosslinked, C = castor oil; D = arachis oil; E = arachis oil, partly crosslinked; F = triglyceride 60% C_{18-12}, 40% C_{18} = Softisan 378® ointment base; G = paraffin oil; H = partial ester C_8—C_{12} = Witten 812 partial ester; I = triglyceride C_8—C_{12} = Miglyol 812®; K = Pur-Cellin® oil = PCL® liquid.

Among the lipids mentioned in Figure 6, that having the greatest spreadability is Pur-Cellin® oil, which is designed to simulate the uropygial gland oil of the duck, and consists of esters of α-alkyl branched fatty acids. The branched structure of the esterified fatty acid leads to special properties, above all strong dissolving power and good wetting properties [72], as well as particularly good spreadability [73].

In investigations on the absorption of salicylic acid from various ointment bases, the best results were obtained with the triglyceride Softisan 378®, though this action is attributed to the partial fatty acid glycerides present, which act as W/O emulsifiers [74].

The fatty alcohols and fatty acids are not absorbed through the skin, since they only pass into the hornified layers but cannot pass through them. They therefore promote penetration, but not permeation.

Whereas ointment bases have different effects on the absorption of absorbable drugs, they do not in general promote sorption of non-absorbable drugs [75]. It has, however, been reported that the synthetic fats Miglyol 812® and Eitanol G® promoted the sorption of a drug that was practically non-absorbable by itself [75].

4.3. Surface Active Agents

Surface active agents (surfactants) can accelerate and increase the absorption of drugs through the skin and mucous membrane. The reason for the increase in the permeability of the tissue membrane is not yet known. It is assumed to be due to the decrease in the surface tension, the improved wetting of the skin, and the improved distribution of the drugs [76].

The surface active agents reduce the surface tension in aqueous solutions and at high concentrations also in organic solutions, until an optimum is reached at the

[67] *G. Valette*, Pharmac. J. *170*, 461 (1953).

[68] *S. E. Svenson, W. P. Delorenzo, R. Engelberg, M. Spooner*, and *L. O. Randall*, Antibiotic Med. *2*, 148 (1956).

[69] *S. Krugman* and *E. Frieden*, J. Pediat. *50*, 16 (1957).

[70] *R. G. Crounse*, J. invest. Dermatology *37*, 529 (1961).

[71] *F. Neuwald, K. E. Fetting*, and *A. Szakall*, Fette, Seifen, Anstrichmittel *64*, 465 (1962).

[72] *G. A. Nowak*, Pur-Cellin und Pur-Cellin-Oel-Dragoco.

[73] *E. K. Rideal* and *J. H. Schulman*, Nature (London) *144*, 100 (1939).

[74] *F. Gstirner* and *R. Elsner*, Arzneimittel-Forsch. *14*, 281 (1964).

[75] *H.-D. Pfau*, Dissertation, Techn. Hochschule Braunschweig, 1964.

[76] *K. Münzel* [2], p. 324.

critical micelle concentration (CMC). Above the CMC, no further decrease in the surface tension occurs. Below the CMC the surfactant molecules are in a disordered state. At the CMC, they form spherical or laminar aggregates (micelles), which consist of about 50 to 150 molecules. On incorporation of an insoluble or sparingly soluble compound into an aqueous solution of an amphiphilic compound, the practically insoluble substance becomes colloidally dispersed ("solubilized") [77]. This process is represented schematically in Fig. 7.

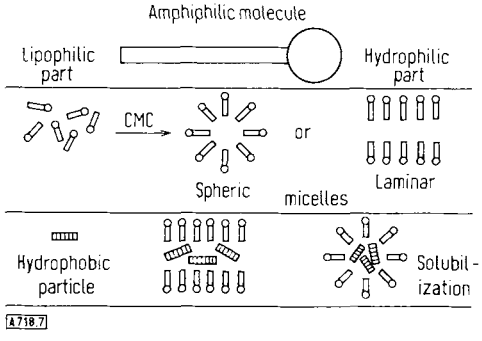


Fig. 7. Mode of action of surfactants as solubilizers [3].

An important property of surfactants is the hydrophile-lipophile balance (HLB), which is found from the saponification value (SV) and the acid value (AV) by means of eq. (3).

$$HLB = 20\ (1-SV/AV) \qquad (3)$$

The properties of the surfactants vary with their HLB values. With HLB values of 1.5–3 they are antifoam agents, 3–7 spreading agents, 3–8 W/O emulsifiers, 7–9 wetting agents, 8–18 O/W emulsifiers, 13–15 detergents, and 15–18 solubilizers.

In many cases, particularly with lipophilic drugs, the sorption-promoting action of the surfactants is undoubtedly due to the improved distribution of the drug in the micelles of the surfactant [78]. The lipid-soluble vitamins A, D, and E, for example, are absorbed much more effectively from sterile surfactant solutions than from oily solutions on parenteral application [79].

The aqueous micelle solutions may be regarded as two-phase colloidal systems, the disperse phase consisting of the colloidal micelles and the continuous phase of water. Any drug present is distributed between the two phases. The degree of partition between the disperse and the continuous phases depends on the partition coefficient K of the drug in the system in question. As free drug is eliminated from the continuous phase by absorption, part of the drug bound in the micelles is released into the continuous phase. The absorption constant in aqueous solution, k, is different from that in surfactant solution, k'. According to *Yamada et al.*, the absorption constants of drugs from surfactant solutions can be calculated as follows [80,81] [eq. (4)]:

$$k' = \frac{f_W}{f_T K + f_W} \times k \qquad (4)$$

where f_W = volume fraction of the water phase = V_W/V; V_W = volume of the water phase; V = total volume of the micelle solution; f_T = volume fraction of the micelle phase = V_T/V; V_T = volume of the surfactant; K = partition coefficient of the drug between water and micelles.

In addition to the decrease in the surface tension and the solubilization the improved wetting is also important to the sorption-promoting action of surfactants. On the one hand the contact area between the drug and the surface of the absorbing organ is increased, while on the other, surfactants improve the wettability of the surfaces of solid particles, and so accelerate dissolution in the aqueous digestive juices on peroral medication. This leads to an increased release of active principle. As an example, Figure 8 shows the influence of a solubilizer on the rate of dissolution of phenacetin [82].

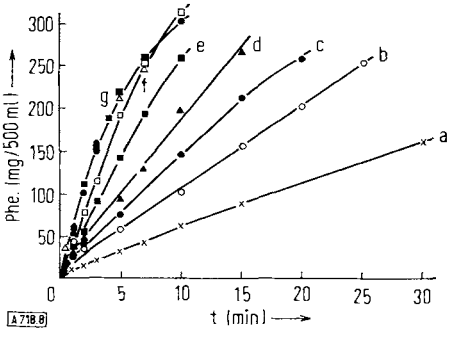


Fig. 8. Influence of the solubilizer Tween 80® on the rate of dissolution of phenacetin having a particle diameter of between 0.21 and 0.3 mm in 0.1 N HCl [82].

Ordinate: Phenacetin (Phe) dissolved. Tween 80 added: a = 0%, b = 0.001%, c = 0.002%, d = 0.005%, e = 0.01%, f = 0.02%, g = 0.05%, 0.1 and 0.2%.

Thus the addition of hydrophilizing agents to tablet preparations [83] leads indirectly to improved absorption since the surfactants used not only lead, as a result of the improved wetting, to faster dissolution and hence to faster release of the drug from the preparation, but can also give better distribution. Furthermore, anionic surfactants probably also influence the cell membranes themselves, with the result that absorption anomalies occur (cf. Section 4.3.2) [79].

It must, however, be mentioned that the three types of surfactants (nonionic, cationic, and anionic) cannot all be considered in the same way as sorption promotors for a given drug. The release of the drug and the absorption may be, not merely unaffected, but actually reduced by a surfactant if the drug reacts with the surfactant to form complexes, *e.g.* of anionic drugs with cationic surfactants or *vice versa*. Incompatibilities of this nature are extremely common [79], so that careful incompatibility studies are always necessary.

However, adverse effects due to interactions between the drug and the surfactant depend not only on the chemical constitutions of the drug and of the surfactant, but also on the concentration of the surfactant. It has been found that surface active agents in general have little or no influence on the effectiveness of drugs below a limiting association con-

[77] *J. W. McBain*: Colloid Science. D. C. Heath & Co., Boston 1950, p. 264.

[78] *W. Saski* and *S. G. Shah*, J. pharmac. Sci. *54*, 71 (1965).

[79] *K. Münzel*, J. mond. Pharmac. (La Haye) *3*, 255 (1967).

[80] *H. Yamada* and *R. Yamamoto*, Chem. pharmac. Bull. (Tokyo) *13*, 1279 (1965).

[81] *H. Yamada*, *T. Ichihashi*, and *F. Kogishi*, Chem. pharmac. Bull. (Tokyo) *14*, 786 (1966).

[82] *P. Finholt* and *S. Solvang*, J. pharmac. Sci. *57*, 1322 (1968).

[83] *W. A. Ritschel*: Die Tablette. Editio Cantor. Aulendorf 1966, p. 117.

centration; from this limiting association concentration up to the CMC they can have a potentiating action, while above the CMC they often reduce the effectiveness of the drug[78].

The dependence of the interaction on the CMC is illustrated in Figure 9 for the case of hexachlorophene and Tween 61® [3]. The incompatibility check in this case was carried out by a microbiological test, as is usual for drugs having an antibacterial action[84]. Addition of Tween 61® up to the CMC had no influence on the size of the inhibition zone in the agar diffusion test with *Staphylococcus aureus* SG 511. Above the CMC there is a steady decrease in activity until the drug becomes completely inactive.

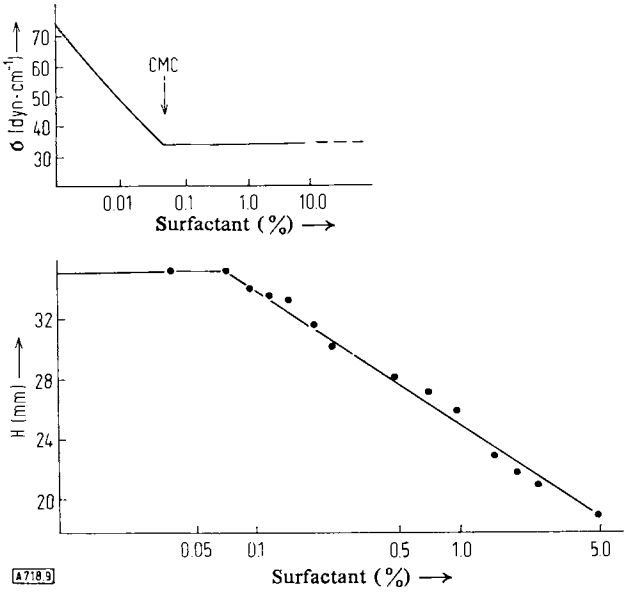


Fig. 9. Influence of Tween 61® on the size of the inhibition zone for hexachlorophene [3].

Top: The CMC of Tween 61® is determined by measurement of the surface tension, and is 0.075%.

Bottom: Addition of Tween 61® in a concentration higher than the CMC leads to a concentration-dependent decrease in activity. Ordinate: Diameter of the inhibition zone (H).

Some surfactants used as sorption promotors are listed in Table 3.

4.3.1. Nonionic Surfactants

Nonionic surfactants include derivatives of sorbitol, sucrose, and polyethylene oxide[85] (see Table 3).

Reports on the influence of nonionic surfactants on absorption are very numerous and often contradictory. The penetration-promoting action of these substances appears in general to be weaker than that of anionic surfactants. The many reported failures to observe sorption promotion and the decreases in absorption are probably mostly due to interactions between the nonionic surfactants and the drugs or to occlusion of the drug in micelles at surfactant concentrations above the CMC. The causes of the penetration-promoting action of nonionic surfactants have been studied in detail by *Levy*[86].

[84] *W. A. Ritschel*, Arzneimittel-Forsch. *18*, 142 (1968).

[85] *W. Drössler* and *R. Voigt*, Pharmazie *22*, 669 (1967).

[86] *G. Levy* in: Prescription Pharmacy. Lippincott, Philadelphia, Pa., 1963, p. 66.

Table 3. Surfactants used as sorption promotors.

Trade name	Composition
Nonionic surfactants	
Span 20	Sorbitan monolaurate
Span 40	Sorbitan monopalmitate [a]
Span 60	Sorbitan monostearate
Span 65	Sorbitan tristearate
Span 80	Sorbitan monooleate
Span 85	Sorbitan trioleate
Tween 20	Polyoxyethylene-(20)-sorbitan monolaurate
Tween 21	Polyoxyethylene-(4)-sorbitan monolaurate
Tween 40	Polyoxyethylene-(20)-sorbitan monopalmitate
Tween 60	Polyoxyethylene-(20)-sorbitan monostearate
Tween 61	Polyoxyethylene-(4)-sorbitan monostearate
Tween 65	Polyoxyethylene-(20)-sorbitan tristearate
Tween 80	Polyoxyethylene-(20)-sorbitan monooleate
Tween 81	Polyoxyethylene-(5)-sorbitan monooleate
Tween 85	Polyoxyethylene-(20)-sorbitan trioleate
G-1702	Polyoxyethylene-sorbitol-beeswax derivative
G-1425	Polyoxyethylene-sorbitol-lanolin derivative
G-1256	Polyoxyethylene-sorbitol-tall oil ester
G-1096	Polyoxyethylene-sorbitol hexaoleate
G-1144	Polyoxyethylene-sorbitol oleate laurate
G-1471	Polyoxyethylene-sorbitol-lanolin derivative
Brij 30	Polyoxyethylene lauryl ether
Brij 35	
Brij 52	
Brij 56	Polyoxyethylene cetyl ether
Brij 58	
Brij 72	
Brij 76	Polyoxyethylene stearyl ether
Brij 78	
Brij 92	
Brij 96	Polyoxyethylene oleyl ether
Brij 98	
Cremophor A solid	Polyoxyethylene stearyl ether
Cremophor A liquid	Polyoxyethylene oleyl ether
Myrj 45	Polyoxyethylene stearate
Mryj 49	Polyoxyethylene stearate
Myrj 51	Polyoxyethylene stearate
Myrj 52	Polyoxyethylene stearate
Myrj 53	Polyoxyethylene stearate
Myrj 59	Polyoxyethylene stearate
Cremophor AP solid	Polyoxyethylene-400-monostearate
Cremophor AP liquid	Polyoxyethylene-400-monooleate
Cremophor EL	Polyoxyethylene ricinoleate
	Saccharose distearate
	Saccharose dioleate
	Saccharose dipalmitate
	Saccharose monostearate
	Saccharose monooleate
	Saccharose monopalmitate
	Saccharose monomyristate
	Saccharose monolaurate
Anionic surfactants	
Texapon Z	Sodium lauryl sulfate
Aerosol OT	Sodium dioctyl sulfosuccinate
Lanette E	Sodium cetyl stearate sulfate
Cationic surfactants	
CPC	Cetylpyridinium chloride
CTAB	Cetyltrimethylammonium bromide
	Benzalkonium chloride
	Benzethonium chloride

[a] Sorbitan is monoanhydrosorbitol ($C_6H_8O(OH)_4$).

A relatively simple method for the study of the effects of surfactants on absorption is the addition of drugs and adjuvants to aquarium water, using goldfish as subjects. This system was used to test the sorption-promoting action of Tween 80® on alcohols and pentobarbital or secobarbital sodium[87]. The quantities of the various alcohols absorbed

[87] *G. Levy, K. E. Miller*, and *R. H. Reuning*, J. pharmac. Sci. *55*, 394 (1966).

did not change appreciably. The absorption of the barbiturate was considerably faster with low concentrations of Tween 80®, but was much slower with higher concentrations. This is probably due on the one hand to a direct inhibiting action of the surfactant on the lipid membrane, and on the other to the formation of a simple but more readily absorbed non-micellar complex between the barbiturate and the Tween 80® [87].

The influence of nonionic surfactants on peroral absorption has been investigated for the case of spironolactone; much higher blood concentrations were found on addition of Tween 80® than when ordinary tablets were used [88,89].

Increased enteral absorption of vitamin B_{12} in rats was obtained with Tween 80® and Tween 85® [90].

Widely differing results have been reported for the use of nonionic surfactants in rectal absorption. Whereas *e.g.* nonionic surfactants in aqueous solution do not improve the rectal absorption of sulfonamides, since the sulfonamides are probably largely occluded in micelles [91], faster absorption was observed with Tween 61® in the investigation of the rectal absorption of salicylic acid from various suppository bases [92,93]. In the investigation of the sorption-promoting action of nonionic surfactants on the absorption of aminophylline and ephedrine from theobroma oil suppositories, it was found that the transfer of drug in the dialysis experiment can be increased by surfactants (having an HLB of 11—14 in the case of aminophylline, and having an HLB of 9 in the case of ephedrine). It is probably impossible to calculate the optimum sorption promotion in advance, and the appropriate nonionic surfactant and its optimum concentration must be determined experimentally for each drug in each base [94]. It has been shown in the case of barbiturates that the rectal absorption is also increased by the addition of nonionic surfactants as penetrant carriers [95].

Numerous reports on percutaneous absorption under the influence of nonionic substances have also been published. Tween 60® considerably improved absorption from a 6% salicylic acid/vaseline ointment on addition in concentrations of from 5 to 10%, and even a 1% addition led to a significant improvement. On the other hand, no appreciable change was observed with sodium salicylate in the same base [96].

It has been found that after treatment for four days with ointment bases consisting of vaseline containing 10% of Span 85®, Tween 85®, or Brij 96®, the phosphorus content of the epidermal phospholipids was increased by up to 90% [97], indicating that the nonionic surfactants influence the membrane structure.

4.3.2. Anionic Surfactants

The anionic surfactants (see Table 3) should be the most effective of the three types as sorption promotors. In addition to the decrease in the surface tension, the improvement of the solubilization, and the increase in wetting, these substances have the further property of being able to influence the cell membrane directly. This leads to absorption anomalies, which are due to complex formation between the sulfonates and sulfates and the calcium and magnesium ions on the intestinal wall.

The view that anionic surfactants are stronger sorption promotors than other surfactants is confirmed by the observation that nickel salts compounded with anionic substances cause eczema, whereas nickel salts combined with nonionic or cationic substances do not. This could be due to an acanthotic effect [modification of the prickle cell layer (stratum germinativum) of the skin] or to denaturation of the epidermal proteins by the anionic surfactants, allowing the nickel salt to penetrate the skin and cause sensitization [98].

Among anionic substances, the laurate ion is reported to have the greatest penetration and the strongest sorption-promoting action [99]. The most important anionic surfactants for pharmaceutical use are sodium lauryl sulfate and sodium dioctyl sulfosuccinate. In an investigation on the enteral absorption of the dye phenol red with anionic, cationic, and nonionic surfactants, only sodium lauryl sulfate and sodium dioctyl sulfosuccinate were found to have a sorption-promoting action [100].

Strophanthin-G can be absorbed both enterally [101] and rectally with sodium lauryl sulfate as a sorption promotor. Strophanthin in a dose of 1 mg/kg, which has no effect on guinea pigs when given rectally, actually exhibits a toxic action on addition of sodium lauryl sulfate [102].

Considerably higher blood concentrations of the following drugs are found on addition of sodium lauryl sulfate to preparations for rectal application: penicillin-G sodium [103,104], streptomycin [104], sodium PAS [105], and chloramphenicol [106]. On addition of sodium lauryl sulfate to Witepsol H 15® suppository base, penicillin-G blood concentrations as high as those observed after intramuscular injection are found in rabbits [107].

On local application of radioactively labeled sodium iodide in hydrophilic ointment USP, the optimum release of the active principle was obtained with the anionic surfactant Sipon ES® (ethoxylated sodium lauryl sulfate) at a concentration of 2%. The release of the drug was retarded when the surfactant concentration was increased [108].

4.3.3. Cationic Surfactants

The cationic surfactants (see Table 3) are mostly quaternary ammonium compounds, which cannot be regarded as inert adjuvants, since they have a more or less pronounced antibacterial action of their own.

[88] *C. L. Gantt, N. Gochman,* and *J. M. Dyniewicz,* Lancet *1*, 486 (1961).

[89] *G. Bauer, P. Rieckmann,* and *W. Schaumann,* Arzneimittel-Forsch. *12*, 487 (1962).

[90] *K. O. Kuda, E. Duran,* and *B. F. Chow,* Proc. Soc. exp. Biol. Med. *103*, 588 (1960).

[91] *K. Kakemi, T. Arita,* and *S. Muranishi,* Chem. pharmac. Bull. (Tokyo) *13*, 976 (1965).

[92] *W. Lowenthal* and *J. F. Borzelleca,* J. pharmac. Sci. *54*, 1790 (1965).

[93] *W. Lowenthal* and *J. F. Borzelleca,* Toxicol. appl. Pharmacol. *8*, 347 (1966).

[94] *J. M. Plaxco, C. B. Free,* and *C. R. Rowland,* J. pharmac. Sci. *56*, 809 (1967).

[95] *J. H. Fincher, D. N. Entrekin,* and *C. W. Hartman,* J. pharmac. Sci. *55*, 23 (1966).

[96] *J. M. Stelzer, J. L. Colaizzi,* and *P. J. Wurdack,* J. pharmac. Sci. *57*, 1732 (1968).

[97] *M. Mezei* and *R. W. Sager,* J. pharmac. Sci. *56*, 12 (1967).

[98] *L. J. Vinson* and *B. R. Choman,* J. Soc. Cosmetic Chemists *11*, 127 (1960).

[99] *F. R. Bettley,* Brit. J. Dermatol. *73*, 448 (1963).

[100] *P. M. Liish* and *J. H. Weikel,* Toxicol. appl. Pharmacol. *1*, 501 (1959).

[101] *D. Krause,* Arzneimittel-Forsch. *7*, 742 (1955).

[102] *V. Eybl,* Pharmazie *12*, 30 (1957).

[103] *O. Gundersen,* Dissertation, Eidgen. Techn. Hochschule Zürich, 1948.

[104] *L. C. Vargas* and *A. B. Izquierdo,* Mitt. dtsch. pharm. Ges. *31*, 153 (1961).

[105] *W. Hennig* in: Arzneiformung, Probleme und Entwicklungen. Deutscher Apotheken-Verlag, Stuttgart 1964, p. 82ff.

[106] *L. Adam, Z. Csath-Stingel, J. Papp, M. Gaspar,* and *L. Domokos,* Bev. Méd. *13*, 356 (1967).

[107] *K. Backe-Hansen,* Arch. Pharmacog. Chem. *64*, 219 (1957).

[108] *K. C. Patel, G. S. Banker,* and *H. G. DeKay,* J. pharmac. Sci. *50*, 300 (1961).

The surface of the skin may be regarded as an ion-exchange membrane, which can adsorb ions on its amphoteric protein surface [109]. Under normal conditions the surface of the skin is negatively charged, so that positively charged ions can be readily adsorbed [110, 111]. This is true of quaternary ammonium compounds, which are generally readily adsorbed, but which penetrate into the skin only if it is broken [*i.e.* when the barrier layer (the stratum corneum) is damaged], or if the quaternary ammonium compounds form absorbable complexes with other substances, or if fat solvents are present [112].

Like other surfactants, quaternary ammonium compounds make wetting easier and allow more intimate contact with the surface by lowering the surface tension. Owing to their high pK values, their strong dissociation, even in alkaline media, and their low lipophilicity, they can form unabsorbable complexes with mucin, an acidic polysaccharide of the stomach and intestine [113]. Their gastrointestinal absorption is consequently often uneven and low. The absorption of quaternary ammonium compounds used for medicinal purposes can, however, be increased by the addition of a physiologically inert quaternary ammonium compound as an adjuvant, since these substances facilitate the absorption of the drug by competitive complex formation with mucin [114].

According to *Levine* [115], quaternary ammonium compounds are absorbed, not only by diffusion, but also because they are partly bonded to an endogenous anion and so transported through the intestinal wall as an adsorbable neutral complex.

Kakemi et al. [116] investigated the effect of surface active sorption promotors on the absorption of sulfisoxazole from theobroma oil suppositories in rabbits. The nonionic surfactant Tween 60®, the anionic sodium lauryl sulfate, and the cationic cetyltrimethylammonium bromide (CTAB) all gave increased release of the drug with increasing surfactant concentration *in vitro*. The highest values were obtained with CTAB. *In vivo* experiments showed that higher blood concentrations could be obtained with all three types of surfactants, but optimum values were obtained at only one particular concentration in each case, and further increases in the surfactant concentration led to a decrease in absorption.

4.3.4. Saponins

The possibility of sorption promotion was first recognized when it was observed [117] that the absorption of glucose from the digestive tract is accelerated by saponins. About 30 years ago, saponins were the only sorption promotors used in pharmacy [118]. It was found that the action of saponins (which differ considerably according to their source) improved the absorption of drugs given at the same time. Thus 0.1% of saponin was added to cod-liver oil emulsions [119].

On peroral administration of calcium, the calcium level in the blood could be increased by 41% by addition of saponin [119] Saponins have also been added to analgesic combinations. The use of saponins as sorption promotors has now almost entirely ceased because of their hemolytic action, their local irritant action, and the fact that they can lead to an accumulation of water in the lungs.

The saponins exist in aqueous solution as colloids, and this may explain their generally poor absorbability on peroral application. With the saponin aescin, for example, micelle formation occurs at a concentration of only 10^{-4} moles/l [120]. The basis of the sorption-promoting action of saponins is not yet known. The decrease in the surface tension and the improved wetting of drugs administered at the same time are undoubtedly only part of the story. Investigations on erythrocytes indicated that the membrane of the erythrocytes which is normally permeable practically only to anions, also becomes permeable to cations under the action of saponins. This leads to hemolysis. The antiedemic action of saponins is due to the fact that they mobilize the protein layer in the capillary wall, and so increase the permeability of the capillaries.

4.4. Enzymes

4.4.1. Hyaluronidase

Hyaluronidase is chemically not a uniform enzyme, but an enzyme complex [121]. It hydrolyzes hyaluronic acid, a component of the mucoprotein base substance or of the binding agents in the intercellular spaces of various tissues; this leads to a decrease in the viscosity, and the tissues consequently become more permeable to liquids.

The use of hyaluronidase as a sorption promotor is based on the observation by *Duran-Reynalds* at the Rockefeller Institute, New York, in 1928, that dye solutions injected together with hyaluronidase spread out more rapidly and over a greater distance in the tissue than in the absence of hyaluronidase. Because of this effect, the hyaluronidase is also known as a spreading factor.

Hyaluronidase is currently extracted industrially from the testes of various animals. It is used as a sorption promotor, as an additive to decrease discomfort due

[109] *B. Idson*, J. cosmet. Chem. *18*, 91 (1967).

[110] *J. J. Parran* and *R. E. Brinkmann*, J. invest. Dermatology *45*, 89 (1965).

[111] *W. A. Ritschel*, Fortschr. Med. *86*, 828 (1968).

[112] *I. H. Blank*, *E. Gould*, and *A. Theobald*, J. invest. Dermatology *42*, 363 (1964).

[113] *R. D. Levine*, *M. R. Blair*, and *B. B. Clark*, J. Pharmacol. exp. Therapeut. *114*, 78 (1959).

[114] *C. J. Cavallito* and *T. B. O'Dell*, J. Amer. pharmac. Assoc., sci. Edit. *47*, 169 (1958).

[115] *R. R. Levine*, Arzneimittel-Forsch. *16*, 1373 (1966).

[116] *K. Kakemi*, *H. Sezaki*, *S. Muranishi*, and *H. Matsui*, Chem. pharmac. Bull. (Tokyo) *15*, 172 (1967).

[117] *F. Lasch* and *S. Brügel*, Naunyn-Schmiedebergs Arch. exp. Pathol. Pharmakol. *116*, 7 (1926).

[118] *F. O. W. Meyer*, Pharmaz. Ztg. *80*, 329 (1935).

[119] *F. O. W. Meyer*, Dtsch. Apotheker-Ztg. *102*, 107 (1962).

[120] *G. Orzechowski*, Z. ärztl. Fortbildung *50*, 1 (1961).

[121] Medizin. Mitt. Schering *12*, 1 (1951).

to subcutaneous and intramuscular injections, for the absorption of excess fluids and blood in tissues, and to increase the effectiveness of local anesthetics [122].

Numerous articles on sorption promotion by hyaluronidase in ointment bases have been published. Increased release of the antibiotics penicillin-G, dihydrostreptomycin, tetracycline, chlortetracycline, hydroxytetracycline, and chloramphenicol was observed *in vitro* when hyaluronidase was added to the anhydrous ointment bases [123].

The investigation of the influence of hyaluronidase on rectal absorption is also interesting. The absorption of antibiotics from theobroma oil suppositories is considerably improved by the addition of hyaluronidase. For example, the absorption maximum for chloramphenicol is reached in less than an hour, and the blood concentration is doubled [124].

Some heparinoids act in the same way as hyaluronidase. The heparinoid sodium polyethylenesulfonate, for example, gives a 20—25% increase in the rate of absorption of radioiodide on percutaneous application [125]. The heparinoid Bayer 5000 HDB-E (sodium salt of a polysaccharide sulfonic acid) can increase the absorption of salicylic acid from the monosalicylate of ethylene glycol to a much greater degree than dimethyl sulfoxide.

4.4.2. Chymotrypsin

According to reports in the literature, chymotrypsin can increase the quantities of penicillin [126] and of tetracycline [127] absorbed on peroral application.

4.5. Complexing Agents

Sorption promotors from the group of complexing agents include ethylenediaminetetraacetic acid (EDTA), disodium hydrogen phosphate, sodium metaphosphate, and citric acid. It is thought that these substances form complexes with the calcium and magnesium ions that seal the pores of the mucous membrane in the intestinal wall, and that this withdrawal of the alkaline earth metal ions increases the general permeability of the epithelium of the mucous membrane. Absorption can be increased by a factor of up to 10 by the use of EDTA as a sorption promotor. The increase in absorption due to EDTA, citric acid, and sodium metaphosphate has been investigated for tetracycline [128] and heparin [129].

The increase in the antibacterial activity of benzalkonium chloride by EDTA is also due to an increase in the permeability of the cell membranes as a result of complex formation with the bivalent metals of the membrane. The positively charged benzalkonium ions can thus become attached to the free sites on the membrane [130].

4.6. Carbohydrates

Some carbohydrates and amino sugars, particularly sorbitol, and glucosamine, are reported to have sorption-promoting properties. It has been found, for example, that the absorption of vitamin B_{12} is greatly increased, both in young and in old patients, when the orally active B_{12} preparations contain sorbitol; moreover, the B_{12} concentrations reached are higher [131, 132]. Sorbitol can also increase the absorption of vitamin B_1 [133] as well as of calcium, strontium, and iron [134].

Glucosamine was initially described as a sorption promotor for tetracycline but further checks failed to confirm this report [135]. On the other hand, a sorption-promoting action due to glucosamine has been observed with sodium salicylate [136].

5. Conclusion

Many individual observations on the promotion of the penetration of various drugs have now been reported. On the bases of these results, it is already possible to deduce certain rules and to draw conclusions concerning the mode of action of sorption promotors. Owing to the great differences between various drugs and the forms in which they are applied, it is impossible to find a universal sorption promotor. It is therefore necessary in drug research to carry out biopharmaceutical studies for each drug and for each preparation form into which it is to be developed, in order to check whether a given adjuvant is suitable for use as a sorption promotor. The thoughtless use of adjuvants must be warned against, since on the one hand, uncontrolled high absorption may increase the toxicity of the drug, while on the other, interaction with the adjuvant could weaken or nullify the action of the drug. Two drug preparations from the same manufacturer, and containing the same drug in the same dose, will not necessarily have the same action, even if the chemically determined contents of the active principle are the same.

Received: December 10, 1968 [A 718 IE]
German version: Angew. Chem. *81*, 757 (1969)
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Transfer Ribonucleic Acids[1]

By H. G. Zachau[*]

Transfer ribonucleic acids (tRNAs) [2] *occur in all living organisms. In biological protein synthesis they accept activated amino acids which are then transferred to growing peptide chains. With molecular weights lying between 25000 and 30000, tRNAs are easily within the reach of today's physical, chemical, and biochemical methods. The primary structures of several tRNAs as well as some relationships between structure and function have been elucidated. Three-dimensional structure, specificity, and mechanism of action are the subjects of present research efforts.*

1. Introduction

The study of transfer ribonucleic acids began with theoretical considerations. Out of the "one-gene – one-enzyme" hypothesis was developed, in the 50's, the sequence hypothesis: the sequence of nucleotides in deoxyribonucleic acid determines the sequence of amino acids in a protein; the nucleotide sequence is translated "colinearly" into the amino acid sequence. At that time practically nothing was known about the mechanism of biological protein synthesis, but one had to assume that amino acids interact specifically with nucleotide sequences, are arranged along them, and are finally joined to form proteins.

Is the binding specificity of amino acids to the nucleic acid template determined by a specific charge pattern or through hydrophobic regions of the nucleotides? Neither suggestion is plausible when viewed from the structural and chemical properties of the molecules involved. Nucleic acids, however, do have a specific hydrogen bond pattern. Therefore *Crick*, in 1955, postulated 20 small "adaptor" nucleic acids to which the 20 amino acids are bound in covalent, high-energy bonds by 20 different enzymes. The amino-acid carrying adaptor molecules would then interact with specific nucleotide sequences of the template through H bonds [3]. In the following years RNA fractions were found [6,7], after several indications of their existence [4,5], which bound amino acids covalently and had all the other properties of *Crick*'s adaptor molecules. The fractions were originally called sRNA (soluble RNA) until the name tRNA (transfer RNA) became established. After the solution of the genetic code and the elucidation of several tRNA sequences, *Crick* refined the adaptor hypothesis (Fig.1) further. Today, as we shall see, it has been proved at least in principle.

tRNA has been isolated from animals, plants, and numerous microorganisms. In all cases the molecular

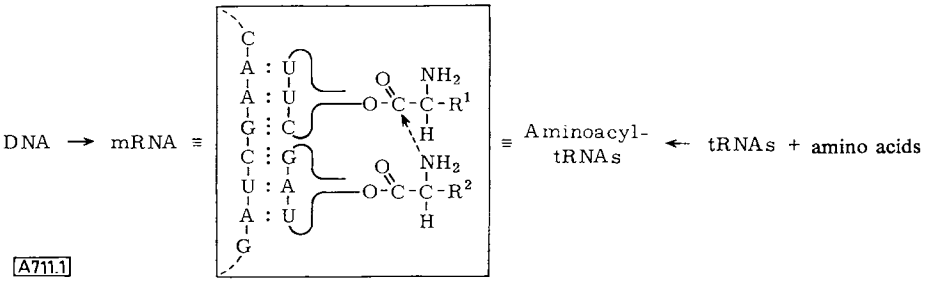


Fig. 1. Schematic representation of the adaptor hypothesis. The aminoacyl-tRNAs are arranged on the mRNA such that the amino acids are linked in the order determined by the mRNA and thus ultimately by the DNA.

weights of the nucleic acids have been between 25000 and 30000, corresponding to chain lengths of 75–85 nucleotides. Specific tRNAs, such as $tRNA^{Ala}_{yeast}$ or

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[1] Parts of this paper were delivered as the Richard Kuhn Memorial Lecture at the General Meeting of the Gesellschaft Deutscher Chemiker at Hamburg in September 1969.

[2] Abbreviations used according to IUPAC-IUB convention: tRNA = transfer ribonucleic acid; $tRNA_{yeast}$ = mixture of tRNAs from yeast; $tRNA^{Phe}$ = phenylalanine specific tRNA; Phe-tRNA = tRNA esterified ("charged") with Phe; mRNA = messenger RNA; DNA = deoxyribonucleic acid; U = uridine; A = adenosine; C = cytidine; G = guanosine; pA = 5'-adenylic acid; Ap or A- = 3'-adenylic acid; $m^{2'}G$ = 2'-*O*-methyl guanosine; m^7G = 7-methyl guanosine; m^2_2G = *N*(2)-dimethyl guanosine; other methylated nucleosides are abbreviated analogously; abbreviations of other odd nucleosides are given with Fig. 2; p or – signifies phosphate; RNase = ribonuclease; DEAE = diethylaminoethyl; fMet = *N*-formyl methionine.

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$tRNA^{Ser}_{yeast}$, were isolated from the mixture of tRNAs obtained from one organism and were found to differ structurally from one another and from the corresponding tRNAs of other organisms ($tRNA^{Ala}_{coli}$, $tRNA^{Ser}_{coli}$). The enzymes postulated by *Crick* were also found. These are the aminoacyl tRNA synthetases which catalyze the reactions

amino acid + ATP $\rightleftharpoons$ amino acyl-AMP + PP_i

and

amino acyl-AMP + tRNA $\rightleftharpoons$ amino acyl-tRNA + AMP.

Several synthetases have been purified. The tRNA-bound amino acids are transferred to the growing peptide chain on the messenger RNA/ribosome complex. (For literature on protein synthesis and genetic code see [8,9]; summary [10].)

Since only a small portion of the literature concerning structure and function of tRNAs will be cited here, the reader is referred to other sources. Isolation and fractionation of tRNAs was last reviewed 5 to 6 years ago [11,12]. More recent collections containing the most important methods are available [13–15]. Physical properties [16] and biological specificity [17,18] of tRNA have been reviewed, as have some aspects of sequence analysis and primary structure [19–23]. Mention should also be made of reviews on enzymatic methylation [24], odd nucleotides [25], and amino acid esters [26] of tRNA. Recent advances in tRNA research may be found in two Symposium volumes [9,27]. In general, if there are several publications pertaining to a specific problem, only the most recent one will be cited.

2. Isolation of Pure tRNAs

Pure compounds are needed for much of the chemical and biochemical research on tRNA. The "soluble RNA" fraction isolated from cells contains more than 20 different tRNAs as well as several other RNA species of low molecular weight. Although a few tRNAs are readily isolable from this mixture, the purification of most tRNAs is time consuming. Countercurrent distribution was the only effective method of separation [28–30] in the early days of tRNA research, and it is still the best method when larger quantities of tRNA have to be fractionated. In recent years partition, ion exchange, and adsorption chromatography, as well as combinations of these methods, have proved useful in the purification of specific tRNAs.

The principles underlying separation by any of the above methods are not fully understood; it is not known which structural characteristics of tRNAs are the basis of the separation. Chain length and nucleoside composition of $tRNA^{Ala}_{yeast}$, which travels slowly on countercurrent separation, are only slightly different from those of $tRNA^{Tyr}_{yeast}$ and $tRNA^{Ser}_{yeast}$, both of which travel with the organic phase. One could postulate that remnants of three-dimensional structure, which tRNAs perhaps still have in organic solution, are responsible for the separation. But relevant experimental data are not available. Three-dimensional structure is definitely involved in the chromatography of tRNAs on basic ion exchangers. At elevated temperatures tRNAs are eluted later, *i.e.* by higher salt concentrations than are needed at room temperature [31]. The simplest explanation for this phenomenon is that the tRNA molecules are partially unfolded at higher temperatures, exposing more phosphate groups for interaction with the ion exchanger. Since separation is particularly effective in the presence of urea or other agents that weaken internucleotide interactions [32], it is not possible that the original three-dimensional structure of tRNA is the determining factor. A more likely factor is the different amount of residual internucleotide interactions under the conditions of countercurrent distribution or chromatography; some tRNAs retain more of their three-dimensional structure than do others.

Hydrophobic side chains on one nucleotide of a tRNA, such as the isopentenyl group of $tRNA^{Ser}_{yeast}$ [33] $tRNA^{Tyr}_{yeast}$ [34], or $tRNA^{Tyr}_{coli}$ [35], are partially re-

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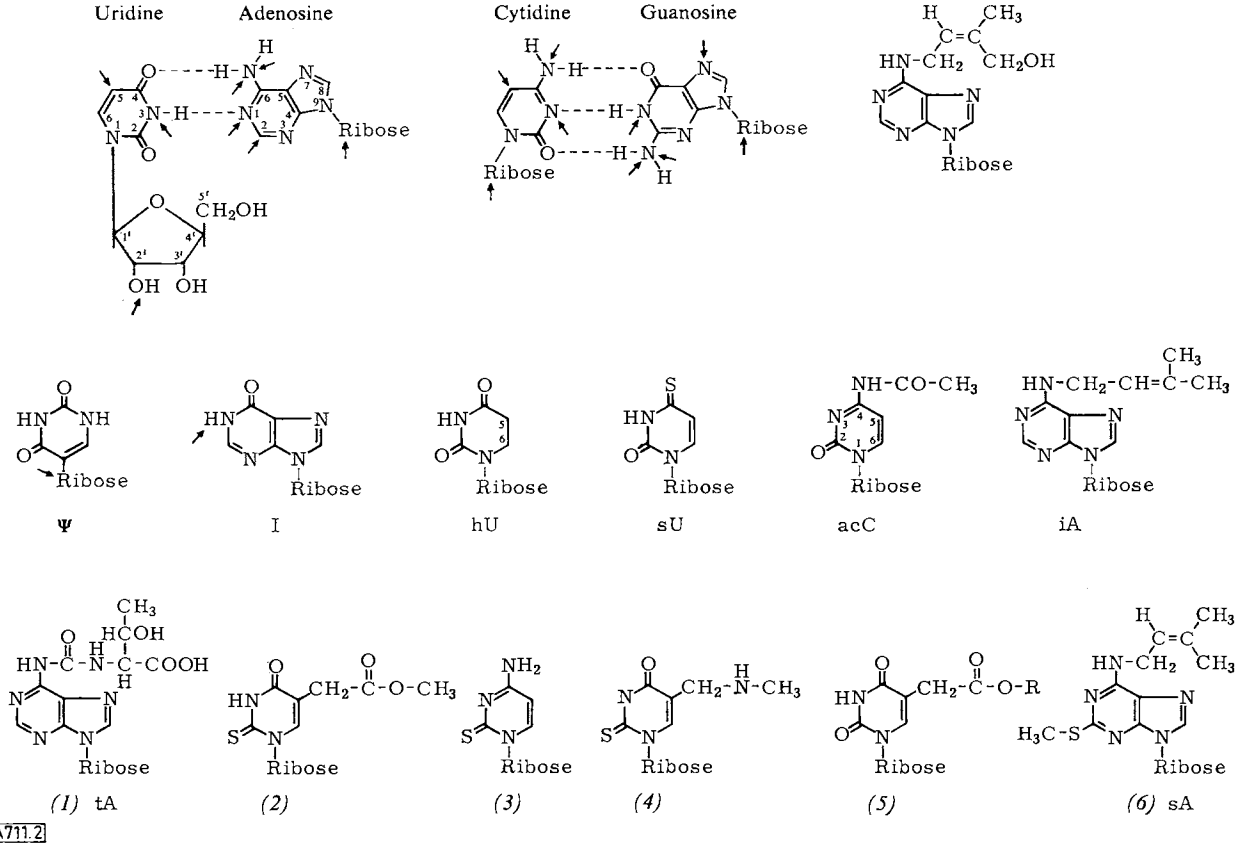
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sponsible for the molecules traveling preferentially with the upper phase. The hydrophobic base Y^+, whose structure is still unknown, has a similar effect in $tRNA^{Phe}_{yeast}$. The effect can be clearly demonstrated in this case since Y^+ can be excised from this tRNA with acid, without breaking the nucleic acid chain or drastically changing its three-dimensional structure [36]. The new product, called $tRNA^{Phe}_{HCl}$, tends to stay more in the aqueous phase during countercurrent distribution. $tRNA^{Phe}_{HCl}$ is also retained less on benzoylated DEAE cellulose [37], whose operating principle is based to a great extent on hydrophobic interactions, than is $tRNA^{Phe}$.

It is surprising that groups which are small in comparison to the whole molecule have such a profound effect on the properties of tRNAs. The findings may be explained by the fact that the hydrophobic groups are localized at an exposed part of an otherwise fairly compact molecule. Y^+ as well as the isopentenyl group are found in the anticodon regions of the tRNAs. The 3′-terminal –C–C–A sequence and tRNA-bound amino acids, which must lie on the surface of the molecule, influence the properties of tRNAs. $tRNA^{Ser}_{yeast}$ with a 3′-terminal –C–C–A migrates further in countercurrent distribution than does the same tRNA with terminal –C–C [38]. Tyr-$tRNA^{Tyr}$ can be separated from free $tRNA^{Tyr}$ by chromatography [39], and the substitution of a tRNA-bound amino acid by an aromatic group (such as phenoxyacetyl) facilitates the separation [40] of the charged tRNA from the other (uncharged) tRNAs.

3. Odd Nucleosides and Biosynthesis of tRNA

Besides the nucleosides A, G, U, and C, found in all RNAs, tRNAs contain more than thirty different odd nucleosides. A few odd nucleosides have also been found in the RNA of ribosomes. Fig. 2



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Fig. 2. Odd nucleosides found in RNA. The arrows indicate positions in which methyl group substitutions have been found. The structures of the nucleosides in the bottom row were determined within the past year [*(1)* [41], *(2)* [42], *(3)* and *(4)* [43], *(5)* [44], *(6)* [45, 46]. See ref. [25] for references regarding the other nucleosides.

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shows the odd nucleosides whose structures had been elucidated up to early 1969. 10–12 other odd nucleosides have been found, the structures of which are not as yet known.

Most odd nucleosides are derived from the four main nucleosides through methylation on C, O, or N; methylation of the base and of the sugar group (2′-*O*-methylribose) has been observed and mono- and dimethyl derivatives have been found. The ability to form hydrogen bonds is decreased in some methylated nucleosides, but not in others (Fig. 2). A nucleoside, found in all tRNAs studied so far, is 5-ribosyluracil or pseudouridine (Ψ) which has a C–C bond between base and ribose instead of an *N*-glycosyl linkage. Not especially noted in Fig. 2 is ribothymidine (T) which is also very common.

Like the other RNAs of the cell, tRNAs are synthesized at particular cistrons of the DNA [47]. Since there are no nucleotides known in DNA which can determine the insertion of odd nucleotides into the tRNA chain, it is assumed that an unmodified, "virgin" tRNA is synthesized first on which the odd nucleotides are formed later through modification of the chain. It is also possible that the three 3′-terminal nucleotides C–C–A, found in all tRNAs, are missing in the newly synthesized tRNA. In animal cells and microorganisms there has been found a CCA-phosphorylase which attaches the three bases onto tRNA in a reaction independent of DNA. Attempts to isolate tRNA precursors are only starting [48].

The formation of some odd nucleotides has been examined rather thoroughly. In the absence of the methyl-group donor methionine certain mutants of microorganisms produce "undermethylated" tRNA which can be transformed *in vitro* into the fully methylated form by the action of specific methylases [24]. Isopentenyl [49] and thio groups [50,51] are also added to the complete tRNA. In $tRNA^{Ala}_{yeast}$ some of the molecules contain a U in position 48, and others contain hU [52]. It seemed therefore reasonable to assume that hU is formed by hydrogenation of U in the complete tRNA chain. C may also be the parent group of hU (or of a dihydro-C which is converted into hU during the working-up procedure) since several tRNAs of *E. coli* contain A–G–C instead of the A–G–hU sequence found in yeast. Valine-specific tRNAs from two different yeast species contain hU and C in analogous positions (see Section 4). Arguing against U as parent of hU is also the finding that incorporation of the U-analog 5-fluoro-U suppresses the formation of T and Ψ but not of hU [52a]. Formation of Ψ from U is probably also accomplished in the complete tRNA but has so far not been demonstrated [53]. The fact that the triphosphate of pseudouridine can be incorporated into RNA *in vitro* does not rule out the possibility that U may be transformed in the RNA chain since RNA-polymerase accepts numerous nucleotide analogs as substrate both *in vitro* and *in vivo*.

Up to now little is known about the function of odd nucleotides. Since certain nucleases do not split next to some odd nucleotides, these nucleotides may have a protective function. Hypotheses concerning a relationship between degree of methylation of tRNA and cell differentiation or malignant growth could not be substantiated [24]. Isopentenyladenosine and other *N*(6)-substituted adenosine derivatives related to the natural cytokinin zeatin are potent plant growth factors. It is unknown, however, whether there is a relationship between their growth activity and their occurrence in tRNA. The role of odd nucleotides in codon recognition and interactions with amino acyl tRNA synthetases will be discussed in Section 6.

Odd nucleotides appear mainly in certain analogous positions of tRNAs. Up to now, however, no regularity has been found in the primary structure as would be the case, *e.g.*, if the cytidines found between several guanidines were always methylated. It should be noted that odd nucleotides are mostly found in regions that are single stranded in the clover leaf model (see Section 5). Their function in these positions could be the stabilization of a particular three-dimensional structure or a contribution to interactions of tRNA with components of the protein biosynthesis system. It is also quite probable that unmodified tRNAs already have a three-dimensional structure similar to that of modified tRNAs, and that the odd nucleotides are found predominantly in single-stranded regions because of easier access of modifying enzymes to these parts.

A surprising regularity was detected recently after purification of numerous tRNAs from *E. coli* and after a study of sA-biosynthesis [53a]: tRNAs with a 3′-terminal A in their anticodons (top line of the code table) frequently have an iA or sA next to this A, while several tRNAs with a 3′-terminal U in the anticodons (3rd line of the code table) contain tA. There is, as yet, no functional interpretation of this finding.

Animal tRNA has more odd nucleotides than yeast tRNA which is in turn more extensively modified than bacterial tRNA. However, even the tRNA of a very low order organism, T4-phage induced tRNA, contains Ψ [54]. It is difficult to believe that this refining of modification in evolution is a "freak of nature". The search for a function of the odd nucleotides remains one of the more interesting problems in nucleic acid biochemistry.

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4. Primary Structures of tRNAs

The elucidation of the nucleic acid sequences of tRNAs represents a major scientific advance. *Holley* and his co-workers were the first to determine the primary structure of a $tRNA^{Ala}_{yeast}$ [52]. Structures of other tRNAs followed: from the yeast *Saccharomyces cerevisiae* ($tRNA^{Ser}_{I+II}$ [33], $tRNA^{Tyr}$ [34, 21], $tRNA^{Phe}$ [55], $tRNA^{Val}$ [56]); from the yeast *Torulopsis utilis* ($tRNA^{Val}$ [57], $tRNA^{Ileu}$ [58], $tRNA^{Tyr}$ [58a]); from *Escherichia coli* ($tRNA^{Tyr}$ [59–61]; $tRNA^{fMet}$ [62], $tRNA^{Met}$ [63], $tRNA^{Val}$ [64]); from rat liver ($tRNA^{Ser}$ [65]); and from wheat germ ($tRNA^{Phe}$ [66]). Tentative structures for $tRNA^{Phe}_{coli}$ [67,68] and partial structures for $tRNA^{Ala}_{coli}$ [69] and $tRNA^{fMet}_{yeast}$ [69a] have also been published. Elucidation of another dozen tRNA structures is under way.

The first step in a sequence analysis of a nucleic acid is its specific enzymatic cleavage into smaller parts. Two endonucleases are known which cleave specifically at certain nucleotides. Pancreas-RNase cleaves next to both pyrimidine nucleotides and most of the odd nucleotides derived from them; T1-RNase, obtained from a microorganism, hydrolyzes the RNA next to G and several G derivatives (Fig. 3). A nuclease which cleaves specifically next to A has not yet been found. The exonucleases listed in Fig. 3 are useful in the determination of nucleotide sequences of oligonucleotides, which are in turn obtained by the action of endonucleases on the nucleic acid. Chemical methods for the stepwise degradation of a chain, which are so important in protein chemistry, have not yet been developed to such a stage that they are universally applicable or usable over a large number of steps in the case of nucleic acids. First results have been reported [69b].

Once the nucleotide sequences of all oligonucleotides formed on cleavage with pancreas- and T1-RNase have been determined, it is possible to reconstruct part of the original nucleic acid chain by comparison of the cleavage products. This process is illustrated for $tRNA^{Ser}_{II}$ from yeast in Fig. 4. It was not possible, however, to reconstruct a fragment greater than about 20 nucleotides by this method. Nucleic acid research is in a more difficult position than protein chemistry as regards the puzzle of sequence analysis. Specific proteases, which cleave next to two or three of 20 possible amino acids, generally afford larger segments than do nucleases that cleave next to one or two out of four possible nucleotides. The amino acid sequence of a protein can therefore be obtained in general by comparison of several rows of peptides formed on complete cleavage with specific proteases.

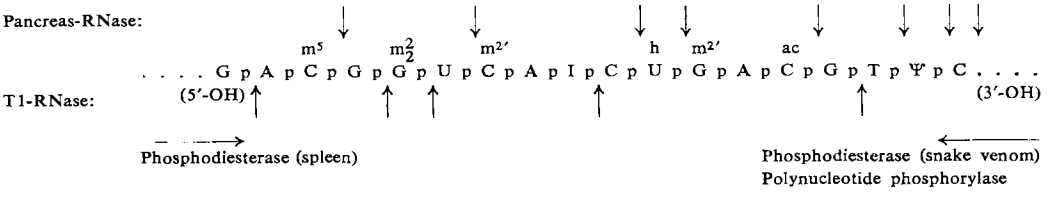


Fig. 3. A hypothetical nucleotide sequence is cleaved by an endonuclease at the positions indicated by arrows. It is degraded by exonucleases from the 5'- or 3'-hydroxyl end, respectively.

Additional methods are needed for nucleic acids. Partial digestion by endonucleases which leads to large fragments of the nucleic acid has proved useful. The method rests on the fact that in the three-dimensional structure of a tRNA certain sequences are more exposed than others and thus more susceptible to nucleolytic attack. A complex mixture of larger and smaller fragments is obtained under mild cleavage conditions. Isolation of the fragments followed by complete cleavage with a nuclease gives information on which oligonucleotides are adjacent to one another within a particular region of the tRNA. 30–40 fragments of $tRNA^{Ser}_{yeast}$ had to be analyzed [70] until the sequences of all overlapping regions were established beyond doubt. Several fragments of importance in the proof of structure are indicated in Fig. 4.

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Several hundred milligrams of pure tRNA were needed for the first complete sequence analysis of tRNAs, during which methods were still being developed. Oligonucleotides were separated by column chromatography; products of the subsequent cleavages were identified by their behavior on paper chromatography, electrophoresis, and by their UV spectra. Even at the last degradation step, on the nucleoside level, enough material is left to characterize possible odd nucleosides present. In the sequence analysis of, *e.g.*, $tRNA^{Ser}_{yeast}$ the structures of the then unknown nucleosides iA and acC (Fig. 2) were elucidated by mass spectrometry and NMR [71], or by degradation and synthesis [72] respectively. iA was isolated and identified simultaneously from unfractionated tRNA [73].

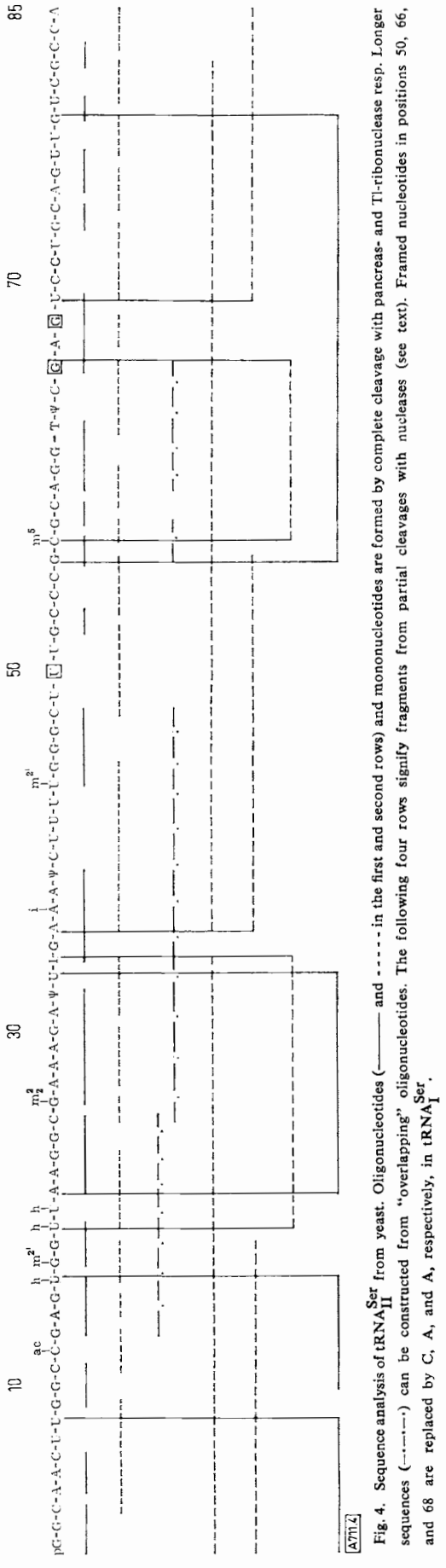


Fig. 4. Sequence analysis of $tRNA^{Ser}_{II}$ from yeast. Oligonucleotides (——— and - - - - - in the first and second rows) and mononucleotides are formed by complete cleavage with pancreas- and T1-ribonuclease resp. Longer sequences (—·—·—) can be constructed from "overlapping" oligonucleotides. The following four rows signify fragments from partial cleavages with nucleases (see text). Framed nucleotides in positions 50, 66, and 68 are replaced by C, A, and A, respectively, in $tRNA^{Ser}_{I}$.

Today it is possible to analyze a sequence using the above methods with as little as 40–60 mg of pure tRNA, provided that no extra material is needed for the elucidation of particularly complicated odd nucleosides. Even less tRNA is needed when radiochemical techniques are employed. *Sanger* and his coworkers have developed methods of sequence analysis using ^{32}P-labeled nucleic acids [74] which have been useful in the elucidation of, *inter alia*, five tRNAs from *E. coli* [59,62–64,67]. Oligo- and mononucleotides are rendered visible by autoradiography and identified by their behavior on two-dimensional electrophoresis. Such methods lead to a considerable saving not only of material but also of time. Difficulties arise only when unknown nucleotides are found since the quantities of material used do not generally suffice for a UV spectrum, to say nothing of chemical degradation reactions. In addition, it is much more difficult to obtain nucleic acids with sufficient specific radioactivity from higher organisms than from microorganisms.

A combination of conventional and radiochemical methods is possible with the help of polynucleotide kinase [75], which transfers phosphate to the 5′-hydroxyl group of oligonucleotides. If one has only small quantities of a nonradioactive nucleic acid, the cleavage products can be marked with ^{32}P [76] and characterized by *Sanger*'s methods. A method in which nonradioactive oligonucleotides are made radioactive through neutron activation [76a] is probably much more complicated.

The nucleotide sequences of the presently known tRNAs show characteristic similarities and differences. In Fig. 5 the sequences are so arranged as to emphasize the similarities. First it should be noted that certain odd nucleotides such as hU, m^2_2G, and m^5C appear predominantly in analogous regions of tRNAs. Certain characteristic distances are the same

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or similar in many tRNAs, such as that from m_2^2G to the anticodon and that between the sequence G–T–Ψ'–C (found in all tRNAs) and the 3'-terminal C–C–A. Similarities and differences in the sequences will be discussed in the following Sections in relation to three-dimensional structure and the various functions of tRNAs.

The oligonucleotides of a $tRNA^{Ser}$ from American baker's yeast[77] are identical with those from $tRNA^{Ser}$ from German brewer's yeast[33] (both *Saccharomyces cerevisiae*). After a discussion about the sequence of $tRNA^{Ala}_{yeast}$ as established by *Holley et al.* this tRNA was recently isolated from the same source but by a slightly modified technique. The $tRNA^{Ala}_{yeast}$ thus obtained is longer by one nucleotide (an extra G between positions 47 and 48) and contains only U in position 48 instead of a mixture of U and hU[77a]. Sequence differences between tRNAs from various yeast strains have been found. $tRNA^{Val}$ from the yeast *Torulopsis utilis*[57] differs from that obtained from *Saccharomyces* (Fig. 5)[56]: the sequence A-G-hU-hU-G-G-hU-C-A-U was found in the hU region; moreover the tRNA is shorter by two nucleotides, *i.e.* by the hU in the S-region and G in position 12 counting from the 3'-terminal A. $tRNA^{Tyr}$ from *Torulopsis*[58a] differs from $tRNA^{Tyr}$ from *Saccharomyces*[34] in 7 positions but has the same chain length. Two groups have found sequences for $tRNA^{Tyr}_{coli}$[60] and $tRNA^{Phe}_{coli}$[68] respectively which differ slightly from those in Fig. 5 and 6. It is not yet certain whether the presence of multiple tRNAs is the cause of these discrepancies. Differences in odd nucleotides, which can be induced by various growth conditions, will be discussed in relation to multiplicity of tRNAs (Section 7).

5. Three-dimensional Structure of tRNAs

tRNAs in aqueous solution certainly do not occur as randomly coiled molecules. The best evidence for a definite three-dimensional structure is the fact the tRNAs can be (reversibly) denatured. As for proteins, there are at least one native, biologically active form and one or more inactive forms of tRNA[78,79].

Since the exact three-dimensional structure of a tRNA is not known one resorts to models. *Holley et al.* recognized after the elucidation of the primary structure of $tRNA^{Ala}_{yeast}$ that certain regions of the nucleotide sequence could form Watson-Crick base pairs (A:U; G⋮C) with other regions of the same molecule[52]. They proposed three possible models: one extended, one angled, and one clover-leaf form. No one model is preferable over the other in that it has a higher percentage of paired nucleotides giving it a more favorable energy state. Alternative models can also be constructed for most of the other tRNAs whose primary structures are known. Clover-leaf models (Fig. 6), however, have been preferred since the elucidation of the first sequences, at first primarily for aesthetic reasons. Meanwhile there are several experimental indications that at least parts of the clover-leaf model must be correct.

Support for the clover-leaf model comes, *inter alia*, from the fact that all known tRNAs can be arranged in that form although the nucleotide sequences are very different particularly in the paired regions. After the first mutation in the evolutionary process which relates $tRNA^{Ser}_{rat}$ to $tRNA^{Ser}_{yeast}$ (19 nucleotides differ) and $tRNA^{Phe}_{wheat}$ to $tRNA^{Phe}_{yeast}$ (13 nucleotides differ) there must have been a selective pressure for change of the opposite nucleotide in a paired region so that the base pairing "fits" again[66]. This train of thought can be extended from tRNAs of different organisms accepting the same amino acid to the various tRNAs of a single organism, assuming that all forms have arisen from a single "Ur"-tRNA[80,81]. The fact that the length of the paired regions remains almost constant over a range of nucleotide compositions is explicable only if these parts of the clover-leaf model play a role in the actual three-dimensional structure.

It is, however, certain that tRNAs are not planar platelets. Clover-leaf models (and other two-dimensional models) can be folded such that single-stranded loops can form further base pairs either with one another or with the 3'-terminal C–C–A sequence. This folding produces more or less compact three-dimensional structures from which the anticodon region and the amino-acid-carrying 3'-terminal A protrude. Three-dimensional models have been discussed by several authors (see below)[82–86].

It has become customary to regard paired, and therefore helical, regions as elements of secondary structure, and to consider any fixation of the paired regions in space, *e.g.*, *via* unpaired regions, as an expression of tertiary structure. Base-pairing through H bonds, however, is definitely not the only stabilizing factor of the three-dimensional structure. Coplanar stacking of bases contributes considerably to the stabilization energy. Thus *Fuller* and *Hodgson*[87] made the plausible suggestion after comparing the nucleotide sequences of several tRNAs and constructing models, that part of the anticodon region of the tRNAs is stabilized by stacking of purine bases. Such models appear closer to reality than two-dimensional clover-leaf models with 7 unpaired nucleotides in the anti-

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		5′-terminal region	hU region
$tRNA^{Ala}_{yeast}$	(77)	pG G G C G U G U	m^1 h G G C G C G U A G U C G G U h A G C G C
$tRNA^{Ser}_{yeast\,II}$	(85)	pG G C A A C U U	G G C ac C G A G U h $m^{2'}$ h h G G U U A A G G C
$tRNA^{Ser}_{rat}$	(85)	pG U A G U C G U	G G C ac C G A G U h $m^{2'}$ h h G G U U A A G G C
$tRNA^{Tyr}_{yeast}$	(78)	pC U C U C G G U	A G C m^2 C A A G U U h h $m^{2'}$ h h h G G U U U A A G G C
$tRNA^{Tyr}_{Coli\ I\ su^-}$	(85)	pG G U G G G G U S	U C C S C G A G C h h $m^{2'}$ G G C C A A A G G G
$tRNA^{Phe}_{yeast}$	(76)	pG C G G A U U U	A G C m^2 U C A G U U h h G G G A G A G C
$tRNA^{Phe}_{wheat}$	(76)	pG C G G G G A U	A G C m^2 U C A G U U h h G G G A G A G C
$tRNA^{Phe}_{Coli}$	(76)	pG C C C G G A U S	A G C U C A G U C h h G G U A G A G C
$tRNA^{Val}_{yeast}$	(77)	pG G U U U C G U	m^1 G G U C Ψ A G U C h h G G U U A U G G C
$tRNA^{Val}_{Coli}$	(76)	pG G G U G A U U S	A G C U C A G C U h G G G A G A G C
$tRNA^{Met}_{Coli}$	(77)	pG G C U A C G U S	A G C U C A G U U h $m^{2'}$ h h G G U U A G A G C
$tRNA^{fMet}_{Coli}$	(77)	pC G C G G G G U S	G G A G C A G C C U G G h U A G C U C
$tRNA^{Ileu}_{yeast}$	(77)	pG G U C C C U U	G G C C C A G U U h h G G U U h h A A G G C
		11 8 6 7 13	6 12 11 13 13 13 10 6 13 13 8 7 13 13 12 12

	anticodon region	S region (miniloop)
$tRNA^{Ala}_{yeast}$	m^2_2 G C U C C C U U I G C I Ψ m^1 G G G A G	A G U
$tRNA^{Ser}_{yeast\,II}$	m^2_2 G A A A G A Ψ U I G A A i A Ψ C U U U	$m^{2'}$ U G G G C U U U G C C C G
$tRNA^{Ser}_{rat}$	m^2_2 G A Ψ G G A C U I G A A i m^3 A Ψ C C A U $m^{2'}$	U G G G G U C U C C C C G
$tRNA^{Tyr}_{yeast}$	m^2_2 G C A A G A C U G Ψ A i A A Ψ C U U G h	A G A U
$tRNA^{Tyr}_{Coli\ I\ su^-}$	A G C A G A C U G+U A A S A Ψ C U G C	C G U C A U C G A C U U
$tRNA^{Phe}_{yeast}$	m^2_2 G C C A G A C U G $m^{2'}$ A A Y A Ψ C U G G $m^{2'}$ m^5	m^7 A G G U C
$tRNA^{Phe}_{wheat}$	m^2_2 G Ψ C A G A C U G $m^{2'}$ A A Y_W A Ψ C U G A $m^{2'}$	m^7 h A G G U
$tRNA^{Phe}_{Coli}$	A G G G G A Ψ U G A A S A Ψ C C C C	m^7 G U G X
$tRNA^{Val}_{yeast}$	A Ψ C U G C Ψ U I A C A C G C A G A	h A C U
$tRNA^{Val}_{Coli}$	A C C U C C C U X A C m^6 A A G G A G G	m^7 G G G U
$tRNA^{Met}_{Coli}$	A C A U C A C U C+A U A+A Ψ G A U G	m^7 G G G X
$tRNA^{fMet}_{Coli}$	G U C G G G $m^{2'}$ C U C A U A A C C C G A	m^7 A G G U
$tRNA^{Ileu}_{yeast}$	m^2_2 G Ψ G G U G C U I A U A t A C G C C A	h A G A U
	8 6 9 8 9 13 8 7 11 11 8 9 6	7 11 8 6

	TΨC region	3′-terminal region
$tRNA^{Ala}_{yeast}$	C U C C G G T Ψ C G A U U C C G G A	C U C G U C C A C C A
$tRNA^{Ser}_{yeast\,II}$	m^5 C G C A G G T Ψ C G A G U C C U G C	A G U U G U C G C C A
$tRNA^{Ser}_{rat}$	m^5 C G C A G G T Ψ C G m^1 A A U C C U G C	C G A C U A C G C C A
$tRNA^{Tyr}_{yeast}$	m^5 C G G G C G T Ψ C G A C U C G C C C	C C G G G A G A C C A
$tRNA^{Tyr}_{Coli\ I\ su^-}$	C G A A G G T Ψ C G A A U C C U U C	C C C C A C C A C C A
$tRNA^{Phe}_{yeast}$	m^5 C U G U G T Ψ C G m^1 A U C C A C A G	A A U U C G C A C C A
$tRNA^{Phe}_{wheat}$	C G C G U G T Ψ C G m^1 A U C C A C G C	U C A C C G C A C C A
$tRNA^{Phe}_{Coli}$	C C U U G G T Ψ C G A U U C C G A G	U C C G G G C A C C A
$tRNA^{Val}_{yeast}$	m^5 C C C C A G T Ψ C G m^1 A U C C U G G G G	C G A A A U C A C C A
$tRNA^{Val}_{Coli}$	C G G C G G T Ψ C G A U C C C G U C	A U C A C C C A C C A
$tRNA^{Met}_{Coli}$	C A C A G G T Ψ C G A A U C C C G U	C G U A G C C A C C A
$tRNA^{fMet}_{Coli}$	C G U C G G T Ψ C A A A U C C G G C	C C C C G C A A C C A
$tRNA^{Ileu}_{yeast}$	m^5 C A G C A G T Ψ C G m^1 A U C C U G C U	A G G G A C C A C C A
	13 7 8 13 13 13 13 12 13 7 8 13 8 6 7 7	7 6 11 11 13 13 13

Fig. 5. Comparison of nucleotide sequences of tRNAs. (Literature references are given in the text.) The numbers in parentheses denote chain length. The following odd nucleotides are still unknown: G+ in $tRNA^{Tyr}_{coli}$, Y in $tRNA^{Phe}_{yeast}$; Y_W in $tRNA^{Phe}_{wheat}$, X in $tRNA^{Phe}_{coli}$, X in $tRNA^{Val}_{coli}$, and C+, A+, and X in $tRNA^{Met}_{coli}$ (A+ is tA in one $tRNA^{Met}_{coli}$, *S. Nishimura, H. Ishikura,* personal communication). Sequences differing from those shown here for $tRNA^{Val}_{yeast}$ [56], $tRNA^{Tyr}_{coli}$ I su⁻ [59], and $tRNA^{Phe}_{coli}$ [67] are discussed in the text. Areas which are double stranded in the clover-leaf models (see Fig. 6) are underlined. The numbers in the bottom line designate the frequency of certain nucleotides in that position (including odd nucleotides which are derived from them).

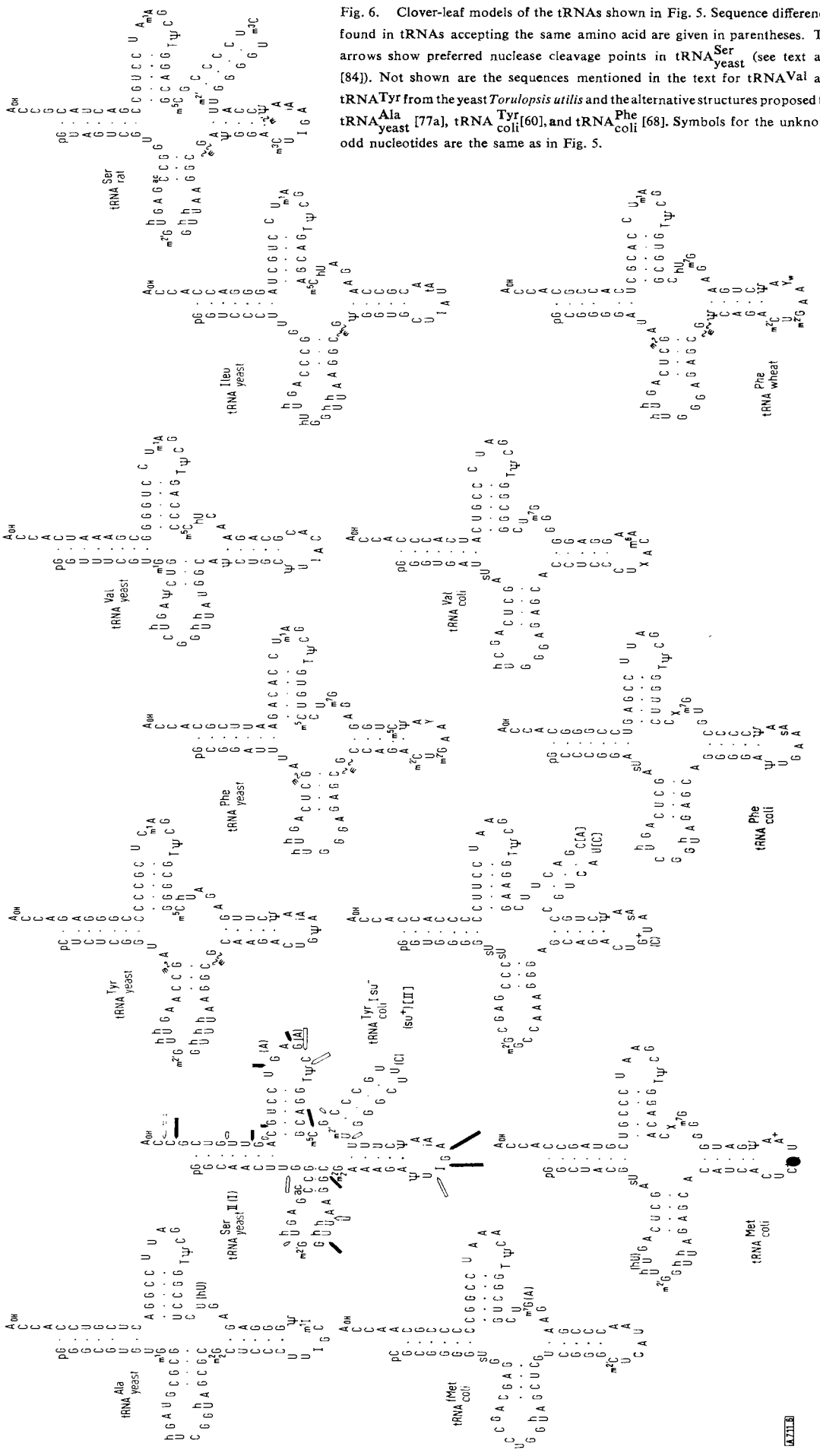


Fig. 6. Clover-leaf models of the tRNAs shown in Fig. 5. Sequence differences found in tRNAs accepting the same amino acid are given in parentheses. The arrows show preferred nuclease cleavage points in $tRNA^{Ser}_{yeast}$ (see text and [84]). Not shown are the sequences mentioned in the text for $tRNA^{Val}$ and $tRNA^{Tyr}$ from the yeast *Torulopsis utilis* and the alternative structures proposed for $tRNA^{Ala}_{yeast}$ [77a], $tRNA^{Tyr}_{coli}$ [60], and $tRNA^{Phe}_{coli}$ [68]. Symbols for the unknown odd nucleotides are the same as in Fig. 5.

codon loop (Fig. 6). If one considers only base pairing, the stem of the anti-codon loop in $tRNA^{Ser}_{yeast}$ for instance could be elongated by one such pair leaving only 5 unpaired nucleotides. Consideration of stacking allows one to construct the anticodon regions of all tRNAs, including that of $tRNA^{Ser}_{yeast}$, in the same manner. Thus the first A of the anticodon loop of $tRNA^{Ser}_{yeast}$ is included in a stacked region instead of being paired with Ψ. The rigidity of the regions stabilized by stacking is probably comparable with that of double-stranded regions of tRNAs. It is therefore not meaningful to apply very strictly the above distinction between secondary and tertiary structure.

There has been no lack of attempts to gain insight into the three-dimensional structure of tRNAs by physical methods. Only a small portion of the work can be cited here: NMR [88]; electron spin resonance [89]; melting curves (temperature-dependence of hypochromicity) [90]; temperature jump methods [90a]; IR spectroscopy [90b]; optical rotatory dispersion [83,91]; circular dichroism [92]; polarization of fluorescence [93]; phosphorescence spectra [94,95]; sedimentation characteristics in the ultracentrifuge [96,97]; flow birefringence [98]; small angle X-ray diffraction [99]; preliminary X-ray studies on tRNA-gel fibers [100]; measurement of exchange kinetics with T_2O [101]; electron microscopy [101a]; determination of chromatographic behavior [102] and kinetics of enzymatic degradation [103,104]. The methods have led to some conclusions concerning the three-dimensional structure of tRNAs. The structures change with temperature, presence of mono- or divalent cation, pH, *etc.*, and are different for uncharged tRNA, aminoacyl tRNA, and peptidyl tRNA. Statements concerning the degree of base pairing and stacking as well as those regarding the conformation of tRNA in solution are still rather tentative. Consideration of some of the more recent data would give preference to somewhat more extended models which are derived from the clover-leaf model by stacking of unpaired nucleotides rather than by formation of many additional base pairs.

It has been possible to obtain indications for elements of the three-dimensional structure and recognition sites of tRNAs (discussed below) by specific chemical [17,105] and enzymatic modification of the molecules. Alkylation and halogenation reactions probably change the three-dimensional structure of tRNAs so rapidly that little information can be gained about the original structure. The same is true of acetylation, acetacetylation with diketene [105a], and oxidation with $KMnO_4$ [106] or OsO_4 [107]. In reactions with formaldehyde [108] and other aldehydes, in the much studied reactions with hydroxylamine and its derivatives, in the deamination with HNO_2 [109], in the reaction with carbodiimides [110], and the oxidation with perphthalic acid [85] it seems that several regions, which are single stranded in the clover-leaf model, react faster than paired regions.

Reagents such as $NaBH_4$ [111] and acrylonitrile [112] are also interesting in that they react preferentially or exclusively with certain odd nucleotides. $NaBH_4$ reduces, *inter alia*, hU and acC. If these nucleotides are part of a tRNA chain, hU is reduced [111] but the acC in position 12 of $tRNA^{Ser}$ is not [113]. This can be taken as an indication that hU is unpaired and acC is protected through pairing, as is predicted from models.

Acrylonitrile, which modifies Ψ and I, does not attack the Ψ in the sequence G–T–Ψ–C found in all tRNAs under a variety of conditions [112] although, according to the clover-leaf model, this sequence is in a single-stranded region. This fact is in agreement with the finding that the G–T–Ψ–C sequence is unusually stable on partial hydrolysis with pancreas-RNase [84]. This region must therefore be protected in some way in the three-dimensional structure.

A promising method for the study of tRNA three-dimensional structure seems to be the partial cleavage

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with nucleases. The preferred points of attack of pancreas- and T1-RNase in $tRNA^{Ser}_{yeast}$ [84] are indicated in Fig. 6. The length of the arrows is approximately proportional to the frequency of cleavage at the points indicated. Most cleavages occur where predicted by the clover-leaf model. This cleavage pattern can be refined by further analyses. The anticodon sequence IGA is particularly labile towards nuclease. It must therefore be in an exposed, single-stranded region; such a position is consistent with its function in the adaptor complex (Fig. 1). The anticodon sequences of most other tRNAs are also particularly labile towards nucleases. Nucleases with a preference for single stranded regions such as the sheep kidney nuclease [114] are valuable tools in the study of tRNA three-dimensional structure [115].

The above physical, chemical, and enzymatic methods are not sufficient to prove a particular three-dimensional structure. It was therefore a great step forward when six independent groups managed to produce tRNA crystals within the past year (for an account see ref. [116]). Although the crystals made so far appear not quite suitable yet for high resolution X-ray structure analysis, it will be only a matter of time until suitable samples will become available and the exact three-dimensional structure of a tRNA or several tRNAs in the crystalline state will be elucidated. tRNA models [82–86], if they are close to the true structures, may be of considerable help in X-ray analysis.

As has been mentioned, tRNAs can exist in several different conformations under physiological conditions. Therefore, in order to describe the three-dimensional structure of tRNAs in solution, it is necessary to pursue other physical methods, chemical modifications, and enzymatic cleavages which supplement X-ray data. These methods may also provide further indications as to the three-dimensional structure of tRNAs before an X-ray structure analysis has been accomplished.

6. Binding and Recognition Sites of tRNAs

6.1. Mode of Action of Binding and Recognition Sites

Each tRNA accepts only its specific amino acid in the enzymatic charging reaction. Reactions with other amino acids are below the limit of error, which is given as 1:10000 for the method used [117]. The codon-anticodon interaction and the transfer of the bound amino acid to the growing peptide chain must *in vivo* also occur with the highest precision since proteins are "molecularly uniform". The limit of error of the assay for wrong insertion is 1:3000 [118]. These data are only valid for natural amino acids. Some amino acid analogs are incorporated quite well into proteins. These analogs "fool" the aminoacyl tRNA synthetases and are not excluded in later steps of protein synthesis. In specially selected mutants of microorganisms [119,120] one has found a higher frequency of incorporation of a natural amino acid in wrong positions ("missense suppression").

A distant goal of research in this field is the explanation of the high precision of protein synthesis through an understanding of the structural elements and interactions of the enzymes, nucleic acids, and ribosomes involved. tRNAs are the most extensively studied macromolecular components of the protein synthesis system, and even for them little is known about the relationship between structure and function. In the search for nucleotide sequences or three-dimensional regions in the tRNA molecule which are responsible for interactions with a macromolecule one can differentiate between two types of structural elements: there must be specificity determining regions which are different for each tRNA, and other regions whose integrity is necessary for an interaction but which are not directly responsible for specificity. These areas, which can be alike in several or all tRNAs, may be called nonspecific binding sites. The distinction facilitates the present discussion, but it may be unnecessary one day when the recognition process is fully understood (see Sections 6.2–6.4).

6.2. Recognition of tRNAs by Various Enzymes

Let us first consider the recognition sites of tRNAs, about which little more is known than that they exist. The 3′-terminal nucleotides of tRNAs – pC, pC, and pA – are added by an enzyme already mentioned, C–C–A-pyrophosphorylase. For this reaction tRNAs must be in the native conformation; denatured $tRNA^{Leu}$ from yeast is a very poor substrate for the enzyme [121]. In the denatured tRNA either the particular recognition site is altered or the total conformation is so different from that of the native tRNA that it is difficult to form an enzyme-tRNA complex. Since there may be only one pyrophosphorylase for all tRNAs one must assume that the enzyme recognizes nucleotide sequences or elements of the three-dimensional conformation which are alike in all tRNAs of a species.

Similar considerations may hold for the structural elements that are responsible for binding of tRNAs to ribosomes and to polymerization enzymes. These interactions are not specific for individual tRNAs. It is known that ribosomes stabilize the tRNA-mRNA complex [122]. The codon-anticodon interaction takes place on the 30S subunit of ribosomes while the amino acid-charged 3′-end of the tRNAs is bound to the 50S subunit [123]. Complexes between tRNAs and polymerization enzymes have also been found [124, 125] but it is not known which regions of tRNAs are involved here.

The enzymes that modify newly formed tRNAs must orient themselves on the three-dimensional structure

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of the tRNAs. As has already been mentioned, odd nucleotides, which are formed by modification, occur predominantly in regions of tRNAs that are single-stranded in clover-leaf models. ^{5}mC, iA, hU, and other odd nucleosides appear in analogous positions of the clover-leaf models; however, tRNAs containing unmodified nucleotides in these positions are also known.

It therefore follows that there must exist some recognition characteristics which are not obvious from the present models. A comparison of the nucleotide sequences in the neighborhood of the odd nucleotides in tRNAs and ribosomal tRNA [126] did not show any regularities. Similarly, it is not known which structural elements cause transformylase to formylate methionine bound to $tRNA_{coli}^{fMet}$ but not that bound to $tRNA_{coli}^{Met}$. *N*-Formyl-Met-$tRNA_{coli}^{fMet}$ is recognized by initiation factors to produce the N-terminal amino acid in many bacterial proteins. Mid-chain Met comes from Met-$tRNA_{coli}^{Met}$. The clover-leaf model of $tRNA_{coli}^{fMet}$ has five unpaired nucleotides at the 3′-terminal end whereas models of other tRNAs have only four (Fig. 6). $tRNA_{coli}^{fMet}$ and $tRNA_{yeast}^{Ser\ I}$ are the only tRNAs known which have the sequence –G–T–Ψ–C–A instead of the usual sequence –G–T–Ψ–C–G. So far no relationship has been found between these features and the particular function of $tRNA_{coli}^{fMet}$.

6.3. Binding and Recognition of Aminoacyl tRNA Synthetases

A particularly well-studied area was and still is the interaction between tRNAs and aminoacyl tRNA synthetases. One is dealing here with the most easily accessible model for the study of specific nucleic acid–protein interactions. These interactions are important at several stages of cell metabolism and particularly its regulation.

In this context the specific binding of repressors to operators may be mentioned. In the case of the lac-operon from *E. coli*, the repressor has been identified as a protein [127] and the operator as a relatively short piece of DNA. mRNA and protein synthesis begin when the repressor dissociates from the operator. It seems then that repressors can recognize nucleotide sequences (or nucleic acid three-dimensional structure).

The first specificity determining step in protein synthesis is the synthetase-tRNA interaction. There is no subsequent check on whether the tRNA is carrying the correct amino acid during the formation of peptide bonds on the ribosomes. This has been very well illustrated in the following experiment [128]. Cys-$tRNA^{Cys}$ was desulfurated with Raney nickel. In protein synthesis the resulting hybrid Ala-$tRNA^{Cys}$ inserts Ala into Cys positions of the protein chain, as expected from the adaptor hypothesis, and not into Ala positions.

The nucleotide sequence of DNA and mRNA determines only which tRNAs are adjacent on the ribosome. Which amino acids are attached to the tRNAs and subsequently built into the protein is determined by the aminoacyl tRNA synthetases which, with high precision, bind and aminoacylate only the cognate tRNA. In relation to the structural elements of tRNAs responsible for the specificity of these interactions one speaks of a "second genetic code" or a synthetase recognition code. Attempts to decipher this code will now be discussed.

The *3′-terminal sequence of tRNAs*, –C–C–A, is certainly involved in the interaction with the synthetase. The amino acid is bound by an ester linkage to the ribose of the terminal adenosine [129], predominantly to the 3′-hydroxyl group of the ribose [26]. This area of the tRNA must be in contact with the enzyme during the charging reaction. Some changes in the structure of the terminal sequence are possible without loss of charging ability, such as omission of one C in the reconstruction of a degraded tRNA with CCA-pyrophosphorylase [130], formation of I from the terminal A with a specific deaminase [131], or oxidation of the 2′- and 3′-OH groups with HIO_4 followed by reduction of the dialdehyde to the primary dialcohol [132]. Oxidation with HIO_4 without subsequent reduction or removal of terminal pA inactivates the tRNA completely. Terminally modified tRNAs are still bound to a greater or lesser extent by their synthetase [133, 134], depending on the type of tRNA and the particular modification. Different tRNAs, after the same modification, behave to a different degree as competitive inhibitors in the charging of the corresponding intact tRNAs [135]. Differences observed in these binding and inhibition studies indicate that formation and properties of synthetase-tRNA complexes differ from one tRNA to another. Attempts to detect competitive inhibition of the charging reactions with synthetic oligonucleotides or tRNA fragments have thus far brought contradictory results. The charging of $tRNA_{yeast}^{Phe}$ at least seems not to be inhibited even by large fragments of this tRNA [136].

Although the –C–C–A sequence, which is the same in all tRNAs, can only be a nonspecific binding region, the attached "*stem*" *of the clover-leaf* could be involved in specific recognition of the synthetase. It has recently been postulated [137] that the three nucleotides in positions 5, 6, and 7 from the 3′-end and the opposing

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three nucleotides of the 5'-end are the main recognition site. As required by the hypothesis, this sequence is different in the various known tRNAs of a species (Fig. 6). The trinucleotide sequence is also different in $tRNA^{fMet}_{coli}$ and $tRNA^{Met}_{coli}$. In spite of this, both tRNAs are charged by the same enzyme. In addition three cases are known of heterologous charging of tRNAs with different trinucleotide sequences, *i.e.* cases in which the synthetases charge not only their cognate tRNAs from the same species but also that from another species ($tRNA^{Ser}_{yeast}$, $tRNA^{Ser}_{rat}$ [65]; $tRNA^{Phe}_{yeast}$, $tRNA^{Phe}_{coli}$ [138]; $tRNA^{Val}_{coli}$, $tRNA^{Val}_{yeast}$ [139]; sequences Fig. 5). The cross-charging experiments do not, however, refute the hypothesis, since the synthetase recognition code, just as the genetic code, could be degenerate. One result not in agreement with the hypothesis is that the charging of $tRNA^{Phe}_{yeast}$ with a synthetase from *E. coli* disappears upon formation of $tRNA^{Phe}_{HCl}$ [138] (see Section 2). This reaction involves a change in the anticodon region and is very unlikely to affect the hypothetical recognition site in the stem of the clover-leaf directly or through changes in three-dimensional structure. But there is a simple explanation: the anticodon region may be another essential binding site for the synthetase. Certain changes in this region (but not all, see below) would then lead to a loss of charging ability although the actual recognition site is intact.

The *anticodon* itself is a good candidate for a synthetase recognition site since it is different for all tRNAs of a species. Attempts to test this hypothesis by comparison of UV-inactivation curves of acceptor and transfer activity [140] have brought as few definitive results as most inactivation experiments using chemical reagents [17,105]. There are, however, three types of experiments which contradict the anticodon as synthetase recognition site. Several very specific chemical changes in or near the anticodon lead to a loss of codon recognition but no loss of synthetase recognition [36,141–143]. Several tRNAs can be cleaved in or next to the anticodon without loss of acceptor activity [144–146,146a]. In addition su^+- and su^--$tRNA^{Tyr}_{coli}$, which differ in the anticodon (Fig. 6), accept the same amino acid [59]; and it has been shown that the same synthetase charges two $tRNAs^{Ser}_{coli}$ that differ in their anticodons [147]. Although these experiments speak against the anticodon playing a role in specific synthetase recognition, they do not exclude the anticodon region as a binding site since such a function could still be performed even by a greatly modified or cleaved nucleotide sequence.

The T–Ψ–C region is the same or similar in several tRNAs and can therefore only be considered as a non-specific binding region. The *hU-containing loop* and the so-called *S-region* are sufficiently different in tRNAs to serve as recognition sites. However, cleavage of $tRNA^{fMet}_{coli}$ in the former [148] and of $tRNA^{Tyr}_{coli}$ in the latter [149] region does not destroy the acceptor activities. In addition, the dihydrouracil ring can be reductively opened without loss of any tRNA activities [111,113].

Some experiments designed to locate the synthetase recognition site were directed at the *odd nucleotides* as possibly playing a role in tRNA specificity. Numerous, partly contradictory, results with "undermethylated" tRNAs have been reported. The activities of these tRNAs seem to differ little from those of normal tRNAs under most assay conditions. The acceptor activity of $tRNA^{Ala}_{yeast}$ is the same whether U or hU is in position 48 [150]. $tRNA^{Tyr}_{coli}$ is charged with the same velocity by the synthetase from *E. coli* whether the A next to the anticodon is not, partly (with an isopentenyl group), or completely (with an additional CH_3-S-group) modified [35]. The sulfur of s^4U of $tRNA^{Met}_{coli}$ can be missing without loss of acceptor activity [150a]. Insertion of 5-fluoro-U instead of U [52a,151], or some other nucleoside analogs, influences acceptor activity as little as ethylation instead of methylation [152] (use of ethionine instead of methionine as alkyl group donor). It is certainly possible that odd nucleotides have a minor effect on the three-dimensional structure which cannot be analyzed by today's methods. A slightly improved binding to the synthetase would be in evolution already a selective advantage of the modified over the unmodified tRNA.

It is interesting to *compare the presently known nucleotide sequences* and clover-leaf models (Figs. 5 and 6; earlier comparisons see [21,27,80,84,105,152a]) with regard to synthetase recognition sites. The total number of identical or different nucleotides in various tRNAs does not seem to be important. $tRNA^{fMet}_{coli}$ and $tRNA^{Met}_{coli}$, which are charged by the same syn-

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thetase, have the same or similar nucleotides in 41 positions. Almost the same number of homologies exist between $tRNA^{Tyr}_{yeast}$ and $tRNA^{Tyr}_{coli}$, for which there is no heterologous charging under most conditions [153]. $tRNA^{Met}_{coli}$ and $tRNA^{Val}_{coli}$, for which no cross-charging should be possible, have 51 homologies. It is worth mentioning that in very similar tRNAs, $tRNA^{Ser}_{yeast}$ and $tRNA^{Ser}_{rat}$ or $tRNA^{Phe}_{yeast}$ and $tRNA^{Phe}_{wheat}$ (66 and 63 homologies, respectively), which can be charged with the heterologous synthetases, the sequence differences (19 and 13 nucleotides, respectively) are found predominantly in the paired regions of the clover-leaves. In general, it seems that heterologous charging is easier and more frequent for tRNAs and synthetases from yeast and those from higher organisms than for those from bacteria. Two cases of an incorrect charging have been found: a Phe-tRNA-synthetase from the cytoplasm of *Neurospora* charges $tRNA^{Ala}_{coli}$ and $tRNA^{Val}_{coli}$ with Phe [154]; Phe-tRNA synthetase from yeast charges $tRNA^{Val}_{coli}$ I, the hU-region of which is very similar to the one of $tRNA^{Phe}_{yeast}$ [154a]. As is obvious from these results the further study of heterologous charging reactions may become quite interesting.

Since the synthetase recognition sites have not yet been localized in a particular region of the tRNAs, and since it is known that tRNAs with altered three-dimensional structure, *i.e.* denatured tRNAs [78, 79], do not accept amino acids, one could assume that *the three-dimensional structure as a whole* must be intact for synthetase recognition. The fact that dimers, trimers, and higher aggregates of $tRNA^{Ser}_{yeast}$ have acceptor activity [155] refutes this assumption. Such activity was confirmed for dimers of $tRNA^{Ala}_{yeast}$ [156]. The conformations of aggregates in solution are certainly different from those of monomeric tRNAs. However, certain parts of the structure may be the same in aggregates and monomers and it is these parts, not the structure as a whole, which must be recognized by the synthetase. Also experiments with tRNA fragments argue against the indispensibility of the whole tRNA for recognition: Heterologous combinations of half molecules of $tRNA^{Phe}_{yeast}$ and $tRNA^{Phe}_{wheat}$ have acceptor activity [156a], as do homologous combinations of fragments in which parts of the tRNA molecules have been omitted [156b,c].

The active sites of numerous enzymes are composed of several amino acids occurring in separated regions of the sequence but brought together through folding of the chains. Similarly, synthetase recognition sites of tRNAs could be composed of several nucleotide sequences which are not adjacent in the primary structure. The stem of the clover-leaf model, the hU- and S-regions, or sequences abundant in purines [21], have been considered as possible candidates. The sequences can be proximate in the three-dimensional structure but need not be. One would certainly assume more than one binding site. Whether one or more of these sites are responsible for the specific recognition is open to question.

The synthetase recognition sites need not lie in analogous regions of all tRNAs. It would simplify the elucidation of the recognition phenomenon if the same regions of the tRNAs were always involved. This is, however, not a necessary assumption.

Work on the synthetase recognition problem will become much easier when the three-dimensional structures of one or more tRNAs are known. It is also necessary to study the structural requirements of binding between tRNA and synthetase separately from those of the actual catalytic step (aminoacylation). Interesting beginnings in this direction are the work on synthetase-tRNA complexes [133, 134, 157, 158]. Information about the forces involved in the binding of synthetase to tRNA [159] and about the functional groups involved in the catalytic step can be obtained from exact kinetic studies of the pH, salt concentration, temperature, and organic medium dependence of the charging of native and modified tRNAs.

Implication of individual regions of tRNAs involved in synthetase recognition can be obtained with the aid of "tRNA-mutants" in which single nucleotides have been exchanged for others [159a].

6.4. The Anticodon

While the structural requirements of the nucleic acid-protein interactions are still vague, those of the nucleic acid–nucleic acid interactions in the adaptor complex (Figure 1) have largely been elucidated. Just the fact that a trinucleotide sequence has been found in all tRNAs, in analogous positions of the clover-leaf model, which is antiparallel complementary to the respective codons, practically proves the adaptor hypothesis and the localization of the anticodon. The occurrence of inosine in several of these sequences was at first surprising. However, it could be correlated satisfactorily with the behavior of those tRNAs in codon recognition by the "wobble" hypothesis [160]. *Crick* postulated that I in the first position of the anticodon could interact with three different nucleotides of the third codon position, *i.e.* with U, C, or A. In addition to A:U and G:C, G:U pairs are possible

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	G C A G C C	U C A U C C	U U C	G U G		U A C	
Codons: (5′→3′)	G C U	U C U	U U U	A U G	A U G	U A U	U A G
			$m^{2'}$				
Anticodons: (3′←5′)	C G I	A G I	A A G	U A C	U A C^+	A U G^+	A U C
	$tRNA^{Ala}_{yeast}$	$tRNA^{Ser}_{yeast}$	$tRNA^{Phe}_{yeast}$	$tRNA^{fMet}_{coli}$	$tRNA^{Met}_{coli}$	$tRNA^{Tyr}_{coli}\,su^-$	$tRNA^{Tyr}_{coli}\,su^+$

Fig. 7. Examples of codon-anticodon pairs. The anticodons have been written in the (uncommon) 3′ ← 5′ polarity in order to show the possibility of base pairing more clearly. C^+ and G^+ in the anti-codons of $tRNA^{Tyr}_{coli}$ su^- and $tRNA^{Met}_{coli}$ are still unknown odd nucleosides with the pairing characteristics of C and G, respectively. Pairing of $tRNA^{fMet}_{coli}$ with GUG, which corresponds to a "wobble" in the first position of the codon, is a pecularity of the chain-initiating tRNA. The mutation observed in suppressor strains, which makes AUC from AUG^+ (3′ ← 5′) in the anticodon of $tRNA^{Tyr}_{coli}$, allows the su^+-tRNA to read the chain terminating codon UAG as Tyr (see text).

in this position. The necessary distance for H-bonds in "wobble" pairs is possible only when the third base of the codon (or the first base of the anticodon) "wobbles" out of the position dictated by the nucleic acid double strand.

While this hypothesis was originally proposed on the basis of only a few data, the anticodon sequences and codon binding experiments that have become known since are in complete agreement: I-containing tRNAs can serve three codons; tRNAs having U or G in the first position of the anticodon can interact with 2 codons (Figure 7). The 61 codons of the genetic code (64 in total, of which 3 are chain-terminating codons) therefore do not require 61 different tRNAs. The high degree of degeneracy of the code has not to be paralleled by a similarly high multiplicity of tRNAs (see Section 7).

Direct proof of the location of the anticodon was provided by the work on $tRNA^{Tyr}_{coli}$ [59]; $tRNAs^{Tyr}_{coli}$ su^+ and su^-, according to structure analyses, differ only in one nucleotide but behave differently in the codon binding assay (Figure 7); the differing nucleotide must therefore lie in the anticodon. Experiments with a fragment from $tRNA^{fMet}_{coli}$ [161] showed that only the anticodon loop and the paired region belonging to it, but not the rest of the tRNA molecule, are essential for codon binding; a fragment containing 19 nucleotides including the anticodon can interact with AUG and GUG on the ribosome.

Nothing is known about the functions of the other odd nucleosides which, apart from I, are found in the anticodon. It is assumed that certain odd nucleosides in the anticodons of some tRNAs are the cause of unexpected behavior in codon binding. The odd nucleotide found next to the anticodon in most tRNAs could be important for the three-dimensional structure of the anticodon loop. Modification of this nucleotide, which barely influences acceptor activity (see above), causes partial [141] or complete [36] loss of the codon-binding ability.

7. Multiplicity of tRNAs and Functions other than Amino Acid Transfer

It is unknown how many different tRNAs occur in a microorganism, a plant, or an animal. As mentioned above, there are certainly more than 20, *i.e.*, more than one tRNA per amino acid. The existence of several tRNAs for the same amino acid is called multiplicity. 40–60 major tRNA species are found in the fractionations of $tRNA_{coli}$ or $tRNA_{yeast}$. This number could be larger for higher organisms. Apart from those tRNAs known to occur in greater amounts, there are always minor peaks and "shoulders" found in chromatography or countercurrent distribution. At least some of these represent actual tRNAs. However, not every peak showing acceptor activity in a fractionation can be associated with an extra tRNA species. Aggregates, various conformations of tRNAs, heterogeneity in the 3′-terminal –CCA group *etc.*, can make the number of tRNAs appear larger than it is. A few cases are mentioned below in which several tRNAs do occur for one amino acid.

One type of multiplicity is a consequence of the degeneracy of the genetic code. Because of the possibility of a "wobble" (see Section 6.4) not 6 tRNAs are necessary for the 6 serine codons; 3 $tRNAs^{Ser}$ are however necessary. Thus one tRNA each for UCU and UCC, UCA and UCG, and AGU and AGC was found to exist in *E. coli* [147]. The I-containing $tRNA^{Ser}_{yeast}$ can serve 3 codons: UCC, UCU, and UCA. $tRNAs^{Ser}$ for UCG and AG^U_C have not yet been found in yeast. These tRNAs are present only in small amounts, if at all [162]. We arrive here at a generally important fact which is also seen for tRNAs from other organisms [163]: the genetic code is universal, *i.e.* it is valid in all organisms, but some organisms seem not to use all codons, since they do not possess the appropriate tRNAs.

A further type of multiplicity of tRNAs was first demonstrated for *Neurospora* [164] and later shown also for other organisms: mitochondria contain some tRNAs which differ from those of the cytoplasm of the cell. Thus a chain-initiating $tRNA^{fMet}$ normally found only in bacteria has also been found in mitochondria from yeast [165] and human tissue culture cells [166]. One of the $tRNA^{Ser}_{yeast}$ species

[161] *B. F. C. Clark, S. K. Dube,* and *K. A. Marcker,* Nature (London) *219,* 484 (1968).

[162] *J. Kruppa,* Diplomarbeit, Universität München 1968; *H. Feldmann,* unpublished experiments.

[163] *C. T. Caskey, A. Beaudet,* and *M. Nirenberg,* J. molecular Biol. *37,* 99 (1968).

[164] *W. E. Barnett* and *D. H. Brown,* Proc. nat. Acad. Sci. USA *57,* 452 (1967); *J. L. Epler,* Biochemistry *8,* 2285 (1969).

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found only in trace amounts could be of mitochondrial origin [167].

Incomplete modification is the third origin of multiple tRNA species. The coexistence of U- and hU-containing $tRNA^{Ala}_{yeast}$ [52] and of unmodified, partially, and completely modified $tRNA^{Tyr}_{coli}$ [35] has already been mentioned (see Section 3 and 6.3).

tRNAs altered in the anticodon could be included in the number of tRNAs occurring in small amounts. Their role in genetic suppression has been elucidated for $tRNA^{Tyr}_{coli}$ [59].

Up to now, such sequence differences as occur in $tRNA^{Ser}_{I}$ and $tRNA^{Ser}_{II}$ from yeast [33], which differ in three nucleotides outside of the anticodon, have no functional explanation.

Some microorganisms have tRNAs that are involved in building amino acids into the cell wall [168]. These tRNAs are probably specialized for this purpose. Also amino acid incorporation into phosphatidyl glycerol seems to work *via* aminoacyl tRNAs [168a].

Animal viruses [169] and bacteriophages [54,170] synthesize their own tRNAs which are different from those of the host cell. Also a phage induced modification of a host cell tRNA has been reported [171].

Some tRNAs from microorganisms in different growth stages [172–175] and from plant [176] or animal tissue [177–180] of different degrees of differentiation gave chromatographic elution profiles which differed from the respective standards. New acceptor activity peaks were found and the disappearance of other peaks observed. However, it has not yet been possible to show that the newly appearing or disappearing tRNAs were different in structure or function from the standard tRNAs. Aggregation or change of conformation can be excluded as origin of the multiplicity by relatively easy experiments; it is more difficult to exclude heterogeneity of the –C–C–A sequence; the primary structure has to be examined in order to distinguish whether two tRNAs differ in extent of modification or in the sequence of main nucleotides. Functional differences, such as codon binding ability, are easier to determine.

Changes in multiplicity as a function of growth stage or degree of differentiation are interesting in relation to the observation that some organisms have no tRNAs or only small amounts for certain codons. Here lies a possibility for protein synthesis regulation independent of the regulation of mRNA synthesis through repression and induction. mRNAs for certain proteins or groups of proteins could contain codons for which special "regulatory" tRNAs are necessary. These tRNAs could have to be newly synthesized or formed by modification of existing tRNAs in certain differentiation stages and degraded in later stages of development.

There is little known about the regulation of tRNA synthesis and modification. Synthesis of tRNA (and rRNA) stops in certain mutants of microorganisms if one of the 20 amino acids is missing [181]; tRNA synthesis seems to be coupled to protein synthesis in these cases. It is definitely known that amino acid activation plays a role in the regulation of amino acid biosynthesis [182,183]. The amino acid itself does not inhibit its own biosynthesis if present in high concentration in the cell. Products of the amino acid activation by aminoacyl tRNA synthetases (perhaps the aminoacyl tRNAs [184]) are involved.

8. Closing Remarks

Research into the structure and function of tRNAs is proceeding so rapidly that important new results will have been published by the time this paper appears. Methods for isolating pure tRNAs are constantly being refined. Several groups are working on the elucidation of tRNA primary structures. Synthesis of a $tRNA^{Ala}_{yeast}$ cistron, a fragment of DNA complementary to $tRNA^{Ala}_{yeast}$, is making good progress [185]. It should be possible to produce the corresponding RNA on this DNA template with the aid of RNA-polymerase. This completely unmodified tRNA is an interesting starting material for many studies, *e.g.* the elucidation of the biosynthesis and the function of odd nucleotides. The problem of tRNA three-dimensional structure should in the foreseeable future be solved with the aid of X-ray structure analysis and other methods. Knowledge of the three-dimensional struc-

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ture will in turn simplify studies of the various binding and recognition sites.

tRNAs are the smallest macromolecular tools of protein biosynthesis. They differ greatly from the other nucleic acids of the cell. Through the peculiarities of their structure they are able to interact specifically not only with the synthetases, but also with ribosomes and mRNA. "It almost appears as if tRNA were Nature's attempt to make an RNA molecule play the role of a protein" [186].

Because of their relatively low molecular weight the tRNAs are still in the range accessible to exact analysis by modern physical, chemical, and biochemical methods. Therefore tRNA research may help in solving some basic questions, such as the relationship of nucleic acid structure and function, and the problem of nucleic acid-protein interactions.

The author wishes to thank his co-workers and colleagues for their cooperation in those studies mentioned in the above paper that were carried out in his laboratory. The work was generously supported by the Deutsche Forschungsgemeinschaft and Fonds der Chemischen Industrie.

Received: April 30, 1969 [A 711 IE]
German version: Angew. Chem. *81*, 645 (1969)
Translated by Dr. *Dagmar Ponzi*, Brooklyn, Mass. (USA)

[186] *F. H. C. Crick*, in [9], p. 3.

Cyclization of Acetylenic Compounds

By W. Reppe (deceased), N. v. Kutepow, and A. Magin[*]

Dedicated to Professor B. Timm on the occasion of his 60th birthday

Cheap acetylene produced by a new process can compete with ethylene as a starting material for the large-scale production of a number of organic products. Hydroquinone and methylated hydroquinones, which are valuable industrial starting materials or intermediates, are obtained by catalytic cyclizations.

1. Introduction

The rapid development of petrochemistry, which has been brought about by the growing demand for fuels, has led to increased production of valuable chemicals. Petrochemistry is concerned not only with the production of organic raw materials (olefins, dienes, polyolefins, acetylenes, aromatic compounds, and other products) on the industrial scale, but also with the development of new catalytic and thermal processes based on petroleum and natural gas. This led *inter alia* to the development of new acetylene processes with the object of making "acetylene chemistry" competitive with "olefin chemistry".

Some time ago acetylene was an irreplaceable starting material for the large-scale production of many organic products, such as vinyl ethers, vinyl esters, vinyl chloride, acrylic compounds, and acetaldehyde. When acetylene chemistry had reached its prime, ethylene chemistry was still in its infancy, since ethylene was more expensive than acetylene and was not available in sufficiently large quantities. The production of ethylene involved laborious processes such as the low-temperature distillation of coke-oven gas, the partial hydrogenation of acetylene, or preparation from acetylene *via* acetaldehyde and ethanol.

Cracking plants with huge capacities have now made ethylene and its homologs very cheap raw materials. Many products formerly produced from acetylene are now produced by new processes based on ethylene. Examples of such new processes are the production of acetaldehyde by *Wacker*'s process, of vinyl chloride by hydroxychlorination, of vinyl acetate from ethylene, oxygen, and acetic acid, of acrylic acid by oxidation of propene, and of acrylonitrile by *Sohio*'s process. Since there is little likelihood that the cost of ethylene will fall still further, acetylene chemistry could compete with ethylene chemistry if the cost of acetylene could be reduced to a level close to that of ethylene. One advantage of acetylene chemistry is that reactions with the extremely reactive alkyne compounds proceed more rapidly and sometimes in better yields than with olefins, which are generally less reactive.

2. Preparation of Acetylene

The processes developed at BASF for the industrial production of acetylene[1,2] by cleavage of light

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[1] *H. Friz*, Chemie-Ing.-Techn. *40*, 99 (1968).

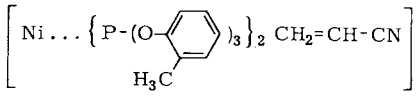
[2] *G. Dümgen, F. Neumayr, W. Teltschik*, and *U. Wagner*, Chemie-Ing.-Techn. *40*, 1004 (1968).

gasoline or of methane with oxygen in a burner are cheaper than the carbide process. Despite the low price of the starting materials, however, this acetylene still cannot compete in price with ethylene. Another process, the immersed flame process [1], was therefore devised at BASF. In this process, crude oil is vaporized with an oxygen-fed flame dipping into a crude oil sump, and the resulting cleavage gas containing acetylene is quenched by the surrounding oil. The immersed flame process is economical, since any crude oil may be used, and the carbon black formed as a by-product can be returned to the immersion burner as an oil-carbon black suspension for combustion. In addition to acetylene, the immersed flame process yields roughly the same amount of ethylene and synthesis gas. The trials carried out so far indicate that the immersed flame process will allow the industrial-scale production of acetylene at a price at which processes based on acetylene can compete with those based on ethylene.

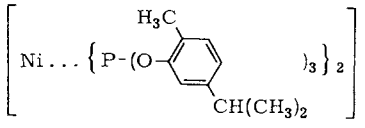
3. Cyclization Reactions

Acetylene or substituted alkyne derivatives undergo a number of cyclization reactions, of which no industrial use has yet been made. Products of such cyclizations include cyclooctatetraene [3, 4], benzene [5], substituted benzenes [5] such as trishydroxymethylbenzene, and other aromatic compounds. Since benzene and its homologs are cheaply available in large quantities by catalytic dehydrogenation of linear paraffins (hydroforming process), the production of benzene by catalytic cyclization of acetylene (*Reppe* [5]) in the presence of carbonylnickel-phosphine complexes such as $Ni(CO)_2[P(C_6H_5)_3]_2$ will not come into use despite the expected lower price of acetylene. On the other hand, the Reppe cyclooctatetraene synthesis and consequently cyclooctatetraene chemistry are becoming more promising as the cost of acetylene decreases, particularly since the cyclooctatetraene synthesis gives a yield of 70 % based on acetylene, and the costs of material and of production are low.

The catalytic cyclization of alkynes discovered by *Reppe* in the 1940's, when applied to propargyl alcohol [5] in the presence of $Ni(CO)_2[P(C_6H_5)_3]_2$ as catalyst, leads in almost quantitative yield to a mixture of 1,3,5- and 1,2,4-trishydroxymethylbenzenes (in a ratio of about 1 : 1). The mixture can be readily oxidized with nitric acid to trimesic and trimellitic acids. The cyclization of propargyl alcohol is strongly exothermic, and proceeds so violently that it can be controlled only at high dilutions, *e.g.* with benzene, and by careful addition of propargyl alcohol. Recent investigations have shown [6] that it can be very readily controlled and proceeds in good yields with practically no resin formation if carbonyl-free phosphite- or thiophosphitenickel(0) complexes such as acrylonitrilebis-(tri-*o*-cresylphosphite)nickel(0) *(1)* and bis(trithymylphosphite)nickel(0) *(2)* or nickel(0) complexes with similar structures are used as the catalyst instead of carbonylnickel-phosphine complexes.



(1)



(2)

Nickel(0) complexes in which the ligands have a branched or bulky substituent (*e.g.* isopropyl, *tert*-butyl, *o*-biphenylyl) *ortho* to the hetero atom that binds the organic residue to the P atom are particularly active catalysts.

For the cyclization of alkynes with these nickel complexes, a solution of the catalyst, *e.g.* in benzene, is heated to 70 °C and the alkyne is added slowly. The reaction, which usually begins immediately, can be controlled by the further addition of the catalyst solution and the alkyne, so that the reaction temperature of 70–80 °C can be maintained without external heat-

Table 1. Cyclic trimerization products of alkynes.

Alkyne compound	Cyclization product(s)	Yield (%)
2-Methyl-1-buten-3-yne	1,3,5-Triisopropenylbenzene 1,2,4-Triisopropenylbenzene	50
Propargyl alcohol	1,3,5-Tris(hydroxymethyl)benzene 1,2,4-Tris(hydroxymethyl)benzene	95 (1:1)
3-Butyn-2-ol	1,3,5-Tris(α-hydroxyethyl)-benzene 1,2,4-Tris(α-hydroxyethyl)-benzene	89 (1:1)
2-Methyl-3-butyn-2-ol	1,3,5-Tris(α-hydroxy-α-methylethyl)-benzene	93
Methyl propiolate	Trimesic acid Trimellitic acid	85
N,*N*-Dimethyl-2-propinyl-1-amine	1,3,5-Tris(dimethylaminomethyl)-benzene	67
N,*N*-Diethyl-3-butinyl-1-amine	1,3,5-Tris(α-diethylaminoethyl)benzene	93
Propargyl ethyl ether	1,3,5-Tris(ethoxymethyl)benzene 1,2,4-Tris(ethoxymethyl)benzene	77 (1:1)
1,4-Butynediol dimethyl ether	Hexakis(methoxymethyl)benzene	72
1,4-Butynediol	Hexamethylbenzene	10–15

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[4] *W. Reppe, O. Schlichting, K. Klager*, and *T. Toepel*, Liebigs Ann. Chem. *560*, 3 (1948).

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[6] *N. v. Kutepow* and *F. Meier*, German Pat. 1159 951 (1961), BASF.

ing. This process is applicable to practically all alkynes that, apart from the CC triple bond, are saturated or unsaturated or also contain functional groups, *e.g.* alkynols, alkynyl ethers, alkynecarboxylic acids and their esters, alkynylamines, and alkynediols. Some examples of the cyclotrimerization of alkynes are listed in Table 1.

The cyclotrimerization of alkynes does not always proceed in good yields. Propargyl chloride, for example, cannot be cyclized at all, and propargyl aldehyde gives only very low yields of benzenetricarbaldehyde. The cyclotrimerization of alkynediols and their derivatives also sometimes gives unsatisfactory yields (see Table 1).

These cyclizations are gaining in importance, not only because the alkynes are becoming cheaper, but also because of the general trend toward the development of new catalytic processes for the production of aromatic compounds. The initiation of this trend was partly due to the gradual closing down of town gasworks and the consequent decrease in the supply of tar products. The syntheses of hydroquinone from acetylene, carbon monoxide, and water and of methylated hydroquinones from propyne, 2-butyne, carbon monoxide, and water, which had been partially investigated earlier, have been re-examined and developed further in the light of experience accumulated in working with acetylene at high pressures.

3.1. Hydroquinone Synthesis

In the early 1940's, *Reppe*[7] discovered that acetylene and pentacarbonyliron react in aqueous alcohol at low temperatures and pressures (50–80 °C, 20–25 atm) to give hydroquinone. This reaction course was surprising in view of *Reppe*'s alcohol synthesis[8]

$$Fe(CO)_5 + H_2O \xrightarrow{\text{Alkali}} H_2Fe(CO)_4 + CO_2 \quad \text{(base reaction)}$$

$$H_2Fe(CO)_4 + 2\,R^1CH{=}CHR^2 + 4\,H_2O \rightarrow 2\,R^1CH_2{-}\underset{\displaystyle CH_2OH}{\overset{\displaystyle |}{C}}HR^2 + FeCO_3 + CO_2 + H_2O \qquad R^1, R^2 = H, \text{alkyl}$$

by analogy with which, the reaction of acetylene, pentacarbonyliron, and water would be expected to give unsaturated alcohols.

The hydroquinone synthesis also proceeds *via* the "base reaction", and is stoichiometric with respect to pentacarbonyliron. It is therefore favored by the addition of basic substances, particularly amines. The presence of a base is not, however, absolutely necessary, since the hydroquinone is also formed in the presence of compounds containing hydroxyl groups, such as water and alcohols. The following equations illustrate the course of the stoichiometric hydroquinone synthesis[7]:

$$Fe(CO)_5 + H_2O \rightarrow H_2Fe(CO)_4 + CO_2 \quad \text{(base reaction)}$$

$$H_2Fe(CO)_4 + 4\,C_2H_2 + 2\,H_2O \rightarrow 2\,p\text{-HO-}C_6H_4\text{-OH} + Fe(OH)_2$$

$$Fe(OH)_2 + CO_2 \rightarrow FeCO_3 + H_2O$$

$$Fe(CO)_5 + 4\,C_2H_2 + 2\,H_2O \rightarrow 2\,p\text{-HO-}C_6H_4\text{-OH} + FeCO_3$$

When bases are used, the hydroquinone yields are about 30 %[9] based on acetylene or alkylated alkynes.

As in all other carbonylations, efforts were made to induce the hydroquinone synthesis to proceed catalytically, *i.e.* instead of using carbonyliron as the carbon monoxide donor, to use carbon monoxide gas under pressure with carbonyliron as a catalyst.

According to *Reppe*, the hydroquinone synthesis can proceed partly catalytically[10] in the presence of complex salts such as $[Fe(NH_3)_6][Co(CO)_4]_2$ and $[Co(NH_3)_6][Co(CO)_4]_2$.

$$2\,CH{\equiv}CH + 3\,CO + H_2O \xrightarrow[80-100\,^\circ C,\ 5-30\ atm]{\text{Catalyst}} p\text{-HO-}C_6H_4\text{-OH} + CO_2$$

Most of the carbon monoxide, as before, is supplied by the carbonylmetal. The absolute yield of hydroquinone in this process is 35–50 % based on acetylene.

By varying the reaction conditions (*e.g.* by increasing the reaction pressure to 600–700 atm, the acetylene partial pressure to about 70 atm, and the temperature to above 170 °C) and by the use of suitable solvents (*e.g.* dioxane) and introduction of the water at a measured rate corresponding to the conversion (*e.g.* by addition of salt hydrates that give off water), the hydroquinone synthesis could be substantially improved in discontinuous experiments at first[11]. Higher hydroquinone yields (up to 70 % based on acetylene) could be obtained by these measures than in the process described earlier. Moreover, a large part of the carbon monoxide required in this process is supplied by the carbon monoxide gas, and not by the pentacarbonyliron, which also acts as a catalyst. Acrylic acid, the ester of hydracrylic acid with acrylic acid, polyacrylates containing iron, and succinic and other acids are formed as by-products of the hydroquinone synthesis.

We are now applying the experience and results accumulated from the discontinuous hydroquinone experiments to a continuous process in small reaction towers. The hydroquinone can be isolated from the crude product by various methods, such as recrystallization from water after removal of the solvent by distillation. A particularly pure hydroquinone is obtained if the solvent dioxane is distilled off together with water and pentacarbonyliron, the impure hydroquinone left behind being sublimed under vacuum and the sublimate stirred with cold toluene.

One advantage of the hydroquinone synthesis with pentacarbonyliron as the catalyst is the low price of the latter as compared with those of other catalysts, such as the ruthenium and rhodium compounds.

Howk and *Sauer*[12] allowed acetylene and carbon monoxide to react in the presence of a halide, carbonyl, or chelate of ruthenium or rhodium in water or alcohol at high temperatures

[7] *W. Reppe* and *H. Vetter*, Liebigs Ann. Chem. *582*, 133 (1953).

[8] *N. v. Kutepow* and *H. Kindler*, Angew. Chem. *72*, 802 (1960).

[9] *W. Reppe* and *A. Magin*, German Pat. 870698 (1944), BASF.

[10] *W. Reppe*, German Pat. 874910 (1951), BASF.

[11] *W. Reppe* and *A. Magin*, German Pat. 1232974 (1965), BASF.

[12] *B. W. Howk* and *J. C. Sauer*, US-Pat. 3055949 (1958), Brit. Pat. 850433 (1958), German Pat. 1135486 (1959), Du Pont.

and high pressures. They used aryl derivatives of group V elements, such as triphenylphosphine and triphenylstibine, as additional activators. The hydroquinone yield in this process is 4—55 % based on the acetylenic compound. The advantage of this process is the small amount of catalyst required, while its disadvantage is the danger of decomposition of the acetylene. Thus after evacuation of the autoclave, the acetylene is dissolved in a strongly cooled solvent, and after heating to the reaction temperature, carbon monoxide is forced in under a pressure of 600–900 atm. When this procedure is used, the system sometimes lies in the acetylene decomposition range before the introduction of the carbon monoxide because of an excessively high acetylene concentration in the gas phase.

In another method, which was discovered by *Pino, Braca,* and *Sbrana*[13], hydroquinone can be prepared from acetylene, carbon monoxide, and hydrogen, *i.e.* in the absence of water or compounds containing hydroxyl groups, with a trimeric carbonylruthenium as the catalyst and in a suitable solvent at 100—300 °C and 50—350 atm, in yields of up to 33 % based on the acetylene that reacts. Small quantities of catalyst are required, and its life is long. The loss of carbon monoxide that results from the formation of carbon dioxide in the presence of compounds containing hydroxyl groups is also avoided.

The Japanese Ajinomoto Company[14] recently discovered another variant of the hydroquinone synthesis, in which acetylene dissolved in water or alcohol (0.1—2 mole/l of solvent) is allowed to react with carbon monoxide or a mixture of carbon monoxide and hydrogen at high temperatures and pressures in the presence of rhodium compounds as catalyst. The reaction is accelerated by halides. The yields based on acetylene are 60—70 %.

One disadvantage of all processes in which rhodium catalysts are used is the fact that owing to the very high price of rhodium, it is absolutely essential to recover the rhodium compounds from the reaction product, and this recovery is expensive and involves difficulties.

The hydrogen required for the formation of hydroquinone in the synthesis using pentacarbonyliron as catalyst is supplied by the tetracarbonyldihydridoiron formed in the base reaction from pentacarbonyliron and water, which reacts with fresh carbon monoxide to give hydrogen and pentacarbonyliron. The course of the reaction is practically based on the water-gas reaction, which is controlled by pentacarbonyliron as the catalyst.

$$Fe(CO)_5 + H_2O \rightarrow H_2Fe(CO)_4 + CO_2$$
$$H_2Fe(CO)_4 + CO \rightarrow Fe(CO)_5 + H_2$$
$$CO + H_2O \rightarrow CO_2 + H_2$$

[13] *P. Pino, G. Braca,* and *G. Sbrana,* German Pat. 1251329 (1964), Lonza A.G.

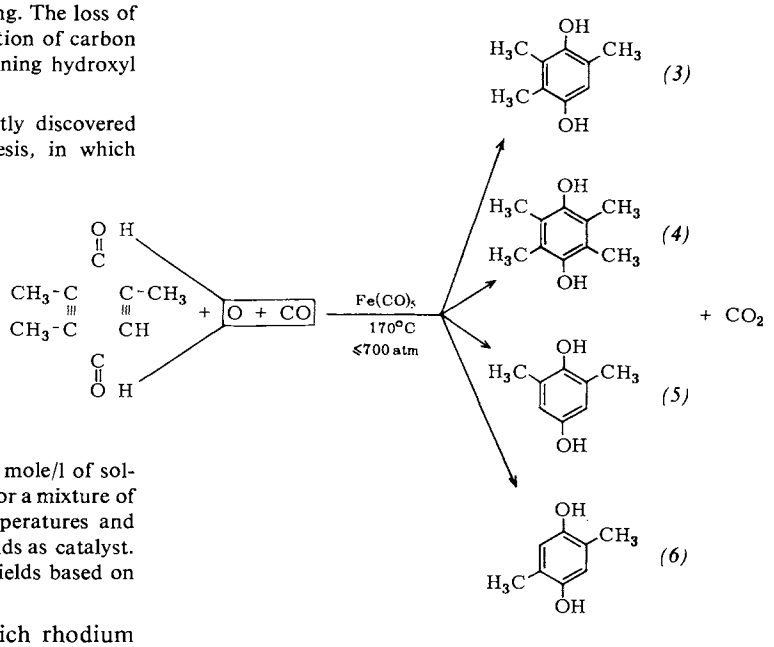
[14] Ajinomoto Co. Inc., French Pat. 1486666 (1966); identical with Japanese patents No. 42162 (1965) and No. 79069 (1965).

3.2. Cyclizations with Alkylated Alkynes

The hydroquinone synthesis with pentacarbonyliron as catalyst is applicable to all alkylated alkynes. Experiments have shown that methylacetylene and dimethylacetylene react more rapidly and under milder conditions than acetylene itself.

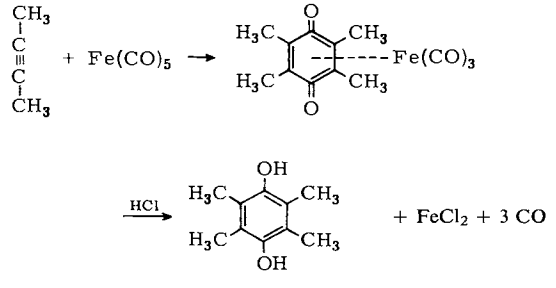
Thus a synthesis of trimethylhydroquinone from propyne, 2-butyne (1 : 1), carbon monoxide, and water with a cheap catalyst such as pentacarbonyliron has been developed on the basis of the process described for acetylene[11]. Trimethylhydroquinone is used in the synthesis of vitamin E.

Together with trimethylhydroquinone *(3)* as the principal product (≈ 55 %), however, tetramethylhydroquinone *(4)* (≈ 22 %) and 2,5- *(6)* (≈ 12 %)



and 2,6-dimethylhydroquinone *(5)* (≈ 11 %) are also formed. The yield of methylated hydroquinones, based on propyne and butyne, is up to 95 %. The formation of trimethylhydroquinone predominates even when the molar ratio of propyne to butyne is appreciably varied.

The course of the synthesis of methylated hydroquinones can be partly explained as a result of experiments by *Sternberg*[15]. This author obtained tetramethylhydroquinone by allowing two moles of dimethylacetylene to react with one mole of penta-



[15] *H. W. Sternberg,* J. Amer. chem. Soc. *80,* 1009 (1958).

carbonyliron under the action of sunlight to give a carbonyliron complex, which he then decomposed with hydrochloric acid.

It may be assumed that the synthesis of the trimethylhydroquinone from methylacetylene and dimethylacetylene proceeds *via* a carbonyliron complex having a similar structure; the complex is decomposed in this case by tetracarbonyldihydridoiron instead of by hydrochloric acid.

For the trimethylhydroquinone synthesis, it is very important to establish the reaction conditions under which it can proceed mainly catalytically.

The catalytic component of the synthesis follows from the percentage contribution of carbon monoxide gas to the total carbon monoxide consumed, the possible sources of carbon monoxide being the carbon monoxide gas and the pentacarbonyliron. Experiments in autoclaves have shown that the catalytic trimethylhydroquinone synthesis is strongly dependent on the pressure (Fig. 1). The synthesis proceeds practically stoichiometrically at 100 atm and 170 °C, but is 85–92 % catalytic at 700 atmospheres and under otherwise identical conditions.

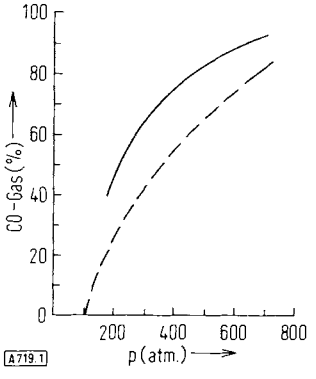


Fig. 1. Influence of the reaction pressure on the catalytic course of the trimethylhydroquinone synthesis at 160—170 °C.
Ordinate: Contribution of CO gas to the total CO consumption (from CO gas and $Fe(CO)_5$); ——: experiments in a 50 l reactor; - - - - -: experiments in a 0.8 l rolling autoclave.

The influence of the temperature on the synthesis is small over a narrow pressure range. Between 155 and 190 °C at 650 to 700 atm, the percentage contribution of carbon monoxide gas to the total carbon monoxide consumption decreases by about 10 % (autoclave experiment).

In addition to the usual advantages of catalysis, a largely catalytic course in this synthesis is even more desirable since iron ions resulting from the decomposition of pentacarbonyliron in a stoichiometric reaction form undesirable, insoluble iron compounds such as iron oxide. Moreover, iron ions react with the methacrylic and dimethacrylic acids formed as by-products to give polymeric iron acrylates containing up to 60 % of iron. All these insoluble compounds can lead to blockages in continuous-process furnaces.

On removal of the by-products and of the solvent, the mixture of methylated hydroquinones formed (referred to in future as the hydroquinone mixture) consists of about 55 % of trimethylhydroquinone and 45 % of other methylated hydroquinones. The influence of the molar ratio of propyne to 2-butyne on the composition of the hydroquinone mixture was therefore studied in autoclaves (see Fig. 2). The curves show that the percentage of trimethylhydroquinone *(3)* reaches its maximum value (55 %) at a molar ratio of propyne : 2-butyne = 50 : 50.

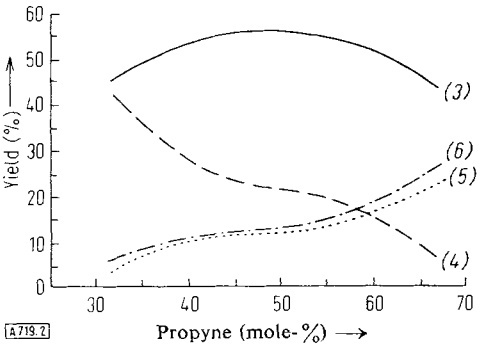


Fig. 2 Influence of the molar ratio propyne: 2-butyne on the composition of the mixture of methylated hydroquinones *(3)—(6)*.

To determine the conversion of propyne and butyne into the hydroquinone mixture as a function of the reaction conditions such as the concentrations of catalyst and of water and the contact time, we carried out experiments in 0.8 l rolling autoclaves.

The reaction mixture used generally contained about 70–80 % of dioxane, 7—9 % of propyne, and 9—10 % of butyne; the remainder consisted of pentacarbonyliron and water.

300—400 atm of carbon monoxide were forced in over the cold reaction mixture. When the reaction temperature of 170—200 °C had been reached, more carbon monoxide was pumped in to bring the pressure to the desired 600—700 atm.

Solvents such as acetone, methylpyrrolidone, and tetrahydrofuran were tried; dioxane was found to be particularly suitable.

The conversion of the alkynes into the hydroquinone mixture increases with increasing catalyst concentration. It is best to keep the pentacarbonyliron concentration below 20 % and to accept a conversion of less than 70 %. Higher carbonyliron concentrations lead to a decrease in the percentage contribution of carbon monoxide gas to the total carbon monoxide consumption, *i.e.* to a decrease in the catalytic component of the synthesis.

The influence of the water concentration in the reaction mixture on the conversion is very great at levels below 4 %. Higher water concentrations offer no advantage (see Fig. 3).

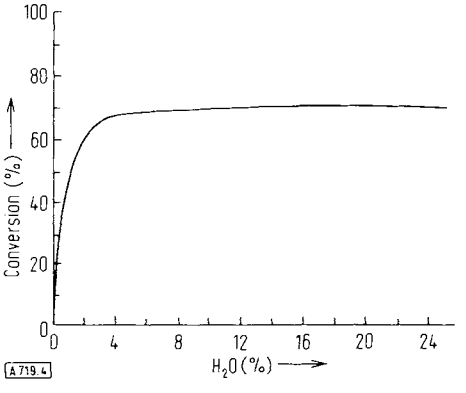


Fig. 3. Influence of the water concentration in the reaction mixture on the conversion of propyne + 2-butyne into the hydroquinone mixture.

In the hydroquinone synthesis, unlike in the trimethylhydroquinone synthesis, the yield and the conversion are reduced by higher water concentrations in the reaction medium, and the water must therefore be added at a measured rate.

While the conversion in the trimethylhydroquinone synthesis varies with the reaction conditions, the yield of hydroquinone mixture is about 95 % based on propyne + 2-butyne, with an approximately adjustable trimethylhydroquinone content of 55 %. The average space-time yield based on the mixture of methylated hydroquinones is about 1.0 in the autoclave experiments, with peak values of about 1.5 kg l^{-1} day^{-1}, corresponding to 0.55 and 0.66 kg l^{-1} day^{-1} respectively based on trimethylhydroquinone.

In the hydroquinone experiments in autoclaves under pressures of 600–700 atm, the content of alkynes in the gas phase (which consists mainly of carbon monoxide) is less than 5 %, *i.e.* well on the safe side of the explosion limit, owing to the ready solubility of alkynes in the reaction mixture. Measurements by *Zieger*[15a] have shown that the decomposition limit of pure acetylene-carbon monoxide gas mixtures at 600–700 atm is around 12 % of acetylene and 88 % of carbon monoxide, and the explosion range is reached only above this acetylene content. Since propyne and 2-butyne decompose less readily than acetylene, and the vapor pressure of the solvent has an inhibiting action on the decomposition, the discontinuous hydroquinone and trimethylhydroquinone experiments described are perfectly safe.

The trimethylhydroquinone synthesis was also carried out continuously in a small trials apparatus.

The feed (200 ml/h), which consisted of dioxane, propyne, butyne, pentacarbonyliron, and water, had approximately the same composition as the reaction mixtures in the discontinuous autoclave experiments. The continuous experiments were generally carried out at 160—200 °C and 600 to 650 atm. The feed was introduced, by means of a metering pump, into the lower part of the furnace together with the carbon monoxide, and the reaction product from the top end of the furnace was allowed to expand past a pressure inspection window into a discharge vessel.

The resulting conversions of propyne and butyne into the methylated hydroquinones were about 50–60 %, with a yield of 95 %. The conversion can be considerably increased by the use of a higher carbonyliron concentration in the reaction mixture.

By optimization of the reaction conditions, it was possible in the continuous experiments to increase the space-time yield of the methylated hydroquinones to about 1.5 kg l^{-1} day^{-1} and that of trimethylhydroquinone to about 0.7 kg l^{-1} day^{-1}.

The methylated hydroquinones *(3)—(6)* in the mixture were determined as trimethylsilyl ethers by gas chromatography and directly by NMR spectroscopy. The very small quantities of iron present in the samples for NMR spectroscopy first had to be eliminated, *e.g.* by vacuum sublimation (0.1—1 torr and up to 180 °C) of the methylated hydroquinones.

It is practically impossible to separate the trimethylhydroquinone from the other methylated hydroquinones by distillation, since all methylated hydroquinones preferentially sublime under vacuum, and must be heated so strongly for distillation that large losses occur by decomposition.

[15a] *A. Zieger* (BASF), unpublished.

Quantitative separation of trimethylhydroquinone and tetramethylhydroquinone by fractional crystallization is impossible, since the two compounds (as is shown by Debye-Scherrer photographs) are isomorphous, and so form solid solutions.

The hydroquinones could be separated in good yields by oxidation to the corresponding quinones and separation of the quinones by vacuum distillation. Hydrogenation of the pure trimethylquinone then gave trimethylhydroquinone. The separation of the methylated quinones by vacuum distillation presents no difficulties, owing to their favorable vapor pressure curves.

Methylated hydroquinones can be oxidized to quinones in various ways. In the stoichiometric method, nitric acid[16], or even iron(III) sulfate in small laboratory experiments, may be used as the oxidizing agent.

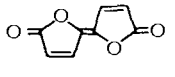
Many heavy metal salts have been examined as catalysts for catalytic air oxidation experiments. An aqueous solution of 3–5 % of $CuCl_2$ and 6 % of NH_4Cl was particularly active. The methylated quinones formed on catalytic air oxidation react with unreacted methylated hydroquinones to give quinhydrones, and they thus block the oxidation. The hydroquinones could be oxidized to the quinones in solvents such as cyclohexane, in which only the quinones dissolve, and the quinones were then separated in a simple extraction apparatus in a yield of 97 %.

To isolate the trimethylbenzoquinone, the quinones were fractionated at 10–70 torr[17]. The trimethylbenzoquinone isolated in this way was almost quantitatively hydrogenated to trimethylhydroquinone in alcohol at room temperature and at a hydrogen pressure of about 100 atm in the presence of Raney nickel.

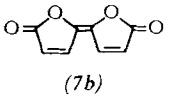
The effective yield of 96–99 % trimethylhydroquinone is 44 % based on propyne and butyne; this value is calculated from the yield of the methylhydroquinone synthesis (95 %), the content of trimethylhydroquinone in the hydroquinone mixture (55 %), and the yields of the oxidation (97 %), the distillative separation of the quinone mixture (90 %), and the hydrogenation of trimethylquinone (98 %). The yield of the quinone distillation can be further improved.

3.3. Synthesis of Unsaturated Dilactones

According to *Reppe*, the reaction of acetylene and carbon monoxide (in a ratio of 1 : 2) in the absence of water and in the presence of complex cobalt catalysts or their components can lead under pressure to heterocyclic compounds, such as the unsaturated dilactone *(7)*, which is obtained as a *cis,trans* isomer mixture[18] [*(7a)*, m.p. 256–257 °C; *(7b)*, m.p. 234 to 235 °C].



(7a)



(7b)

[16] *H.-I. Joschek* (BASF), unpublished.

[17] *H.-I. Joschek* (BASF), unpublished.

[18] *W. Reppe* and *A. Magin*, DAS 1071077 (1965), BASF.

The catalysts consist of octacarbonyldicobalt or cobalt salts and compounds such as ketones or nitriles, which can form complexes with $Co_2(CO)_8$, *e.g.* with the following composition [19]:

$$[Co(L)_n]^{2\oplus}[Co(CO)_4]_2^{\ominus} \quad \begin{matrix} L = \text{ketone or nitrile} \\ n = 1-6 \end{matrix}$$

The reaction proceeds at 40–100 °C with a dilactone yield of 15–40 % based on acetylene; coumarin is formed as a by-product. Substituted acetylenes give correspondingly substituted dilactones. It has also been suggested [20] that the reaction be carried out at 50–3000 atm and 60–175 °C.

4. Closing Remarks

Some of the cyclic compounds described may prove interesting as starting materials and intermediates. The condensation of trimethylhydroquinone with isophytol, for example, yields DL-α-tocopherol (vitamin E). A cheap hydroquinone can also be used for the preparation of anthraquinone by oxidation to *p*-benzoquinone, Diels-Alder reaction of the latter in a molar ratio of 1 : 2 with butadiene [21], and air oxidation of the resulting octahydroanthraquinone in ethanolic potassium hydroxide solution. The yield of anthraquinone based on benzoquinone is about 85 %. The synthesis of unsaturated dilactones may open up a new route to suberic acid if acetylene is available at a favorable price, since such dilactones can be readily hydrogenated with platinum catalysts in polar solvents to give suberic acid.

The cyclization of alkynes shows that if these compounds can be obtained at a reasonable price, they can be used for the production of cheap cyclic intermediates. The economic aspect becomes even more attractive if even cheaper materials such as carbon monoxide and water are used as well as acetylenes.

Received: July 11, 1969 [A 719 IE]
German version: Angew. Chem. *81*, 717 (1969)
Translated by Express Translation Service, London

[19] *W. Hieber*, German Pat. 953796 (1954), German Pat. 1083264 (1958), BASF.

[20] *J. C. Sauer*, German Pat. 1054086 (1955), Du Pont.

[21] *I. G. Farbenindustrie*, German Pat. 494433 (1930).

Modern Analysis[1]

By H. Kienitz[*]

Dedicated to Professor B. Timm on the occasion of his 60th birthday

The important advances being made in modern analytical methods are indicative of the fundamental changes that are occurring in the theory and practice of "analytical chemistry". "Information optimization" demands a new approach in teaching and research, and calls for the integration of chemistry with other scientific and technical disciplines.

1. Introduction

Analysis may be defined as the gaining of information about the qualitative and quantitative composition and about the steric structure of substances and chemical species. The modern paths to this type of information differ in method (chemical and physical processes), in execution (accuracy, speed, economy, and possibility of automation), and with regard to acquisition, critical examination, and representation of the results. The analyst's knowledge, discretion, and experience are applied to the task of choosing the optimum path, which best suits the manifold factors involved and the analytical problems, and provides an adequate and correct result.

A survey of the problems and sectors of analysis is given in Table 1.

Although much scientific progress and industrial development has only been made possible by the results of analytical investigations, analysis has unfortunately still not received full recognition as a subject in its own right. The manufacture of inorganic and organic products can no longer be carried out without constant analytical supervision. Trace and micro methods of analysis have found a place in every field of applied natural science, and have helped us to understand processes that were formerly beyond the reach of quantitative examination.

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[1] Based on a lecture read at the General Meeting of the Gesellschaft Deutscher Chemiker at Hamburg on September 18, 1969.

Table 1.

Problems of analysis:

1. Qualitative analysis of a mixture of substances (for elements, ions, atomic groupings, functional groups, or components)
2. Quantitative analysis of parts or of the whole of a mixture of substances
3. Qualitative analysis of a chemical species (single molecule, macromolecule, unit cell)
4. Quantitative analysis of a chemical species (number and steric arrangement of the atoms and atomic groupings)

Sectors of analysis:

1. Sampling and sample preparation
2. Analytical procedure
   - A. Methods
     - a) chemical
     - b) physical, with alteration of the substance
     - c) physical, without alteration of the substance
   - B. Conditions, imposed
     - a) by the analytical problem
     - b) by the substance to be investigated (quantity, nature, and state)
   - C. Requirements
     - a) accurate, comprehensive, critical
     - b) fast
     - c) economical
     - d) automatic
3. Critical evaluation of the analytical result. Drawing of conclusions from this result

In this article we shall consider some modern developments selected from the many aspects of the analyst's work.

2. Analysis of Inorganic Solids

The sampling of inorganic solids presents interesting and often difficult problems. Sampling is the first step in the sequence sampling – sample preparation – analysis – data processing. A sample taken from a quantity of material that is often many orders of magnitude greater should be representative.

Whether or not sampling is satisfactory depends on the requirements; thus, the requirements for a preliminary analysis (accuracy ±10%) are less rigorous than those for an analysis for commercial purposes (accuracy ±1 or even 0.2%). Sampling errors are in general fully reflected in the final result. The number and size of the samples to be taken are determined statistically by the homogeneity of the material, the uniformity of its density (separation of the components), and its particle size. The probability of inclusion in the sample should be uniform for the material as a whole. This is possible, in general, only if the material is in motion. Mechanized sampling therefore always uses a moving stream of material, such as the material transported by a conveyor belt, the sample being taken on the basis of quantity or of time. This is followed by gradual mechanical reduction of the size of the sample, which is also comminuted in stages. Large-scale units capable of sampling with a reproducibility of a few tenths of one percent have been constructed in recent years for the metal and potash industries.

The influence of inhomogeneities in a solid sample on the analytical result increases as the region covered by the analytical process decreases. Thus inhomogeneities are of practically no importance in neutron activation analysis, whereas they have an appreciable effect in X-ray fluorescence analysis and a strong effect in mass and emission spectrometry.

The detection limits and application ranges of some chemical and physical methods are shown in Figure 1.

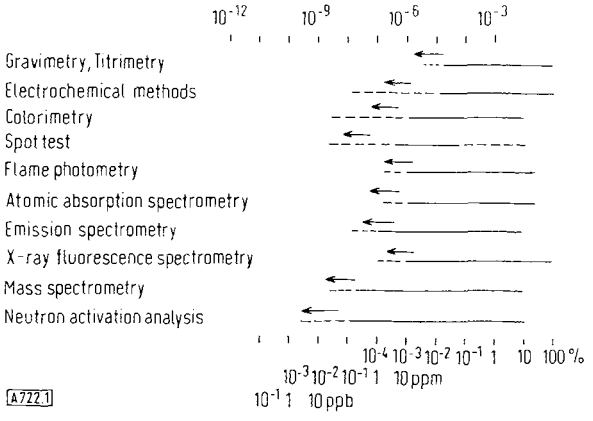


Fig. 1. Detection limits (←) and application ranges (- - - ——) of important analytical methods.

The element specificity of these methods is generally satisfactory, though masking can occur (*e.g.* in the analysis of metals) in both emission and mass spectrometry. The problem of masking can often be overcome by combination with chemical methods.

The detection limits for atomic absorption spectroscopy have recently been improved by two orders of magnitude by evaporation of the samples in graphite cells, with the result that they are now close to the limits for emission and mass spectrometry.

Wider use of neutron activation analysis has been hindered by the lack of neutron sources with adequate neutron fluxes (apart from nuclear reactors) and of detectors with narrow energy bands. The situation has been improved by neutron sources that produce neutron fluxes of up to 10^{10} n/cm² by the T(d,n)He reaction; fast neutrons are particularly desirable for the analysis of elements of the first short period, which are only weakly activated by thermal neutrons in the reactor because of their small cross section. However, activation with fast neutrons has the disadvantages that the detection limits for activation in reactors (neutron flux 10^{14} n/cm²) cannot be reached for heavier elements, and that very short-lived nuclides are formed in most cases. The detection limits for the light elements nitrogen, oxygen, fluorine, and phosphorus, on the other hand, are between 10 and 100 μg for a neutron flux of 10^9 n/cm².

The resolving power of scintillation detectors with NaI crystals and photomultipliers, such as are used for the measurement of the radiation from the activated elements, is only about one tenth of that of the semiconductor detectors that have recently come into use. Thus the relative energy half-width of the ^{60}Co γ line at 1.33 MeV is 5.9% (80 keV) when measured with an NaI(Tl) crystal, but only 0.45% (6 keV) with a Ge(Li) detector (Fig. 2).

In neutron activation analysis, in which several nuclides are activated during the irradiation, many individual nuclides can be both identified and used for very selective quantitative determinations on the basis of the typical maxima of their gamma spectra and the rate of decay of their radiation, corresponding to the half lives. Wet separations of the nuclides formed on irradiation can thus be largely avoided.

Special mention should be made of the extreme difficulty of the preparation of calibration standards for trace determinations. Conflicting results, often differing by several orders of magnitude, depending on the method (particularly in the ppm range), are not un-

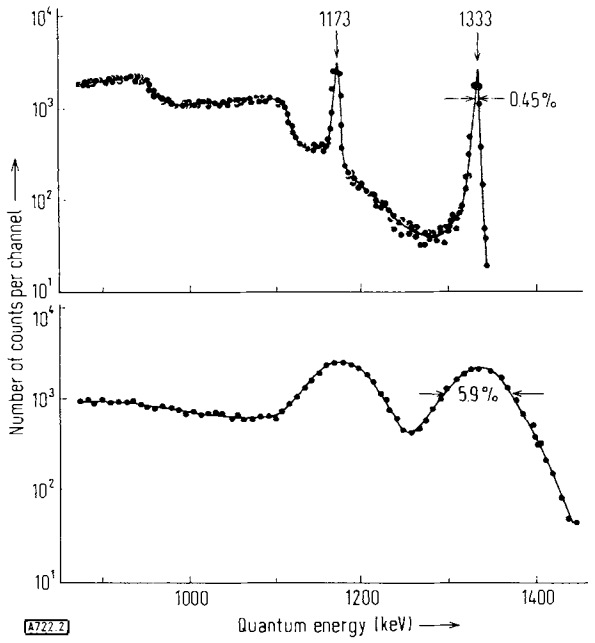


Fig. 2. Comparison of the energy spectrum of ^{60}Co recorded with a germanium detector (top) and with a scintillation detector using an NaI crystal (bottom).

common. Absolute values might be obtained by mass spectrometry if the ion sources had fixed ion yields for known ionization probabilities without interelement effects; the results are, however, at best only semiquantitative. Reliable calibration standards are therefore essential in trace analyses, whether by mass spectrometry or by any other method. Zone melting can be used for the purification and subsequent doping of samples whose melting points are not too high (≈800 to 1000 °C). Since it is very difficult to avoid inhomogeneities and contamination during the mixing, fusing, or sintering of samples, the only way of obtaining quantitative standards for trace concentrations is by chemical analysis, though some uncertainty remains even here because of possible contamination during concentration.

For compact inhomogeneous samples, where we are interested not in an average analysis but in the investigation of individual phases and their distribution in an area or volume, the examination can be carried out after mechanical or chemical separation of the phases, or otherwise by point analysis of small surface or volume elements (on ground surfaces or their sections) without phase separation.

The principal methods for the analysis of solids are surveyed in Figure 3.

Point examination of solid samples can be achieved with the aid of electron, ion, or laser beams. A region about 30 μm in diameter is evaporated from the sample *e.g.* with a laser beam to form a crater. The vapor is ionized with auxiliary electrodes and analyzed by emission or mass spectrometry. The electron beam of a "microprobe" has a diameter of ≈2 μm. It produces element-specific secondary X radiation at the surface of the sample, and the spectrum and intensity of this radiation are determined with proportional counter tubes. The scanning of the surface may also be carried

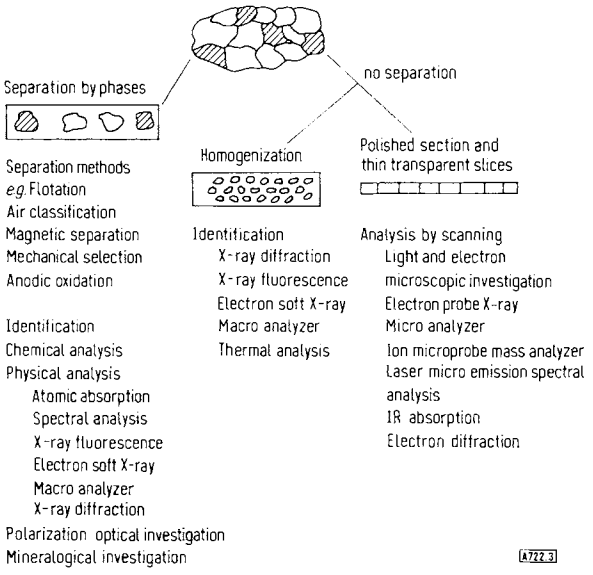


Fig. 3. Analysis of solids.

out with an ion beam, the secondary ions produced being led to a small mass spectrometer. The electron and ion microprobes give only semiquantitative analytical information for local areas; the distribution of the phases in a surface region can, however, be found very accurately by measurement of the relative areas.

With the macroprobe, the area irradiated with electrons (about 2 cm^2) is several orders of magnitude greater than with the microprobe. The X-rays produced at the surface of the sample are again used for qualitative and quantitative analysis. This is a good method for the determination of the light elements boron to sulfur. Macroprobe analysis is more sensitive to surface impurities than X-ray fluorescence analysis; moreover, its use is confined to electrically conducting samples (or samples with a conducting coating).

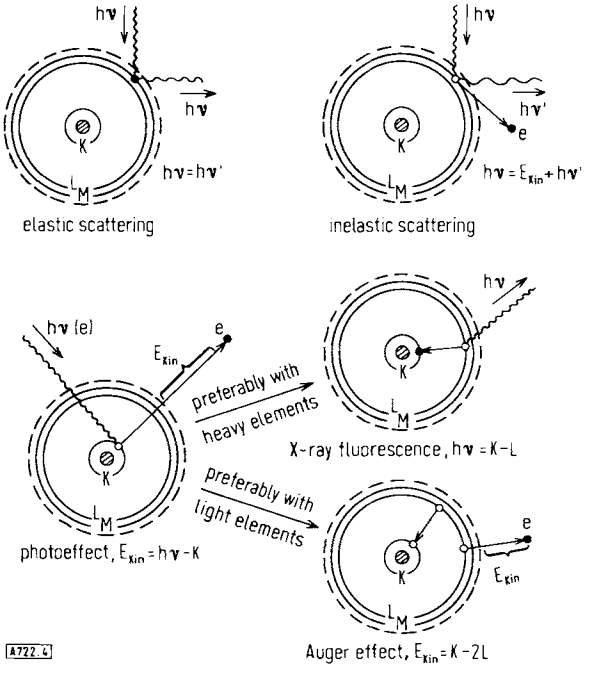


Fig. 4. Interaction of X-rays (or of electrons) with matter.

X-ray fluorescence, microprobe, and macroprobe analyses are based on atomic processes in which electrons or X-ray quanta interact with the electrons of an atom (Fig. 4).

The photoeffect involves the ejection of electrons from the inner shells by the incident X-ray quanta. The bonding state of the emitted electron can be deduced from its kinetic energy and the energy of the absorbed quantum. The vacancy left by the ejected electron is then filled by outer electrons, the energy liberated being released as an X-ray quantum (X-ray fluorescence) or in the form of a secondary emitted electron (Auger electron). For the ejection of inner electrons, the X-ray quanta may be replaced by electrons of corresponding energy.

The possibilities offered by spectroscopy based on the emission of Auger electrons will be merely mentioned here. This method can be used for the analysis of surfaces (the topmost one or two layers of atoms), and has a high detection sensitivity, particularly for light elements. It is possible in this way to detect partial coverages of 0.1 (and in special cases down to 0.01) layer of atoms. The method is therefore very promising for use in problems of catalysis, adsorption, corrosion, and surface diffusion.

The photoelectric effect, in which electrons are released from the inner (K or L) shells of an atom by X-ray quanta ($Al_{K\alpha}$ or $Mg_{K\alpha}$ radiation) has recently acquired growing analytical importance. The emitted electrons are separated in a magnetic field according to their energy distribution (ESCA, *E*lectron *S*pectroscopy for *C*hemical *A*nalysis). The element-specific energy distribution of these secondary electrons is shown in Figure 5.

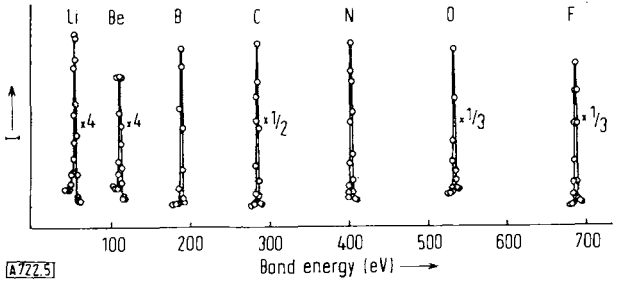


Fig. 5. Photoelectron signal of the elements of the second period (K shell).

Since the kinetic energy of the emitted electrons varies by several electron volts (1 eV $\triangleq$ 29 kcal/mole), according to the bonding state of the atoms, conclusions may be drawn, for example, regarding the bonding state of the two differently bound sulfur atoms in thiosulfate or of the differently bound iodine atoms in iodide or iodate. This method, which possesses considerable potential for the analysis of organic compounds, will be dealt with again in Section 4.

Development trends in the analysis of inorganic substances, taken as a whole, point to the need for the determination of traces, non-destructive methods of analysis, and methods that allow at least semiquantitative analysis of the smallest possible areas or volumes. There is also an increasing demand for methods that are capable of being automated.

3. Chromatography

F. F. Runge, who discovered aniline in coal tar, separated the components of dyes into brightly colored ring-shaped zones by placing a drop of a solution in the middle of a sheet of blotting paper. He mentioned this process as early as 1822, in his dissertation, and in 1850 he published a book "Zur Farbenchemie, Musterbilder für Freunde des Schönen und zum Gebrauch für Maler" (Color chemistry, patterns for lovers of beauty and for artists). Though he had discovered the basis of paper chromatography, and even introduced the "development" of colorless into colored zones, he had no thought of an analytical method. *C. F. Schönbein*, *F. Goeppelsroeder*, and *E. Fischer* also used this method during the last century for the separation of ions of inorganic salts, as well as of dyes, and it was finally introduced into analysis by *M. Tswett* as "chromatography" (derived from the Greek τὸ χρῶμα, the color). He resolved the dye leaf-green into green and yellow zones in separating columns packed with an adsorbent.

Separations of this type (on "two-dimensional" thin layers in thin layer or paper chromatography, and on "one-dimensional" columns in liquid or gas chromatography) are still referred to as "chromatography", though they are no longer used only for the separation of colored components. Chromatography has grown into an essential analytical tool, particularly gas chromatography, which can be traced back to *A. T. James* and *A. J. M. Martin*, and even to *A. Eucken* and *E. Cremer*.

Efforts are being made in all chromatographic methods to improve the separation and the detection. In the two-dimensional thin layer and paper chromatography, the separation and the specificity for certain groups of substances are improved by the successive use of diffusion effects in two directions or by the simultaneous use of different physical effects, as in electrophoresis. The detection is often based on specific color reactions. Thin layer chromatography, and to some extent also paper chromatography, have recently been developed into quantitative methods, and variances of less than 3% have been obtained for repeated determinations. Refinements are continuously being made to the technique of these methods in order to increase their basically rather limited separatory efficiency.

In the one-dimensional separation methods of column and capillary (liquid and gas) chromatography, the detection of the eluted substances is almost ideally solved for gas chromatography. The detectors are characterized by very high sensitivity over a very wide dynamic range, and combination of this with substance-specific methods (particularly with mass spectrometry, as a combination of two trace and micro methods) is particularly effective. Though liquid chromatography is also capable of giving very good separations, the problem of the detection of the eluates is still unsolved. Physical effects in the liquid phase cannot be expected to give detector signals of the same order of magnitude as those obtained in the gas phase; transfer detectors, which transfer the liquid

eluate of liquid chromatography into a flame ionization detector, side-step the problem instead of providing a true solution.

Though the substance specificity of the flame ionization detector is poor, the value of gas chromatography is that it can tell us that a substance originally thought to be pure actually contains at least as many impurities as there are additional signals in the chromatogram, apart from the principal component. It is now known that even the "purest substances" are generally accompanied by traces of numerous other substances. The uncontrolled use of analytical methods in which a substance is examined "en bloc" is thus no longer justifiable, and a chromatographic analysis should always be carried out either beforehand, simultaneously, or afterwards to enable the interpretation of the results to be completed. This is true even of the so-called highly specific methods, apart from the purely element-specific ones.

Whereas further appreciable progress in gas chromatography is to be expected only in fast and high-efficiency separations and in the ultra-trace and maximum-selectivity fields, the development of classical column chromatography into modern liquid chromatography in columns has just begun.

In gas chromatography, the techniques used in present-day practice are still lagging appreciably behind the latest developments (Fig. 6).

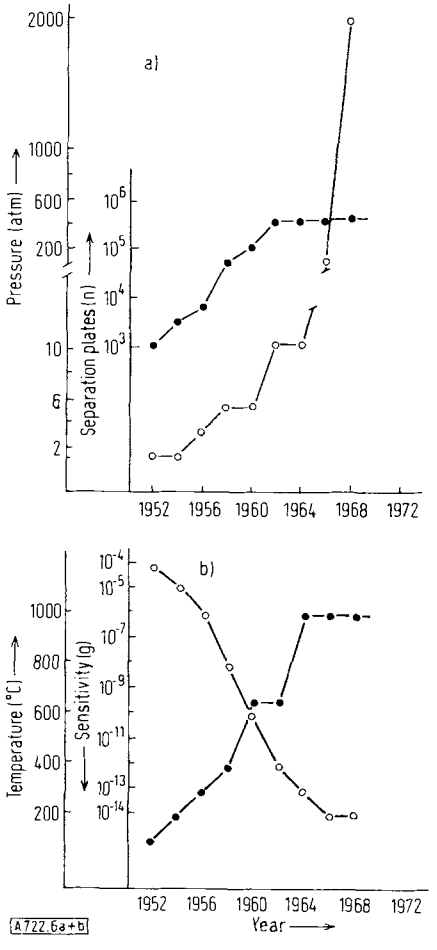


Fig. 6. Development of gas chromatography: a) Pressure (o); number of separation plates (•) — b) Sensitivity (o); temperature (•).

The present stage of development can be summed up as follows. While retaining its extremely broad scope, gas chromatography has become the most accurate quantitative method for the analysis of volatile or decomposable organic substances. The substance to be detected enters the detector at a low concentration, *i.e.* in the ideal state from the physical and measurement points of view; the matrix, *i.e.* the carrier gas, is extremely pure. Variances of down to 0.01 % are quite possible. Gas chromatography allows analyses to be carried out over the concentration range of from 10^{-5} to 100 %; in special cases, volatile stable substances in gases can be detected down to a concentration of 10^{-10} %. One sample can be resolved into as many as 400 (and in special cases up to 1000) chemical species. Quantitative determinations take about 1 to 20 min and require about 10^{-3} g of sample, though 10^{-6} to 10^{-8} g would be sufficient if it were possible to prepare and transport such small quantities of material. More than 100000 chromatographs were in use in laboratories and factories in 1968; only a few percent of these are used in process chromatography, though gas chromatography is excellently suited for automation.

The existing practical achievements are not yet enough. It is expensive to obtain information that can be evaluated directly (on-line) with a computer. Mechanization has not yet gone far enough; though semi-automatic gas chromatographs are already commercially available, their operation is unchecked and uncritical. The separating power, sensitivity, and speed in routine analyses are generally lower by more than two orders of magnitude than they need be, and in some cases than the levels required on economy grounds. For example, up to 3000 separation plates per instrument are often accepted where up to 100000 are needed to detect the components in question. The sensitivity of ordinary commercial instruments is so low that it is just possible to recognize traces at a concentration of 10^{-4} % (ppm), though traces in the 10^{-7} % (ppb) range should be detectable, and these are the very components that are often found to be of immense importance both in chemical and in biochemical processes.

Gas chromatography is today making a decisive contribution to the utilization of the capabilities of structure-specific and structure-identifying methods, and the combination of chromatographic methods is becoming increasingly important (Fig. 7).

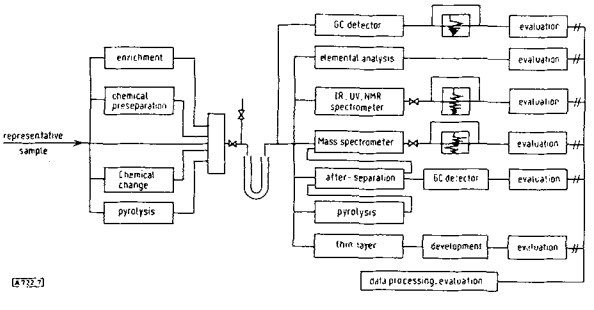


Fig. 7. Possibilities for the combination of gas chromatography with other analytical methods.

Little can be said yet about the state of modern liquid chromatography, except that the expected broad development has probably started this year. The first instruments allowing fast column chromatography with high entry pressures and high separation efficiencies with programmed gradient elution have

Table 2. Survey of chromatographic separation methods.

Mobile phase	Stationary phase	Pressure (atm)	Temperature (°C)	Geometry	Name of method	Applications and capabilities
Gas	Liquid [a]	0.1 to 10 (2000) [d]	Up to about 500 [d]	Tube dia. 0.01 to 10 mm, length a few cm to km	Gas partition chromatography	General: gas chromatography. For volatile or decomposable substances that can be converted into volatile or decomposable derivatives. Qualitative and above all quantitative analysis of all substances that are soluble in the mobile phase in seconds to minutes
Gas	Solid [b]	0.1 to 10 (2000)	−210 to 1700	Tube dia. 0.1 to 10 mm, length a few cm to 0.1 km	Gas adsorption chromatography	
Gas	Solid [c]	0.1 to 10 (2000)	−210 to 1700	As above	Gas diffusion chromatography	
Vapor (in the supercritical state)	One of the above three	[e]	[e]	As above	Dense gas chromatography	
Liquid	Liquid [a]	[d, f], depends on T	[d, f], depends on p	Tube dia. 0.1 to 10 mm, length a few cm to 0.1 km	Column chromatography with secondary names indicating the nature of the separation process, of the stationary phase, or of the material or physical programming	General: liquid chromatography. For all substances that are soluble in the mobile phase. Qualitative and quantitative analysis in seconds to hours
Liquid	Solid [b]	As above	As above	As above	As above	
Liquid	Solid [c]	As above	As above	On layers	Thin layer chromatography	
				On paper	Paper chromatography	
				In a thin film of the stationary phase on an inert rough-surfaced support	Thin film chromatography	

[a] On porous support or wall. [b] Absorbent. [c] Microporous, inert (*e.g.* glass, metal, ceramics, molecular sieve, clathrate former).
[d] Possibly programmed. [e] Depends on the supercritical data for the mobile phase. [f] Depends on the separating system.

already been constructed; however, they are still much more complicated than modern gas chromatographs. In a typical example, almost 8000 separation plates are obtained per meter of column length (diameter 2 to 3 mm) at a rate of 40 separation plates per second.

An intermediate position between gas chromatography and liquid chromatography is occupied by "dense gas chromatography", which is chromatography in the supercritical fluid state, in which elution is carried out at carrier gas pressures of up to 2000 atm. Intermolecular forces in polymers having molecular weights of up to several hundred thousand can be broken down, thus permitting separations far superior to those achievable by gel permeation chromatography. During this kind of chromatography in the supercritical region of the carrier gas, a temperature of 40 °C is sufficient to volatilize substances which would hardly have been thought to behave in such a manner, *e.g.* carbohydrates such as ribose, arabinose, xylose, and glucose at pressures of about 1400 atm in carbon dioxide.

All chromatographic methods require at least one mobile and one stationary phase.The separation of the substances in question is based on differences in the migration rate, solubility, complex formation, adsorption, and includability, and the pressure, temperature, and geometry of the system play a very important part. All possible intermediate stages and combinations are possible between "solution", "chemical bonding", "adsorption", and "sieve effect", and in general, none of these principles acts alone. It is therefore problematic to use names that involve the mechanism of action. Modern chromatographic methods are not only a decisive part of modern analysis; they also, *per se*, provide a constant feedback to the theory and practice of physicochemistry and chemistry.

4. Structural Analysis of Organic Compounds

It has been found convenient to classify organic compounds according to the manner in which the C atoms are linked. They are described according to their carbon skeleton, according to whether the C chains are linear or branched, according to whether they are single carbocyclic or heterocyclic rings or ring systems, and according to the size of the rings and the bonding of the members. Functional groups are inserted in or attached to the carbon skeleton or the heterocyclic nucleus and give rise to the great variety and complexity of organic compounds. The ordering principle of "skeleton" and "functional group" is also followed in the nomenclature. It would be particularly useful if the information and results of a structural analysis also fell into these categories.

Table 3. Comparison of some methods of structural analysis.

Method	Sample	Information
Infrared spectroscopy (microwave spectroscopy) Absorption of infrared light (or microwaves) due to excitation of vibrations and internal rotations of molecules	Solid, liquid, solution, gas or vapor 1—10 mg, in microcells from 10 μg	Structural elements and ring systems of atomic skeletons consisting of carbon and hetero atoms, functional groups, hydrogen bonds, symmetries, isomerism
Raman spectroscopy Scattered radiation whose frequency is the difference between the frequency of the incident visible light and the frequency of the excited molecular vibrations	Solid, liquid, solution 50 mg — 10 g, with laser excitation from 1 mg	As infrared spectroscopy; selection rules of the normal vibrations make the two methods complementary; valuable for symmetrical molecules
Electronic spectroscopy Absorption of ultraviolet and visible light according to the electron levels in molecules	(Solid), liquid, gas, vapor, dilute solution 0.1—10 mg	Double bonds and single electrons, particularly conjugated systems, *e.g.* aromatic compounds, heterocyclic systems with aromatic character
Nuclear magnetic resonance Absorption of radio waves due to resonance of nuclear spin moments in a magnetic field	Solution 5—100 mg	Structural elements and functional groups on the basis of the environment of protons or of nuclei that exhibit nuclear magnetic resonance (*e.g.* ^{13}C, ^{19}F, ^{29}Si, ^{31}P); determination of the hydrogen (proton) content of chemical compounds and groups
Electron spin resonance Absorption of radio waves due to resonance of electron spin moments in a magnetic field	Solid, liquid, solution 1—200 mg 5—100 mg	Detection and determination of free radicals, their structure and electron distribution
Optical rotation, circular dichroism Rotation of the plane of polarized light, difference in absorption of right-handed and left-handed polarized light as a function of wavelength	Liquid, solution 1—200 mg	Relative and absolute configuration of centers of asymmetry, conformation of asymmetric molecules
Mass spectrometry Mass and relative abundance of molecular ions and fragment ions formed on ionization of molecules usually by electron bombardment or strong electric fields	Gases, liquids, and solids that can reach a vapor pressure of 10^{-5} torr at 300 °C without decomposing $\ll$0.1 mg	Molecular weight, elemental composition, detection of hetero atoms on the basis of the natural isotope abundances, structural analysis by specific breakdown of molecules on electron bombardment
X-ray diffraction, neutron diffraction Interference of X-ray or neutron beams as a result of diffraction by the electron clouds or nuclei of the atoms of the oriented molecules in the crystal	Single crystal 1—10 mg and 0.1—1 g respectively	Determination of the complete molecular structure, steric arrangement of the atoms (distances, angles); hydrogen atoms can also be located by neutron diffraction

Some methods of structural analysis are listed in Table 3. Only those most commonly used at present will be considered in this section.

The desire to identify directly the structural units and functional groups in a molecule is satisfied to some extent by X-ray analysis (Table 4).

Table 4. Advantages and disadvantages of X-ray analysis.

Advantages	Disadvantages
Information about the entire intramolecular and intermolecular geometry	No elucidation of partial structures possible; it is always necessary to consider all the atoms in the molecule
Substance is still intact after the analysis	Substance ($\approx$0.1 mg) must exist as a single crystal ($\approx$0.1 mm^3); time required for a structural analysis 4—12 weeks

Figure 8 shows the result of an investigation by *Hoppe, Hecker, et al.*[2] on a neophorbol derivative; the perspective representation of the centers of gravity of the atoms (to the right of the electron density diagram) clearly shows a system of four rings, the two acetoxy groups, and the *p*-bromobenzoyloxy group, which, with its heavy bromine atom, was introduced to facilitate the processing of the X-ray diffraction data (fixing the phase angle).

The method can in principle be used for all compounds that exist as single crystals, whether inorganic or organic and with ionic or molecular lattices. An X-ray structure analysis always gives a picture of the complete electron density distribution in a unit cell of a crystal. It is consequently necessary to include all the atoms of the unit cell in the calculations, so that one cannot, for example, confine one's attention to a specific functional group and ignore the rest of the molecule. The method is a particularly important tool for the determination of partial conformations and absolute configurations, *e.g.* of natural products, or for the investigation of solid-state reactions of inorganic compounds for topochemical analysis by determination of intermolecular and intramolecular distances in the crystal.

Owing to the advances in automatic data acquisition and processing, it is no longer necessary to use a derivative containing a heavy atom, provided that the molecule consists of not more than 50 atoms (apart from hydrogen atoms). Measurements on many isomorph-

[2] *W. Hoppe, F. Brandl, I. Strell, M. Röhrl, J. Gassmann, E. Hecker, H. Bartsch, G. Kreibich,* and *Ch. v. Szczepanski,* Angew. Chem. *79*, 824 (1967); Angew. Chem. internat. Edit. *6*, 809 (1967).

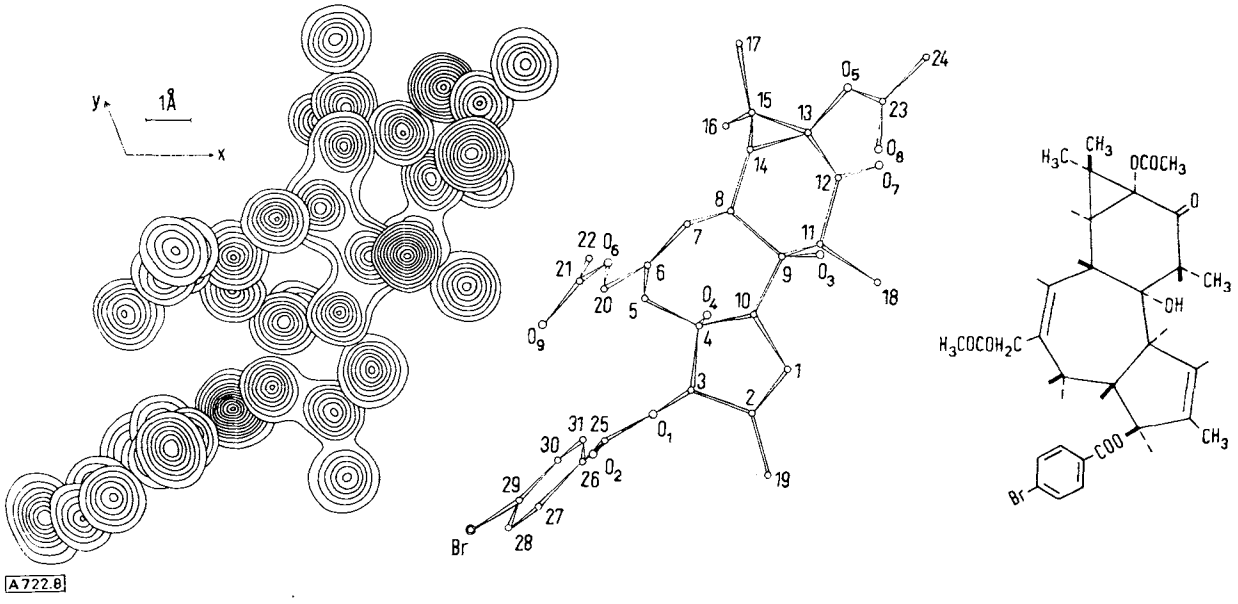


Fig. 8. Fourier analysis of neophorbol 13,20-diacetate 3-*p*-bromobenzoate.

ous derivatives are necessary in the case of large molecules; the structure of these molecules can be conclusively established if there are enough derivatives, personnel, and computer time available. The time required for a medium-large molecule containing 30 atoms apart from hydrogen is 4 to 12 weeks; the time increases roughly linearly with the number of non-hydrogen atoms up to 50 atoms, but much more rapidly beyond 50.

As can be seen from Table 3, IR, Raman, NMR, and mass spectrometry, in complete contrast with X-ray analysis, give only structural elements and environmental and symmetry relations of atomic groupings in molecules, as well as their fragmentation on electron and photon bombardment and in very strong electric fields.

The manner in which the results of the various methods can be combined to find the structure of a molecule is shown below; the information provided by the various methods is indicated, and their effectiveness is compared with that of other methods.

In connection with automatic data processing and combined interpretation, it is necessary to realize that there are basically two types of analytical information, *i.e.* information from which conclusions can be drawn directly and information from which structural elements can be recognized with the aid of empirical tables.

IR spectroscopy yields only information of the second type. The precise information obtained depends on the region of the spectrum. Very characteristic and relatively reliable information about functional groups (such as OH, NH, C≡N, C=O, C=C, C=N) is found between about 3700 and 1550 cm^{-1}, while types of substitution on aromatic rings and heavy atom substitution can be recognized from the wagging vibrations between about 900 and 400 cm^{-1}. In the region between these two, which corresponds mainly to the skeletal vibrations of the molecule, considerable frequency changes occur as a result of changes in structure, and this region cannot be used directly as a source of structural information. This region, however, is very substance-specific (fingerprint region), and is therefore particularly useful for the identification of organic compounds.

For example, the following indirect information can be obtained from the IR spectrum of ethyl *trans*-cinnamate:

Wave number (cm^{-1})	Assignment
685/715 770	C_6H_5R
1174	α,β-unsaturated ester (non-aromatic)
1271	C=C–C–O–R ‖ O
1495 1580	C_6H_6
1638	C=C (olefinic)
1712	C=O (acid or ketone or α,β-unsaturated ester)

We must now ask ourselves whether the information can be improved by the use of more sophisticated apparatus, *e.g.* by an increase in resolution. The answer is negative as far as the spectra of liquids and also of most solids are concerned, since the limit of resolution in these two cases is the natural band width. For gases, on the other hand, increased resolving power can lead to resolution of broad bands into narrower component bands (rotational structure), though this fact is not generally used in normal determinations of the structures of organic compounds. The greater accuracy of the position of the absorption bands, however, can in some cases be of additional value (groups with a C=C function between 1650 and 1800 cm^{-1}).

Raman and IR spectroscopy are based on the internal vibrations of the molecules, the so-called normal vibrations, which appear in accordance with selection rules determined by the physical principles of the

methods; thus a change in the dipole moment during vibrations leads to IR absorption bands, while a change in polarizability gives Raman lines.

Raman spectra, like IR spectra, give only empirical information. The two methods are complementary, since according to the selection rules, which are based on molecular symmetry, vibrations may be *e.g.* IR-active and forbidden in the Raman spectrum or *vice versa*, or they may be allowed or forbidden in both.

A recent important development in Raman spectroscopy is the use of lasers (He/Ne) as Raman light sources. Smaller quantities [a few μl (mm³)] can be used for measurements of this type, even when the substance is colored or slightly turbid; crystalline powders can also be used, with the result that the lattice vibrations of solids can now be readily measured. New possibilities for the determination of the crystallinity of high polymers have appeared, and it seems to be possible to determine the length of polymer chains. Finally mention should be made of the ease of measurement of the degree of polarization of Raman lines, and hence of determining the symmetry of normal vibrations, which is also of value in structural analysis, by excitation with lasers (Fig. 9).

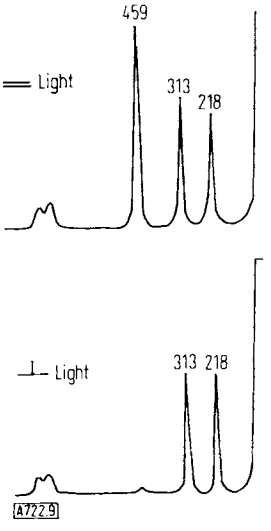


Fig. 9. Polarization measurements in the Raman spectrum of CCl_4.

Unlike infrared spectroscopy, mass spectroscopy gives information that permits direct conclusions as well as providing empirical information (cf. Fig. 10).

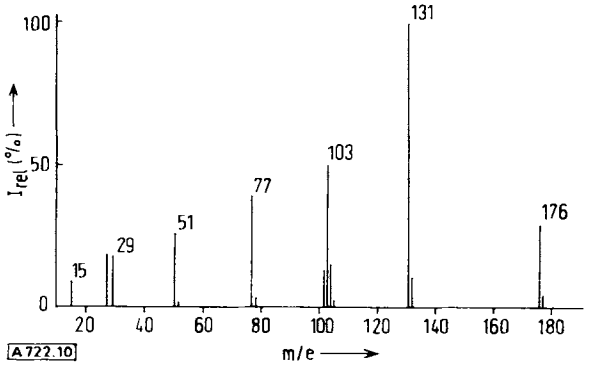


Fig. 10. Mass spectrum of ethyl cinnamate.

Direct statements:

Peak of highest mass number at *m/e* 176	→	Mol. wt.: 176
Even molecular mass number	→	No N atom or even number of N atoms
Absence of isotope multiplets	→	No halogen atoms
$M^+/M^+ + 1 = 100/10.5$	→	10—11 C atoms

Empirical statements:

Key fragments *m/e*	15	→	CH_3
	29	→	C_2H_5
	77	→	C_6H_5 (monosubstituted aromatic compound)
Peak differences *m/e*	176 → 131	45 →	C_2H_5O- O ‖ $-C-$
	131 → 103	28 →	$-CH=CH-$
	103 → 77	26 →	C_6H_5

The value and the direct applicability of the information obtained from isotope multiplets is demonstrated in Figure 11. Such information shows conclusively the nature and number of certain hetero atoms.

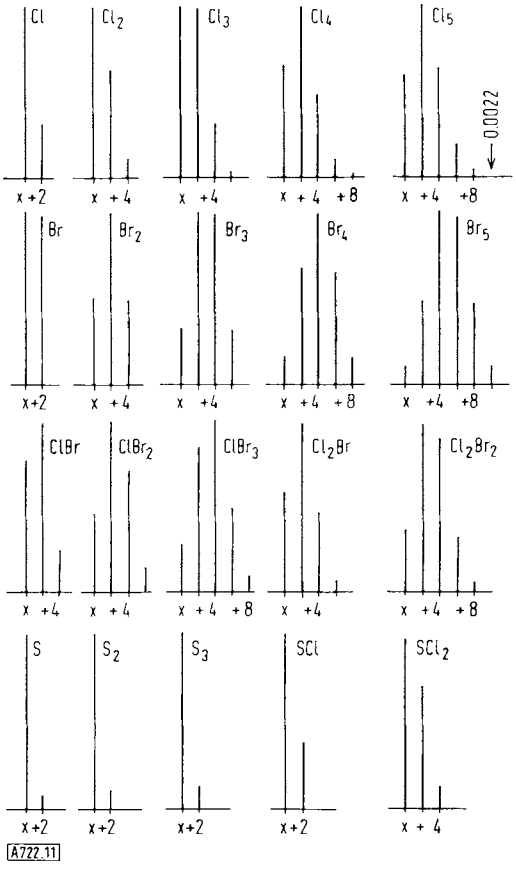
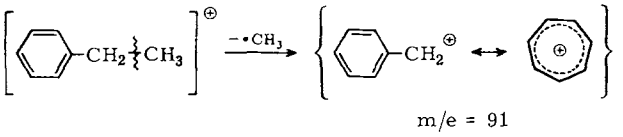


Fig. 11. Characteristic halogen and sulfur isotope multiplets.

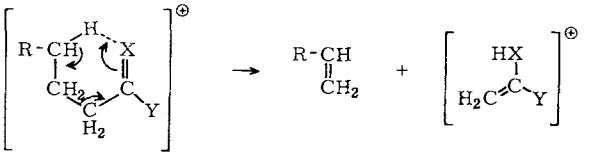
To see how the ions other than the molecular ion are interpreted in the spectrum of ethyl cinnamate (Fig.10), let us consider briefly the fragmentation processes that take place in the ion source of the mass spectrometer. These processes depend both on the energy balance of the bond cleavages involved in the fragmentation and above all on the stability of the positive and neutral particles formed. Thus the fragmentation of ethyl-

benzene, for example, is primarily controlled by the formation of the stable tropylium ion:



m/e = 91

The fragmentation paths and mechanisms are therefore molecule-specific rather than group-specific, since the formation of certain fragment ions depends energetically on the competition of different atomic groupings. In addition to the fragmentation of single bonds, rearrangements frequently also occur, subject to certain steric conditions; though these further complicate the fragmentation mechanisms, they are readily recognizable in many instances, and are then very specific. An example is the "McLafferty rearrangement":



When X = O and Y = OH, the ion of mass 60, which is characteristic of acids with more than three C atoms, is formed.

A rough interpretation of a mass spectrum can be made with the aid of empirically compiled tables of characteristic "key fragments" (*e.g.* ethyl cinnamate: mass numbers 15, 29, 77 correspond to CH_3, C_2H_5, and C_6H_5) and typical mass differences (45 $\triangleq$ C_2H_5O; characteristic of ethyl esters).

Specific syntheses of derivatives of the substance under examination and partial chemical degradation can often be of great value in structural determinations. Strongly polar substances that cannot be evaporated without decomposing are converted into derivatives that can be vaporized without decomposing (silyl ethers, trifluoroacetates, *etc.*).

It is sometimes difficult to recognize the molecular peak. For aliphatic alcohols, ethers, and carboxylic acids, as well as for branched aliphatic hydrocarbons, the intensity of this peak is usually less than 2% of the sum of the intensities of all the other signals, whereas aromatic and alicyclic compounds give very intense molecular peaks. If, however, the ionization method is changed from electron bombardment to field ionization, or if the ionization voltage in electron bombardment ionization is reduced, the peak of the molecular ion becomes quite predominant, despite the lower overall intensity of the spectrum (Figs. 12 and 13).

Wider use of field ionization mass spectrometry has been hindered in the past by the low overall intensity of the spectra. With carbon whiskers as electrodes in a field emission ion source, however, it has recently become possible to obtain sensitivities as high as those

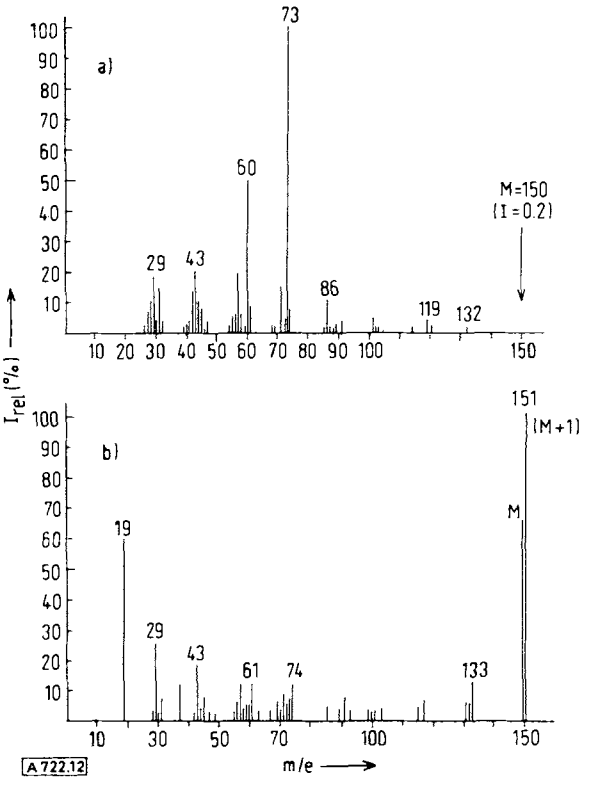


Fig. 12. Mass spectra of D-ribose a) with electron bombardment ionization [3] and b) with field ionization [4].

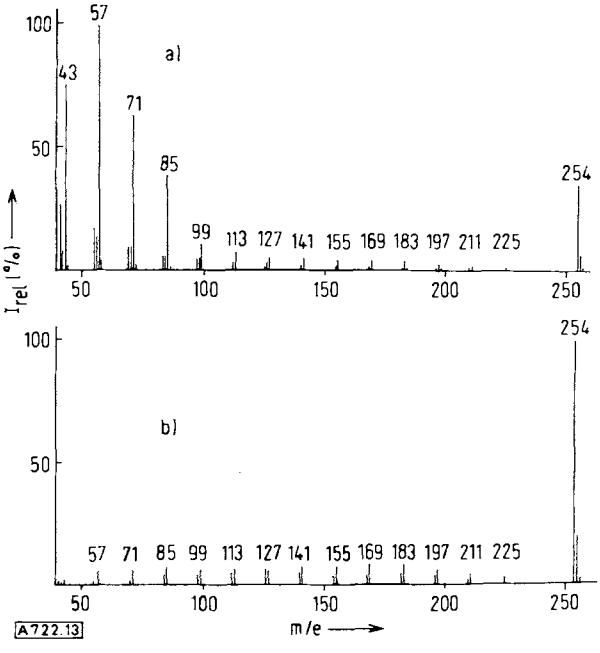


Fig. 13. Mass spectra of octadecane with ionization energies of a) 70 eV and b) 17 eV.

achieved by conventional electron bombardment ion sources [5].

Here again we are faced with the question whether the information value of mass spectrometry could be im-

[3] *K. Biemann*: Mass Spectrometry. McGraw-Hill, London 1962, p. 350.

[4] *H. D. Beckey* in *W. L. Mead*: Advances in Mass Spectrometry. Vol. 2. Institute of Petroleum, London 1966, p. 48.

[5] *H. D. Beckey*, Lecture read to the GDCh Section "Analytische Chemie" at Freiburg in April 1969.

proved *e.g.* by an increase in the resolving power. Even instruments having an average resolution $m/\Delta m$ of 2000–3000 resolve a signal of mass number 28 due to N_2 and CO. A tenfold increase in resolution allows the separation of lines with higher mass numbers (Fig. 14), so that the elemental compositions of fragment ions and molecular ions can now also be given. The usual accuracy of mass determinations is about

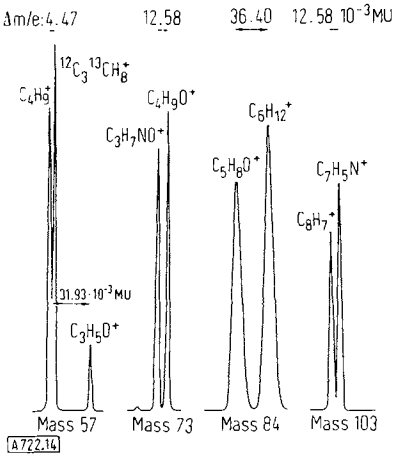
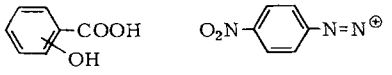


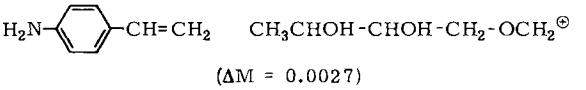
Fig. 14. Ion pairs separated by high-resolution mass spectrometry.

±0.0025 to ±0.003 mass units. An unknown compound *e.g.* having a molecular weight of 587.3444 ± 0.0029 could have any of the formulas $C_{28}H_{49}N_3O_{10}$, $C_{29}H_{45}N_7O_6$, $C_{33}H_{49}NO_8$, and $C_{34}H_{45}N_5O_4$. An elemental analysis giving the results C: 70.65, N: 4.90, and O: 16.65%, with a cryoscopically determined molecular weight of 290 ± 5, would give the empirical formulas $C_{17}H_{23}NO_3$, $C_{17}H_{25}NO_3$, and $C_{17}H_{21}NO$; a mass-spectrometrically determined molecular weight of 289 would rule out the second and third of these formulas.

Combination with elemental analysis is particularly important if a molecule also contains other hetero atoms, such as F, S, and P, that are either isotopically pure or have no characteristic isotope ratios. Styrene, C_8H_8, is practically indistinguishable from pentanethiol, $C_5H_{11}SH$, ($\Delta M = 0.0034$), and benzene, C_6H_6, cannot be distinguished from fluoropropanol, C_3H_7OF ($\Delta M = 0.0021$). The same is true for the molecular ions and the fragments:



($\Delta M = 0.0013$)



($\Delta M = 0.0027$)

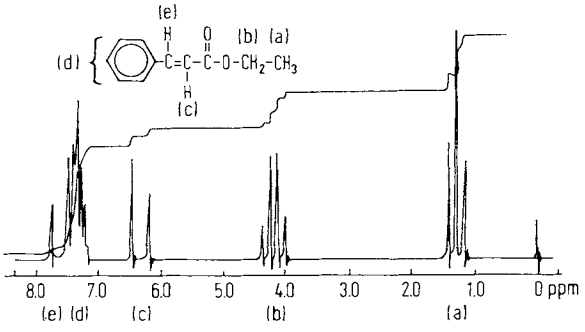
The advantage of high-resolution mass spectrometry, despite certain limitations, can be seen *e.g.* in the mass spectrum of ethyl butyrate; instead of mass numbers, elemental compositions are now given for the peaks of the spectrum:

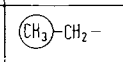
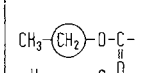
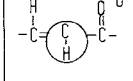
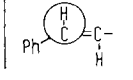
m/e			
116	$C_6H_{12}O_2$	$C_2H_8N_6$	$C_4H_{10}N_3O$
101	$C_5H_9O_2$	CH_5N_6	$C_3H_7N_3O$
89	$C_4H_9O_2$	–	$C_2H_7N_3O$
88	$C_4H_8O_2$	–	$C_2H_6N_3O$
73	C_4H_7O	–	$C_2H_5N_3$
	89 = M–C_2H_3		
	88 = M–C_2H_4		
	73 = M–C_3H_7		
	81 = M–C_2H_5O		

When arranged schematically in the form of an "element map", they can be interpreted more easily than when they are simply listed according to their mass numbers.

In principle, the elemental compositions can be calculated and an element map can be constructed with the aid of tables; since it is convenient in any case to use computers in the processing of high-resolution mass spectra, this task may also be incorporated in the program.

To illustrate the information obtainable from a nuclear magnetic resonance spectrum, let us again take the example of ethyl *trans*-cinnamate (Fig. 15).



Chemical shift (ppm)	Multiplicity	Coupling constant (Hz)	Intensity	Assignment
1.28	3 (Triplet)	7	3	
4.23	4 (Quartet)	7	2	
6.40	2 (Doublet)	16	1	
7.35	n (Multiplet)	-	5	
7.70	2 (Doublet)	16	1	

A 722.15

Fig. 15. ^{1}H-NMR spectrum of ethyl *trans*-cinnamate.

The area under the multiplet having a given shift corresponds to the number of protons, and the ratios of the areas are thus equal to the ratios of the numbers of protons in various environments. The chemical shifts and coupling constants for various atomic groupings can be found in empirical tables. The triplet a and the quartet b in the spectrum correspond to an ethyl group, and the two doublets c and e to a –CH=CH– group. The two hydrogen atoms could also be *cis*, but this would be shown by the coupling constant: *cis* ≈ 8 Hz, *trans* ≈ 16 Hz. The higher-order multiplet d, in which five non-equivalent protons couple with one another, is more complicated; it can be interpreted (cf. Fig. 16), though the interpretation is not necessary for the structural analysis, particularly in this case.

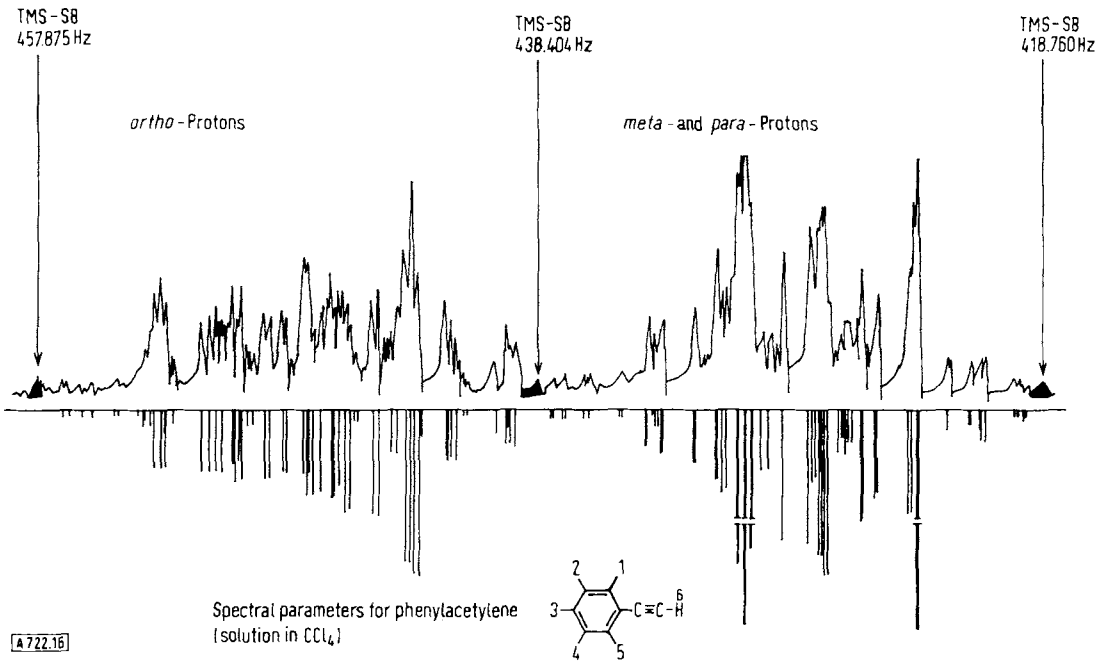


Fig. 16. Experimental and calculated NMR spectrum of the *o*, *m*, and *p* protons of phenylacetylene.

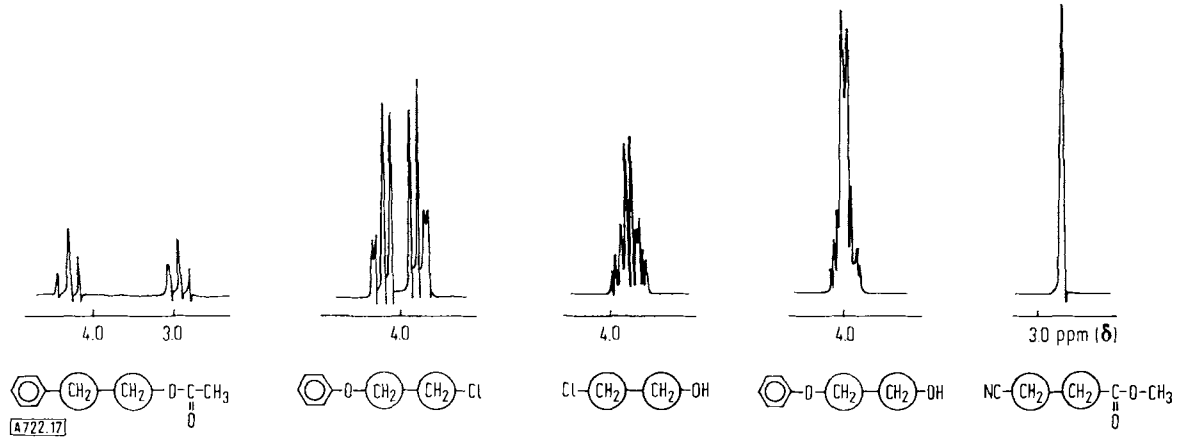


Fig. 17. Spin-spin coupling for the A_2X_2 system.

An example of the transition from lower-order to higher-order NMR multiplets is shown in Figure 17.

Neighboring CH_2 groups carry groups that can induce different intramolecular fields. The multiplet structure is characterized by the coupling constant J, the shift difference $\Delta\delta\nu$, and their ratio $J/\Delta\delta\nu$, *i.e.* the coupling factor. In the case of the A_2X_2 system, *i.e.* the two CH_2 groups, we should expect two triplets in the first order (Fig. 17, left). In the spectra from left to right, not only do the signals move closer together ($\Delta\delta\nu$ becomes smaller), but their structure also becomes more complicated, until they finally degenerate into a singlet. The structure of the multiplet is determined by the coupling factor which is <0.25 for the first order of the multiplet. If, on the other hand, it is >0.25, complicated multiplets of higher order are obtained.

As in IR and mass spectroscopy, it is reasonable to hope that the structure of the NMR multiplet might become clearer if the "resolution" were increased. This would require a decrease in the signal width, which would in turn be possible only by an increase in the constancy of the magnetic fields (fundamentally an increase in the constancy of the temperature) and of the measuring frequency. One order of magnitude (from $\nu/\Delta\nu = 2 \times 10^8$ to 2×10^9) might be gained in this way, but a natural limit is imposed by the relaxation of the internal motion of atomic groups in the molecules. It is commonly thought that the "resolution" can be improved by increasing the magnetic fields, *e.g.* from 14100 gauss and a measuring frequency of 60 MHz currently used in routine work to 23500 gauss and 100 MHz; instruments working with 51700 gauss and 220 MHz have been available for two years. A further increase in the field strength and measuring frequency still seems possible.

In connection with this development of nuclear magnetic resonance instruments, one speaks of an increase in the "resolution" of the spectra with the magnetic field strength. This is not, however, true of the resolution as usually defined in spectroscopy. On the other hand, the chemical shift increases very appreciably with increasing magnetic field strength. In the parlance of optical spectroscopy, which should be

used to describe this effect, the angular dispersion of a 220 MHz instrument is greater by a factor of 3.7 than that of a 60 MHz instrument. The multiplet groups move apart as the field strength and measuring frequency are increased, but the multiplet structure simultaneously becomes simpler. This is understandable if one considers that the coupling constants are independent of the field strength, whereas the shift difference increases with increasing field strength. The coupling factor $J/\Delta\delta\nu$, which determines the structure of the multiplicity, accordingly becomes smaller, and the multiplets become simpler.

This effect is shown in Figure 18. The same spectrum (60 MHz) of 2-chloroethanol is shown twice on the left, and the spectrum of the phenyl ether is shown (top right) for comparison. A greater difference in the shielding constants leads to a greater shift difference, and hence to a smaller coupling factor, so that the structure of the multiplet becomes simpler. In the lower right-hand diagram, which shows the 220 MHz spectrum of 2-chloroethanol, the external field is greater and the same effect is thus observed.

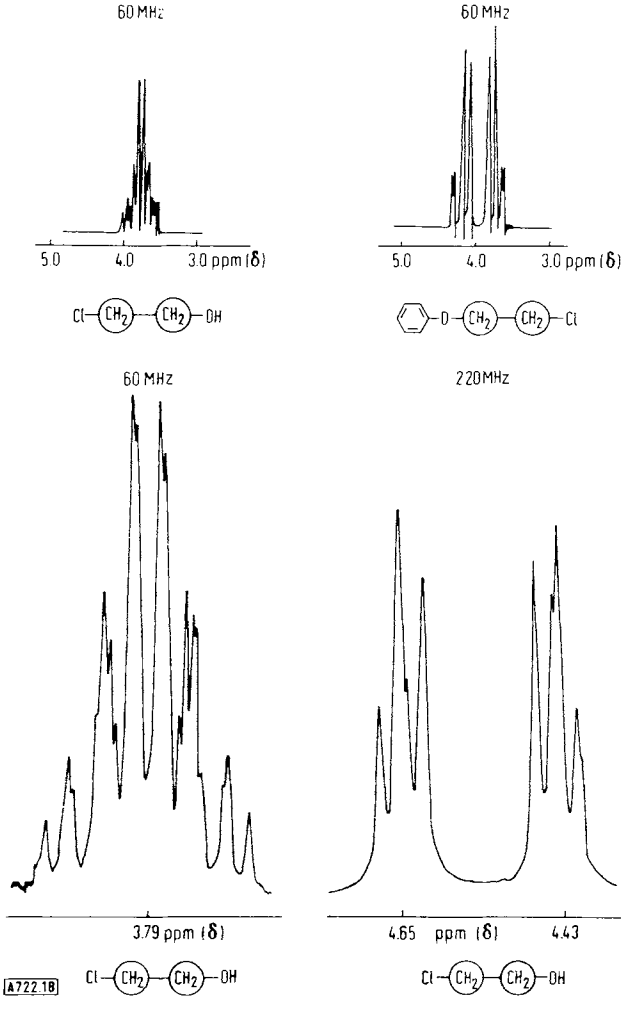


Fig. 18. ^{1}H-NMR spectra of 2-chloroethanol and its phenyl ether at various measuring frequencies.

To sum up, therefore, we can say that an increase in the field strength and measuring frequency moves the multiplets apart, and so disentangles them and makes them simpler; however, this is accompanied by a loss of information. It should also be mentioned that the signal-to-noise ratio is appreciably improved (by a factor of 3–5) by the change from 60 to 220 MHz.

It is convenient to leave the data processing and all the steps in the evaluation of information from IR, Raman, NMR, and mass spectroscopy to a computer, which can also carry out searches and comparisons in stored empirical tables of the structural elements, and can take over the functions of memory, learning, and searching:

1. Automatic data collection and conversion into a form suitable for interpretation (*e.g.* determination of mass numbers and elemental compositions in mass spectra, separation of overlapping bands);
2. Comparison with catalogs of spectra;
3. Input of reliable preliminary information;
4. Output of structural data in the form of partial structures and the arrangement of structural parts;
5. Comparison of the results obtained by different methods.

As a result of these combined integrated interpretations, the computer yields structural elements, partial structures, or complete structures, depending on the difficulty of the problem. It will provide self-consistent proposed structures as well as structures that still involve some uncertainty, and it will also list any conflicting results and negative findings. Decisions between various possibilities and the selection of the eventually proposed structure (possibly after further investigations based on intermediate results) remain the work of the chemist. The most reliable confirmation of an analysis is generally a total synthesis.

The substance whose structure is to be analyzed must be substantially pure. Separation methods, particularly chromatographic, are of great value in this connection, both preparatively and analytically as a purity check. The combination of separation and determination methods has already been described for the case of gas chromatography and mass spectrometry.

A method that should be of great importance for structural analyses in the future is one reported two years ago by *Siegbahn*[6], who named it ESCA. This method makes use of the photo-ionization of atoms by relatively soft X-ray beams (cf. Section 2). *Siegbahn* used a magnetic separation system in his electronic spectrometer. The Varian Company, which undertook the development of instrumentation for the method (also known as induced electron emission spectroscopy, IEES), introduced electrostatic separation with a multichannel store; it is possible in this way to resolve spectra with a sharpness of separation of 1 eV. Figures 19 and 20 show the corresponding spectra of acetone and ethyl trifluoroacetate, in which substitution effects on the carbon are clearly shown by a change in its bond energy (E_B) (according to *Siegbahn*). Manufacturers have recently announced the production of instruments, which no longer separate the photoelectrons in a magnetic field but by a time-of-flight principle in an electric field at a resolutions of

[6] *K. Siegbahn et al.*, Nova Acta Regiae Societatis Scientiarum Upsaliensis, Ser. IV, *20*, 1 (1967).

1 eV; these instruments will probably ensure that this new method will soon take its place alongside other methods of molecular spectroscopy. Moreover, in this case, an integrating interpretation is also possible with the aid of a computer.

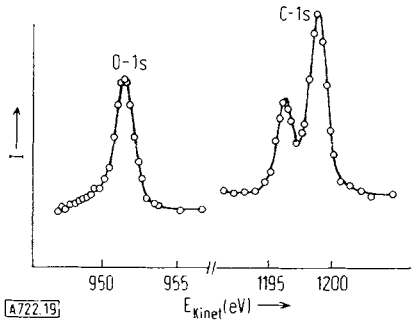


Fig. 19. ESCA spectrum of acetone.

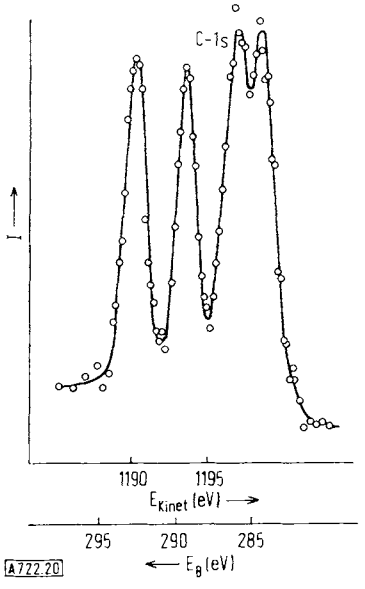


Fig. 20. ESCA spectrum of ethyl trifluoroacetate.

X-ray structure analysis provides the structure of the entire molecule, though the demands on time and work are still relatively severe. The molecular spectroscopy methods can never yield direct information about a carbon skeleton in structural analyses; they cannot show directly the presence of rings, chains, or branching. Recognition of typical ring vibrations is possible only by modern laser Raman spectroscopy employing polarization measurements, so that, with the exception of the aromatic six-membered ring, methods of molecular spectroscopy can recognize functional groups and the environments of atoms, as well as isolated steric arrangements, which can often be combined to give partial or total structures only on the basis of a well founded chemical knowledge.

5. Data Processing in Analysis

Some possibilities offered by the use of electronic data processing equipment in analysis are shown in Figure 21. Analog signals are accepted at a rate of 10000 or

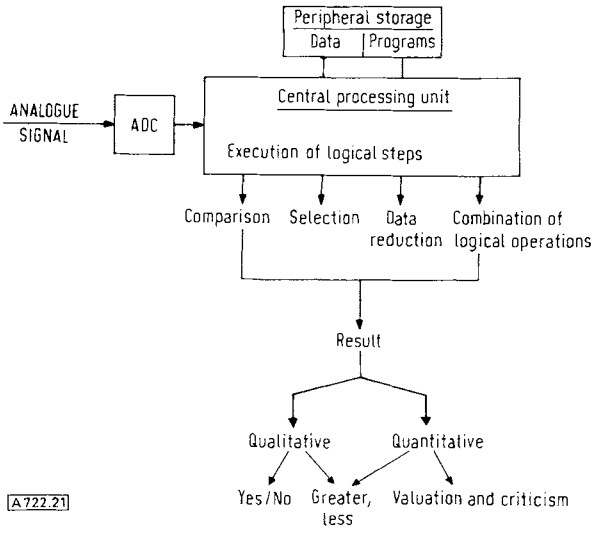


Fig. 21. Use of a computer for analytical problems.

more values per second by an analog-to-digital-converter, which passes the resulting digital values to the core memory of the computer. The data can be further processed directly in time-sharing operation during the data collection. Where the information flow is high, the incorporation of a temporary store in the peripheral equipment is often advisable in order to relieve the central unit. The information can then be recalled later, or may be passed on, after packing, to a larger processor. Using data and programs from storage units, the computer can compare, select, condense, and relate the data by logical operations, in such a way as to obtain an intermediate or final result.

An obvious step is to employ calculating machines, from small desk models to large computers, for pure calculating tasks in the processing of analytical results. With skilled programming, not only of analytical parameters, but also of standardization factors, names of substances, operating terms, *etc.*, a small computer can prepare a complete analytical account, thus easing considerably secretarial work in the laboratory and largely eliminating errors involved in calculation, transfer of data, and writing; it can, moreover, carry out comparisons with theoretical values, summation checks, calculation of standard deviations or errors in multicomponent systems. However, such a machine cannot be expected to perform special tasks corresponding to the capability of a full-scale computer.

In the examples mentioned so far, the computer is used merely as a calculating machine whose program includes a comparison with a reference value. However, it becomes much more directly involved in the analysis if it is also used for data acquisition and processing. As a calculator it simply derives an analytical result on the basis of existing experimental values, whereas in data acquisition and processing the computer itself obtains values that can be used in analysis from a large number of individual values, and manipulates these further to obtain an intermediate or final result.

This can be illustrated for the case of a titration. The end point of a titration is usually determined visually on the basis

of a color change; as soon as this color change occurs, the tap of a buret is closed and the value is read off. In electrochemical titration, the titration curve (volume of titrant used against the potential difference) can be recorded, and the end point of titration is then determined graphically as the point of inflection of the curve. It is well known that the points of inflection are indistinct, particularly when there are several potential steps, so that it is difficult to determine these points accurately. If the potential difference as a function of time is fed into the computer as a large number of individual measurements (*e.g.* every 10—15 ms), care being taken to ensure that the addition of titrant is exactly linear with time (the volume per unit time should also be accurately measurable), the computer can find the point of inflection by differentiation (formation of the first, and if necessary also the second, derivative) with much greater accuracy than is possible by hand.

The computer can also take over the data processing in the evaluation of gas chromatograms, particularly where signals overlap or where the base line is not constant. The earlier planimetric method of manual evaluation, which was subject to considerable errors (1—3%), has been steadily replaced by electric integrators, which give very good reproducibility (≈0.3%). However, these offer only an incomplete solution to the problems of base-line drift and the separation of overlapping signals. A computer, on the other hand, can fully correct for the base-line drift by constructing a tangent at the beginning and end of a signal, or of a group of overlapping signals, and determining the area above the tangent. To separate overlapping signals, an approximate gaussian curve is determined from the signals, in a chromatogram, and for the overlapping signals, the two gaussian curves are sought whose superposition best reproduces the measured signal. The simple procedure of dividing superimposed signals into area elements by vertical lines is sufficiently accurate in many cases if the assignment of the area elements is correct.

All these computer evaluations depend on the recording of the true experimental values. This is seriously affected by noise in the measurement signals and their disturbance by isolated signals due to sudden voltage or current surges, and considerable expense is involved in the elimination of these interfering factors.

As in gas chromatography, a computer can also be used in mass spectrometry for data acquisition, processing, and reduction and for obtaining analytical results.

The question of economy is also important. As is shown in Figure 22, the times taken for the various steps of the analysis differ considerably.

If the preparation of the sample and the measurement take a long time in relation to the evaluation, the use

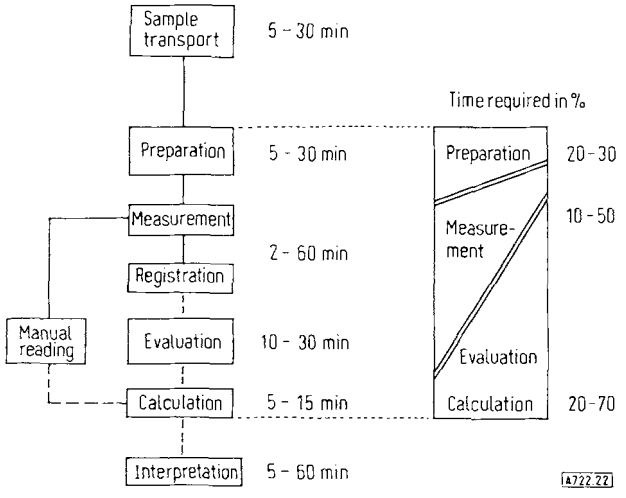


Fig. 22. Time taken for the various steps in analysis.

of a computer is not normally justified. It is advisable in such cases to modify the procedure, rationalize or mechanize individual steps, or improve the measuring method. If the number of samples for routine examination is very large while the amount of calculation is small, a programmable desk calculator or digital data collection, *e.g.* with a tape punch for off-line evaluation on a larger computer, may be advantageous.

The direct connection of smaller or larger data processing units is recommended whenever the collection and evaluation of the experimental values accounts for a medium or major part of the total work of analysis. In physical methods it is usually the collection of the experimental values that involves a great deal of manual work, which is simple, but requires care and concentration (gas chromatography, mass spectrometry); the use of medium sized computer systems is profitable in such cases.

If the times for measurement and for evaluation are roughly the same without a computer, the measuring process becomes rate-determining with automatic data processing. It is then desirable to speed up the measuring process. An example of this is gas chromatography, where the operating speed could be considerably increased, but where this has been of no interest until now because of the long times taken for the evaluation. This is a case in which the use of computers has had repercussions on the method itself.

In view of its cost, the fullest possible use should be made of a data processing system. This condition is satisfied in particular in routine operation, *e.g.* in round-the-clock industrial analyses, particularly when the data flow is matched to the capacity of the computer by connection of a large number of analytical instruments. Extremely high data flows from individual measuring instruments also justify the use of a computer for these instruments alone, provided that they are used often enough (*e.g.* in high-resolution mass spectrometry). These computers, which are intended for a single field of use, and which operate for long periods with the same program, can be profitably used with the minimum equipment for this purpose, particularly if they also take over the duties of supervision (regulation) of the measuring instrument and optimization of the measured values (improvement of the signal-to-noise ratio) (*e.g.* in nuclear magnetic resonance).

The preparation and control of the measuring processes can be carried out by a small computer. The experimental data are reduced by this computer, and may be passed to a large computer for further processing. In X-ray structure analysis, for example, the intensities of several thousand reflections from one crystal are measured with a diffractometer, which is controlled by a small computer. This computer optimizes the measuring process for each reflection, corrects the experimental values, and passes them in a reduced form to a large computer. An attempt is now made, with the aid of a suitable program, to assign phases to the measured structure amplitudes, in order to obtain a

model of the structure by a three-dimensional Fourier analysis. This model is then refined by the computer by optimum matching with the experimental data. The control of the diffractometer by the computer may be compared to automatic process control in industry, and is probably the first process to reach this level of perfection in the field of measurement.

This opens up whole new vistas for the role of computers in analytical work, though the applications at present are still rather trivial. Its role as a pure calculator is widened, and it also assumes control functions over the analytical instruments. In emission spectroscopy, for example, one measurement may be repeated several times; the mean of the individual results is used to calculate the standard deviation, which is then compared with the expected standard deviation of the analytical method. If the result is greater than the expected value, the computer decides to repeat the analytical measurement. The new result, together with the standard deviation, provides the basis of a criticism that either the sample may be inhomogeneous or the analytical method is unsatisfactory. The analyst himself must now draw his conclusions, but the basis of his decisions is provided by the computer.

Other duties of the computer are distinguishing between systematic and random errors and verifying the correctness of results. It is not difficult for the computer to store a large number of repeated measurements, find their statistical mean, and check their statistical distribution. If the distribution differs from the gaussian or other suitable distribution, the errors in the measuring process are not only purely random ones.

The error of the method is found by repeating the entire measuring process several times, and occasional measurements on calibration samples confirm or refute the correctness of the measuring process. All the intermediate calculations involved in this procedure are carried out by the computer, which provides the analyst with the quantities required as a basis for decisions, or may even itself indicate the satisfactoriness or uncertainty of analytical findings.

It is now beyond all doubt that the resulting speed of the whole measurement and evaluation operation and the increase in the accuracy and correctness of the results that is generally possible are leading to a new era in analytical work, with the scientific and economic consequences that follow from it. In recognition of the economic importance of analysis, it has become our duty to encourage and force through the decisions that are necessary to our entry into this new era.

6. Automation in and with Analytical Chemistry

The possibility of influencing an analytical process by decisions suggests a comparison with control and regulating functions in chemical processes (Fig. 23).

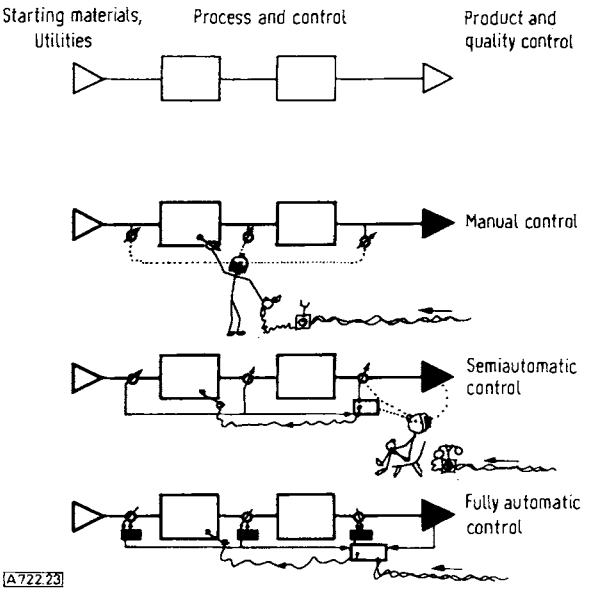


Fig. 23. Control, regulation, and automation. Stages in the unloading of the human operator in chemistry (symbolic: two-stage process).

Three stages of process control are known in industrial production, *i.e.* control (manual control), regulation (semiautomatic control), and automation (fully automatic control). In manual control, information provided by measuring instruments on the basis of the instantaneous state of the process is translated into commands by human agents. The process is thus under human supervision, and the quality of the product and the economy of production depend on the efficiency and availability of labor.

In semiautomatic process control, the same information as is used in manual control is fed into data converters. These are regulating instruments with no automatic checking or critical functions, which convert the information supplied into commands in accordance with a fixed program or simply in such a way as to maintain a predetermined state. An important characteristic of a good regulator is the ability to convert the information into commands in such a way that the desired action occurs as quickly and as accurately as possible. Data feedback allows optimum matching of the commands to the prevailing state. However, all these features cannot be compared to the specific characteristics shown by a human agent controlling a process. Though the regulator does the mechanical operations faster, better, and more continuously than a human operator, it lacks the checking and decision-making functions and the ability to adapt to different states. As the demands made by process control become more stringent, therefore, the usefulness of semiautomatic control diminishes. The stage of full automation is then necessary.

Full automation means a high degree of replacement of human activities by machines, and includes checking, decision-making, and adaptation functions. Checks can be made only by comparison of data. Decision-making and adaptation require the observation and evaluation of a change in data with time. Tasks of this nature are within the capabilities of computers. Automation in the chemical industry is thus characterized by the use of a computer, which compares data, follows their trend, and uses this as a basis for commands.

It can be seen from Figure 24 that the various steps leading from sampling, *via* the measuring process, to the analytical result can be considered in the same scheme as was used for process control (cf. Figure 23).

Manual analysis, in which a sample is subjected to transformation and measurement, has reached only the semiautomatic stage even when complex instruments are used for the production and collection of data, since the state of the sam-

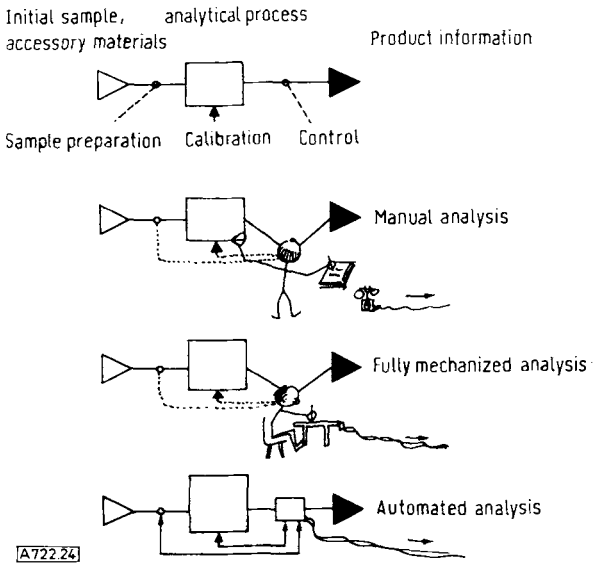


Fig. 24. Stages in automatic analysis: manual analysis, fully mechanized analysis (with checking, correction, and evaluation by human operators), and automated analysis.

ple is (unconsciously) checked by a human operator and corrected if necessary, and since the human operator must also check and correct the information produced, *e.g.* by unconscious comparison or with the aid of a calibration analysis. Transformation of the results of the measurements is sometimes necessary. It is always necessary to check in some way whether the information is "correct enough".

Analytical measurements with "automatic" instruments are comparable to semiautomatic process control. These instruments should, however, be described as automatic only if the criteria of automation (checking, correction, decision-making, and adapting) are satisfied. An automatic vending machine is much more automatic than an "automatic" titrating instrument, since it checks a coin inserted and decides whether to deliver the goods or not (*e.g.* if foreign money or a button has been used instead of the correct coin). Though an automatic vending machine can be deceived, or may refuse to deliver the goods even when a gold coin has been inserted, this error characteristic does not alter the difference between automation, as a high level of checked, corrected, and adapted mechanization, and mechanization without checking and decision-making functions.

The instruments usually referred to as automatic analysers, as well as "automatic" combustion equipment for element analyses and "automatic" titrating instruments, are instruments that function in accordance with a control program, but which contain no idea of automation. Phrases like "automatic laboratory" refer at best to the evaluation, and never to the analytical process. An automatic apparatus should be[7] an assembly of mechanism and instruments that forms an informationally closed system. The quality of being "informationally closed" is essential to the process taking place in a truly automatic apparatus. One can also say that an automatic apparatus must carry out this process in accordance with the "input/output" principle, which states that material and/or informative input quantities are processed internally with no help from external agencies, and that the results are again definite material and/or informative output quantities. The process is often specified expressly as in automatic "computer". Unlike in a machine or instrument, the individual steps in the operation of an automatic apparatus need not be predictable either in their nature or in their duration, but are varied within preset limits by internal regulating and control processes. For this purpose control signals and/or response signals are used to vary the actuating variables of the mechanisms and to match them to one another. The characteristics of the object to be acted upon must also be determined directly and introduced into the data cycle.

Where the input quantities are fixed, we speak of programmed automatic systems. Units for the elimination of variable input quantities in the form of random variables, deviations, or perturbing quantities are also known as automatic regulators or controllers. However, many units correspond to both concepts.

For true automation, the individual steps in analytical chemistry (sampling, measuring, and data processing) must be automated, *i.e.* provided with automatic checking, correction, and adaptation to changed conditions.

These requirements are already largely satisfied in data processing, and perfectly practicable proposals have been made for automatic analytical instruments. In sampling, on the other hand, the requirements can scarcely be met even in the simplest cases. Systems of two or more phases and components with different densities and volatilities raise problems that have not even been adequately thought out, far less solved.

Requirements that must be satisfied by analytical instruments for automatic process control are given below. It should be noted that an analytical method, however important it may be to the process, is incomplete unless it incorporates a checking system corresponding to the human criticism that always intervenes between sampling and evaluation of the measurements in analysis in the laboratory.

This checking system involves the storage, comparison, and checking of changes and rates of change within the analytical system. The calibration functions and the reference standards must be supervised and automatically corrected in case of deviation, as must the input of the correct measurement data.

The internal checking is a special characteristic, and one that is obviously necessary for a production process. The instrument itself decides whether the output analysis result is probably correct or whether it should be rejected. The process control learns from this decision. An automatic system must therefore constantly make yes-or-no decisions that are often difficult for a human worker.

These checking and decision-making functions are natural in automatic computers. The calculating programs always contain a loop that checks whether the calculation and logic steps carried out are correct. It is also usual with punched tapes to carry out this check by cross footing of the punched holes. Two internal checks must be distinguished for the analytical instrument:

1. the automatic checking of the function of the instrument itself and

2. the insertion of analysis of a calibration mixture at regular intervals and the detection of excessively large non-systematic errors.

The demands on the sampling system become increasingly stringent with increasing measuring sensitivity of the analytical method. The sampling reliability decides whether the (now very high) outlay on analysis and measuring equipment is justified and whether the conclusions drawn from analytical results, which are sometimes of great economic importance, are correct. It is known that the sampling, like the analysis itself, contains a systematic error that depends on the procedure and a non-systematic error that can be influenced only by the method. Whereas the magnitude (more accurately the standard deviation) of the non-systematic error can be determined by a sufficiently large number of repetitions of the measurements, the discovery and elimination of systematic

[7] Z. anal. Chem. *237*, 81 (1968).

sampling errors is sometimes very difficult. The automation of sampling is more difficult than the automation of the analytical measuring process.

The elimination of signals due to temporary strong fluctuations and to periodic fluctuations in the process is another testing problem in the automatic control of plants.

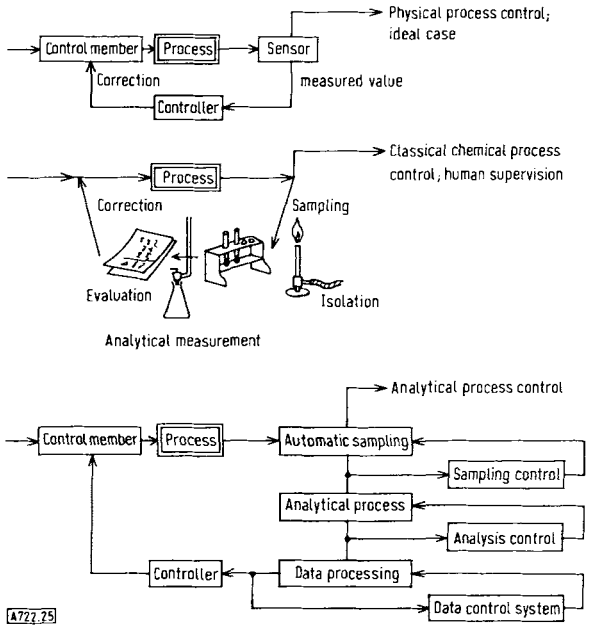


Fig. 25. Analytical data for the control or regulation of a chemical process.

Finally, Figure 25 shows the ideal combination of an automated analysis for the regulation of a chemical process.

7. Conclusion

It should be clear from the developments outlined above that modern analysis has little in common with the analytical chemistry of two or three generations ago, which is still being taught in technical colleges. The modern chemist must therefore bring himself up to date, and acquaint himself with this important branch of knowledge, which links together chemistry, physics, mathematics, biology, and medicine, as well as many branches of technology. Analysis can now claim to be an independent field of instruction and research.

Analysts with a good training in inorganic and organic chemistry, with wide knowledge and experience in analytical methods as a whole, and with a deeper knowledge of some special fields are required today in research and industry. They should be familiar with mathematics, physical measuring techniques, electronics, data processing, information theory, and logic, to enable them to take part in the development of a rapidly growing new field, *i.e.* the logical, exhaustive, and correct evaluation of analytical information from material processes, and their critical appraisal and reduction to the essential facts: the optimization of information.

The author is grateful to the staff of the Physikalisch-Analytisches Laboratorium der BASF, and particularly Dr. Günzler, Dr. Kaiser, and Dr. Seidl, as well as Dr. Brügel and Dr. Witte, for stimulating discussions.

Received: June 16, 1969 [A 722 IE]
German version: Angew. Chem. *81*, 723 (1969)
Translated by Express Translation Service, London

COMMUNICATIONS

Malonodithioamide from Dimethylaminomalonodinitrile and Hydrogen Sulfide

By *H. Eilingsfeld* and *M. Patsch* [*]

Dedicated to Professor B. Timm on the occasion of his 60th birthday

N–C bonds in quaternary ammonium salts can be cleaved reductively, *e.g.* electrolytically [1] or with sodium amalgam [2]. We have observed that even hydrogen sulfide is able to cleave an N–C bond, with reduction of the carbon released, in the case of certain ammonium salts and tertiary amines. This reaction of dimethylaminomalonodinitrile *(1)* with hydrogen sulfide leads to the formation of malonodithioamide *(4)* in very good yields.

The reaction takes place particularly readily at room temperature in pyridine and in pyridine/glacial acetic acid and ethanol/tertiary amine mixtures. Since malonodinitrile in alcohol adds one hydrogen sulfide to only one nitrile group with formation of cyanothioacetamide [3], while malonodithioamide is formed from dimethylaminomalonodinitrile under the same reaction conditions, it is assumed that the cleavage of the dimethylamino group takes place after the H_2S addition. Under certain reaction conditions (*e.g.* in benzene at 0 °C) we have been able to isolate dimethylaminomalononitrilemonothioamide *(2)* and dimethylaminomalonodithioamide *(3)*. Both products react with hydrogen sulfide in the above mentioned solvents to give the compound *(4)*.

$$(CH_3)_2N{-}CH(CN)_2 \xrightarrow{H_2S} (CH_3)_2N{-}CH\begin{matrix}CS{-}NH_2\\ CN\end{matrix}$$
(1) *(2)*

$$\xrightarrow{H_2S} (CH_3)_2N{-}CH(CS{-}NH_2)_2 \xrightarrow{H_2S} CH_2(CS{-}NH_2)_2$$
(3) *(4)*

The ammonium salt *(5)* [4], which can be prepared by *N*-alkylation of *(1)*, also reacts with hydrogen sulfide to give *(4)*.

$$[(CH_3)_3N{-}CH(CN)_2]^{\oplus}\ p\text{-}CH_3{-}C_6H_4{-}SO_3^{\ominus}$$
(5)

In order to explain the course of the reaction *(3)* → *(4)* we assume that a nucleophilic substitution by SH at the nitrogen takes place, similar to that postulated in the alkaline hydrolysis of chloroamines [5]. However, results of our previous investigations do not rule out a free radical mechanism.

The thiohydroxylamine derivative which one would expect to be formed along with malonothioamide in the cleavage of *(3)* is not stable under the reaction conditions, as the behavior of sulfenamides shows; disulfide and amine are formed.

In the case of compounds of similar structure such as aminomalonates and α-phenyl-α-dimethylaminoacetonitrile we have not been able to split off the amino group with hydrogen sulfide. Attempts have been made to cleave the N—C bond in *(3)* with thiophenols or alkylthiols; however, the reactions proved to be of a complex nature.

Preparation of malonodithioamide (4)

Hydrogen sulfide is passed into a solution of *(1)* (10.9 g) in pyridine (40 ml) and glacial acetic acid (10 ml) over a period of 10 hours at 20–25 °C. Compound *(4)* precipitates out on cooling the solution; yield 11 g (82%), m.p. 185–195 °C (decomp.) [212 °C (decomp.)[6]].

Received: February 5, 1969 [Z 997 IE]
German version: Angew. Chem. *81*, 741 (1969)
Publication delayed at authors' request

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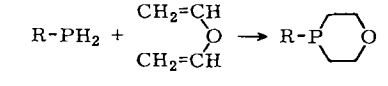
Perhydro-1,4-oxaphosphorins

By *P. Tavs*[*]

Dedicated to Professor B. Timm on the occasion of his 60th birthday

Until recently only few cyclic phosphines have become known that contain, in addition to phosphorus, another hetero atom not directly bonded to phosphorus[1–3]. This communication reports on the synthesis of perhydro-1,4-oxaphosphorins[3], the phosphorus analogs of morpholine.

UV irradiation[4] of an approximately 3% ethereal solution of an equimolar mixture of alkylphosphines RPH_2 and divinyl ether for 20–40 h leads to the heterocyclic tertiary phosphines *(1)–(4)* (work-up by distillation).



	R	B.p. (°C/torr)	Yield (%)	^{31}P chemical shift (ppm) [5]
(1)	n-C_8H_{17}	109–110/0.5	51	+52
(2)	n-$C_{12}H_{25}$	155–157/0.5	57	+52
(3)	n-$C_{14}H_{29}$	150–152/0.1	40	—
(4)	n-$C_{18}H_{37}$	211–212/0.5	42	—
(5)	H	45–48/16	7	+79 (J_{P-H} = 185 Hz)

Their structures follow from the $-CH_2-O-CH_2-$ signal in the 60-MHz NMR spectrum[6] (τ = 6.1–6.5) and the absence of a P–H absorption in the IR spectrum (2300 cm^{-1}). Compounds *(1)–(4)* react rapidly and quantitatively with methyl bromide in ether at 0 °C (quaternary salt of *(1)*, m.p. 97 to 98 °C; that of *(2)*, m.p. 139–140 °C) and with sulfur in boiling benzene (sulfide of *(1)*, m.p. 35–36 °C, recrystallized from pentane; that of *(2)*, m.p. 31–32 °C, recrystallized from methanol).

Reaction of 1 mole of PH_3 with 1 mole of divinyl ether in 500 ml of pentane with addition of 0.05 mole of azoisobutyronitrile[4] in an autoclave at 78–80 °C for 12 hours yields the unsubstituted heterocycle *(5)*, P–H absorption at 2250 cm^{-1}, molecular weight (determined by mass spectrometry) 104. In the 220-MHz NMR spectrum, the resonance signal of the equatorial and of the axial ring protons of *(5)* is resolved into four multiplets: τ = 6.0, 6.8 ($O-CH_2-$) and τ = 8.0, 8.5 ($P-CH_2-$)[7]. The P–H signal appears at τ = 6.85 (J_{P-H} = 185 Hz, further splitting into triplets). β,β'-Diphosphinodiethyl ether, b.p. 83–85 °C/0.5 torr, P–H absorption at 2290 cm^{-1}, is formed in 10% yield along with compound *(5)*. The fragment of highest mass in the precision mass spectrum of the former compound is $C_4H_{11}OP_2^+ = (M-H)$. Its 220-MHz NMR spectrum shows two multiplets at τ = 6.85 ($O-CH_2$) and τ = 8.5 ($P-CH_2$), as well as the P–H signal at τ = 7.5 (J_{P-H} = 193 Hz, further splitting into triplets).

UV irradiation of compound *(5)* and an excess of 1-octene in ethereal solution leads to 4-octylperhydro-1,4-oxaphosphorin *(1)* in 68% yield.

Received: February 5; revised: March 18, 1969 [Z 1000 IE]
German version: Angew. Chem. *81*, 742 (1969)
Publication delayed at author's request

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[5] 85% H_3PO_4 as internal standard. I am grateful to Prof. *E. Fluck*, Universität Stuttgart, for recording and discussing the spectra.

[6] All the ^{1}H-NMR spectra were recorded in C_6D_6 using TMS as internal standard; the spectrum of *(5)* was measured in deuteriotoluene. I am grateful to Dr. *W. Brügel* and Dr. *C. Witte*, Badische Anilin- & Soda-Fabrik, Ludwigshafen, for recording and discussing the 220- and 60-MHz spectra.

[7] The $-OCH_2$ and $P-CH_2$ multiplets coalesce when the sample is heated to 90 °C.

Novel Pigments from Dichloromaleimides

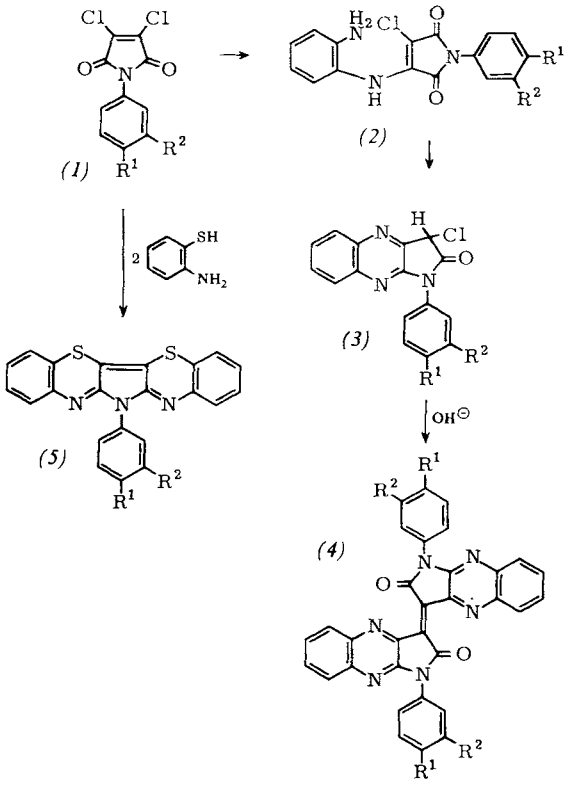
By *P. Dimroth* and *F. Reicheneder*[*]

Dedicated to Professor B. Timm on the occasion of his 60th birthday

We have prepared the novel pigment systems 1,1'-diphenyl-2,2',3,3'-tetrahydro(3,3'-bipyrrolo[2,3-*b*]quinoxaline)-2,2'-dione *(4)* and 7-phenylbenzothiazino[2',3' : 3,2]pyrrolo-[4,5-*b*]benzothiazine *(5)* by reaction of dichloromaleimides with *o*-phenylenediamines and *o*-aminothiols respectively. Both classes of compounds are intensely colored and exhibit pigment-like character.

The reaction product *(2)* expected[1] to be formed by reaction of *N*-phenyldichloromaleimide *(1)* with *o*-phenylenediamine, *e.g.* by heating the components in glycol monomethyl ether, cyclizes with elimination of water during recrystallization (*e.g.* from DMF) to give the quinoxaline derivative *(3)* in very good yields. When heated with bases such as alcoholic sodium- or potassium hydroxide, amines, or magnesium oxide, compound *(3)* undergoes condensation with elimination of HCl and formation of the isoindigoid dye *(4)*. The same reaction takes place when the substituted compounds

(1) and *(2)* are used as reactants. The derivatives of *(4)* (R^1 = R^2 = H, red-violet; R^1 = Cl, R^2 = H, Bordeaux; R^1 = OCH_3, R^2 = H, violet) thus obtained have a pigment-like character (insolubility, thermostability, weather resistance, coloring power); they are suitable, *e.g.* for the coloring of lacquers, PVC, polystyrene, polyamides, and polyolefins.



(5)	R^1	R^2	Color	Suitable for coloring:
(a)	H	H	orange	styrene, hard PVC, printing inks
(b)	Cl	C_6H_5—NH—CO	yellow	styrene, hard PVC, printing inks
(c)	Cl	*p*-C_6H_5—NH—CO-C_6H_4—NH—CO	yellow	lacquers, PVC, thermoplastics
(d)	*p*-C_6H_5—NH—CO-C_6H_4—NH—CO	Cl	orange	lacquers, PVC, thermoplastics

If *N*-phenyldichloromaleimide is allowed to react with *o*-mercaptoaniline instead of *o*-phenylenediamine (*e.g.* by boiling under reflux for 6 hours in glacial acetic acid — recrystallization from *N*-methylpyrrolidone) the polycyclic compound *(5a)*, a brilliant, intensely orange colored compound, is formed. The reaction can be carried out with any substituted dichloromaleimide and *o*-aminoarenethiols and thus affords a method for the preparation of a new class of yellow to red pigments. Red pigments in particular are obtained by anellation of the mercaptoaniline — sometimes by using 2-amino-1-thionaphthol — or by using derivatives of *N*-aminodichloromaleimide (*e.g.* *N*-benzoylaminodichloromaleimide). Yellow pigments are formed when imides having electron donors in the alkyl group (*e.g.* chlorine, *N*-chloroamide) are used in the reaction.

Received: February 5, 1969;
revised: June 18, 1969 [Z 18 IE]
German version: Angew. Chem. *81*, 742 (1969)
Publication delayed at authors' request

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1,3-Di(*tert*-butyl)-2,4-dichlorodiazadiphosphetidine

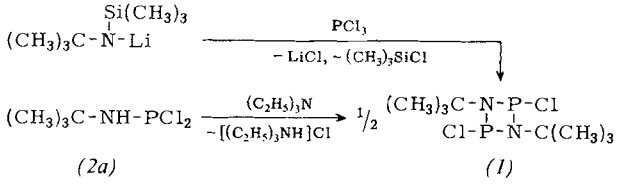
By *O. J. Scherer* and *P. Klusmann*[*]

The existence of four-membered phosphorus(III)-nitrogen ring compounds of the general composition $(RNPCl)_2$ (compounds in which R = C_6H_5 [1] and CH_3 [2] have, for example, been described) has been disputed on the basis of results of recent investigations [3,4].

We have now been able to prepare 1,3-di(*tert*-butyl)-2,4-dichlorodiazadiphosphetidine *(1)* by two different methods:

(i) by reaction of lithium *tert*-butyltrimethylsilylamide with phosphorus trichloride

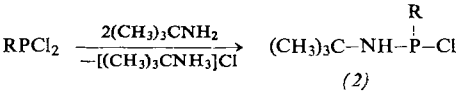
(ii) from *N*-*tert*-butylaminodichlorophosphine *(2a)* by elimination of HCl (yield 60%)



Compound *(1)*, colorless crystals having m. p. 42—44 °C (b. p. 90—93 °C/0.1 torr), is readily soluble in ether, benzene, and CCl_4. A 1:2:1 triplet (J^{31}PNCCH = 1.0 Hz) ascribable to the $(CH_3)_3C$ group can be observed in the ^{1}H-NMR spectrum (60 MHz). The alternative compound, $(CH_3)_3CN(PCl_2)_2$, was excluded by elemental analysis (*e. g.* Cl calc.: 25.8%; exp.: 25.1%).

Attempts to carry out substitution reactions on *(1)* with dimethylamine or methyllithium led only to complicated mixtures of substances.

N-Alkylaminodihalogenophosphines $RNHPX_2$ [5,6] and *N*-alkylaminohalogenoalkylphosphines RNHPRX [7], compounds of type *(2)*, have been little investigated; the majority of these compounds are not particularly stable at room temperature. If *tert*-butylamine is added dropwise with cooling to PCl_3 or $RPCl_2$ (both components being diluted with ether), thermally stable *N*-*tert*-butylaminochlorophosphines *(2)* are formed in various yields; these products can be purified by distillation and are readily soluble in benzene and ether.



(2a): R = Cl; yield 30% (*ca.* 20% of *(1)* is simultaneously formed); b.p. 53—58 °C/6 torr, m.p. −40 to −38 °C; J^{31}PNCCH = 2.2 Hz.

(2b): R = CH_3; yield 40%; b.p. 48—52 °C/5 torr, J^{31}PNCCH = 1.3, J^{31}PCH = 11.0 Hz.

(2c): R = $(CH_3)_3C$; yield 80%; b.p. 35—36 °C/0.1 torr; J^{31}PNCCH = 1.0, J^{31}PCCH = 13.3 Hz.

Unlike compound *(2a)*, compounds *(2b)* and *(2c)* do not form diazadiphosphetidine derivatives on addition of bases.

Preparation of (1):

A solution of $(CH_3)_3C[(CH_3)_3Si]NLi$ (73 mmoles) [prepared from $(CH_3)_3CNHSi(CH_3)_3$ (10.6 g, 73 mmoles) and *n*-C_4H_9Li/hexane solution (33.0 ml, 73 mmoles)] in ether (50 ml) is added slowly and dropwise with stirring at room temperature to a solution of PCl_3 (10.0 g, 73 mmoles) in ether (100 ml). After the exothermic reaction the mixture is filtered through a G3 frit, the filtrate is concentrated under vacuum (water pump), and the residue is heated to 130 °C in order to complete the elimination of $(CH_3)_3SiCl$. Fractional

distillation of the filtrate at reduced pressure yields 7.5 g (75 %) of pure *(1)*.

Received: July 1, 1969; revised: July 8, 1969 [Z 47 IE]
German version: Angew. Chem. *81*, 743 (1969)

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Hexapotassium μ-Thiobis(hexacyanomolybdate(IV)), a Novel Molybdenum Complex

By *A. Müller* and *P. Christophliemk*[*]

Passage of H_2S into an alkaline molybdate solution containing a large excess of KCN affords green, crystalline hexapotassium μ-thiobis(hexacyanomolybdate(IV))-4-water $K_6[(CN)_6MoSMo(CN)_6] \cdot 4H_2O$ *(1)*. The values obtained in a series of elemental analyses correspond to the composition given for the complex. Several experiments yielded products whose analyses, IR and electronic spectra, and powder photographs were in agreement with one another.

The solid-state IR spectrum of *(1)* in nujol shows the following main absorption bands (in cm^{-1}): νOH 3490; νCN 2133, 2123, 2112 (measured at high resolution, ±1 cm^{-1}); δOH 1660; δCN(?) 630; δCN, νMoC, and ν_{as}MoSMo: 485, 443, 387, 376, 356.

Electron absorption spectrum (aqueous solution): 620 nm ($\varepsilon = 1.4 \times 10^2$ l $mole^{-1}$ cm^{-1}), 369 (10^5), 295 ($\approx 10^3$), 263 ($\approx 2 \times 10^3$), and 232 ($\approx 10^4$). Whereas the first band is to be ascribed to a d→d transition, that at 369 nm, which has an exceptionally high intensity, is due to an electron transfer π(S)→d(Mo). The shift of this band toward shorter wavelengths compared with thiomolybdates without a bridging sulfur atom[1,2] is physically meaningful; the increased intensity compared with the corresponding band of thiomolybdates appears to be characteristic of an Mo-S-Mo group. The three remaining bands lie in the region expected for d(Mo)→π*(CN) transitions[3,4,5]. The solid-state electronic spectrum of *(1)* is identical with the solution spectrum between 650 and 300 nm. Since the solid-state electronic spectra of *(1)* and of the anhydrous complex *(2)* are in agreement with each other, it appears unlikely that water is coordinated to molybdenum; such a bonding would raise the coordination number of molybdenum to 8.

The molar conductivity Λ (18 °C, H_2O; $v = 10^3$ l $mole^{-1}$) of 665 cm^2 Ω^{-1} $mole^{-1}$ was to be expected for a complex salt that dissociates into seven ions. Complex *(1)* is diamagnetic both in the solid state and in aqueous solution. The five most intense lines in the powder photograph have the *d* values (relative intensities): 8.34_6 (92), 7.62_8 (64), 7.02_5 (74), 3.77_0 (55), 3.04_8 (100) Å.

The anion $[(CN)_6MoSMo(CN)_6]^{6-}$ can be precipitated from aqueous solution as $[Cr(NH_3)_6]_2[(CN)_6MoSMo(CN)_6] \cdot 4H_2O$, whose IR spectrum is analogous to that of the potassium salt.

Procedure:

H_2S is passed into a concentrated solution of potassium molybdate containing a five-fold excess of potassium cyanide (*e.g.* 40 g of MoO_3 + 90 g of KCN in 250 ml of 25% KOH) until the solution assumes an intense green color. On addition of acetone, a dark green oil is precipitated which solidifies on repeated washing with acetone, ethanol, and methanol. The crude product, which still contains a considerable amount of potassium molybdate, is recrystallized from aqueous solution with methanol until the IR spectrum no longer contains a band between 1200 and 800 cm^{-1}. The pure salt *(1)* is pale to grass green; the yield amounts to about 20%, referred to MoO_3. The anhydrous salt *(2)* is obtained when *(1)* is dried over P_4O_{10} in vacuum at 100 °C for two days.

Received: June 25, 1969; revised: July 30, 1969 [Z 52 IE]
German version: Angew. Chem. *81*, 752 (1969)

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The Catalytic Mixed Oligomerization of Butadiene and Alkynes

By *W. Brenner, P. Heimbach, K.-J. Ploner*, and *F. Thömel*[*]

Reaction of butadiene with 2-butyne (molar ratio 10 : 1) on Ni^0-triphenylphosphine catalyst leads to the formation of 4,5-dimethyl-*cis,cis,trans*-1,4,7-cyclodecatriene[1,2] (yield based on reacted butadiene ≈85% at 25% conversion; referred to 2-butyne >90% with ≈100% conversion). Equally good yields of ten-membered ring compounds can be

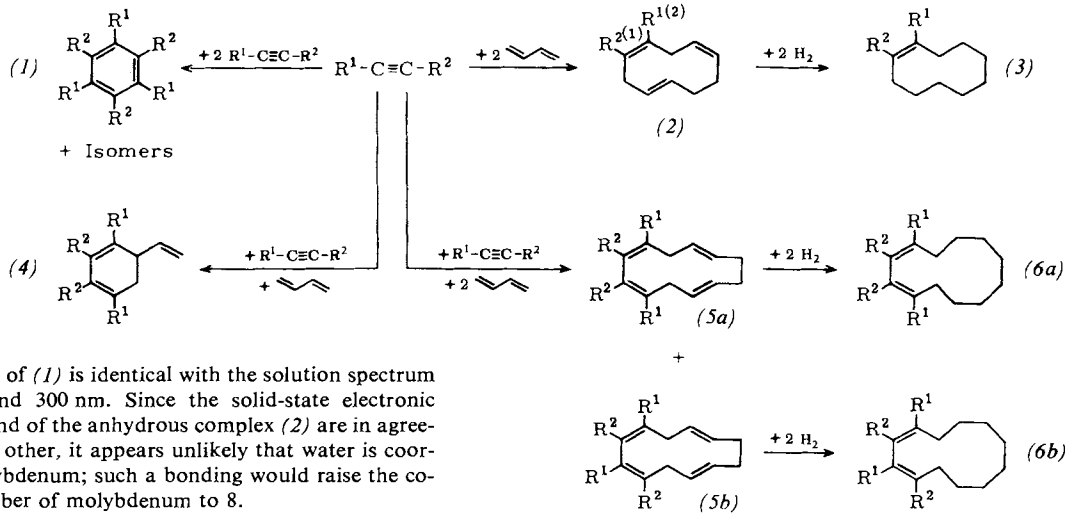


Table 3. Physical data of the previously undescribed mixed oligomers.

Alkyne used	Product	B.p. (°C/torr) [m.p. (°C)]	n_D^{20}
1,4-Dimethoxy-2-butyne	*(3)*, $R^1 = R^2 = CH_2-O-CH_3$	106–108/0.2	1.4901
1-Methoxy-2-pentyne [a]	*(3)*, $R^1 = CH_2-O-CH_3$, $R^2 = C_2H_5$	75/0.1	1.4913
Phenylacetylene	*(4)*, $R^1 = C_6H_5$, $R^2 = H$	[93–94]	
2-Butyne	*(5)*, $R^1 = R^2 = CH_3$	[59]	
1,4-Dimethoxy-2-butyne	*(6)*, $R^1 = R^2 = CH_2-O-CH_3$	162/0.2 [b]	1.4985
1-Methoxy-2-pentyne [a]	*(6a)*, $R^1 = CH_2-O-CH_3$, $R^2 = C_2H_5$	85–90/1 × 10^{-4} [b]	1.5025
1-Methoxy-2-pentyne [a]	*(6b)*, $R^1 = CH_2-O-CH_3$, $R^2 = C_2H_5$		1.5002

[a] Prepared from the sodium salt of methyl propargyl ether and ethyl bromide in liquid NH_3. B.p. 120 °C/760 torr; $n_D^{20} = 1.4235$. [b] The three compounds of type *(6)* were isolated in the pure form by preparative gas chromatography.

prepared if alkyl-substituted alkynes or alkynes in which the functional groups are separated from the triple bond by at least two methylene groups are used[3,4]. In addition, we could isolate further mixed oligomers of type *(4)* and *(5)* from butadiene and alkynes; these were identified by IR, ^{1}H-NMR, and mass spectroscopy.

Table 1. Dependence of yields of mixed oligomers on the molar ratio of butadiene : 2-butyne and on the catalyst. Reaction temperature 20 °C [3].

Catalyst	Butadiene : 2-butyne [a]	*(1)*, $R^1 = R^2 = CH_3$	Yield [b] *(2)*, $R^1 = R^2 = CH_3$	*(5)*, $R^1 = R^2 = CH_3$ [c]
Ni^0	1 : 1	3.3	21	17
Ni^0 +	1 : 1	3.2	83 [d]	3.2
$(C_6H_5)_3P$	10 : 1	0.3	76 [e]	0.9
Ni^0 +	1 : 1	2.3	58	19
$(C_6H_5O)_3P$	10 : 1	0.8	44	1.2

[a] Molar ratio at the beginning of the reaction.
[b] Wt.-% in reaction product.
[c] Small amounts of the *cis,cis,cis,trans* isomer is formed along with the *cis,cis,trans,trans* compound.
[d] Yield based on reacted 2-butyne ≈78%.
[e] Yield based on reacted 2-butyne >90%.

At higher alkyne concentrations, twelve-membered ring compounds *(5)* and aromatic compounds *(1)* are formed in higher yields. The twelve-membered ring compound *(5)*, $R^1 = R^2 = CH_3$, can be prepared from 2-butyne and butadiene in much better yields if triphenylphosphite-Ni^0 is used as catalyst instead of triphenylphosphine-Ni^0 (see Table 1).

The formation of the various mixed oligomers is dependent to a great extent on the nature of the substituents at the triple bond (see *e.g.* Table 2).

Two of the three isomeric twelve-membered ring compounds *(6)* are formed in the reaction of 1-methoxy-2-pentyne. So far we have been able to prepare a mixed oligomer of type *(4)* in about 20% yield from butadiene and 2-butyne (1 : 1) using Ni^0-catalysts containing no phosphorus ligands. Reaction of two molecules of phenylacetylene and one molecule of butadiene on Ni^0-triphenylphosphine catalyst at −10 °C leads to the formation of a 1,3-cyclohexadiene derivative in 25% yield[5]. That the phenyl groups are situated in the 1,4-position is confirmed, *inter alia*, by the UV-spectrum (λ_{max} = 343 nm, ε_{max} = 25770 l mole^{-1} cm^{-1} in hexane; cf.[6]). Furthermore, the compound can be isomerized quantitatively to 2′-ethyl-*p*-terphenyl (m.p. 38–39 °C, λ_{max} 264 nm, ε_{max} = 21000 l mole^{-1} cm^{-1} in hexane, cf.[7]) by potassium *tert*-butoxide in dimethyl sulfoxide.

Other catalytically formed cyclic mixed oligomers having the molar composition butadiene: alkyne = 3 : 1 and 2 : 3 have not as yet been isolable in the pure form.

Experimental

Bis(cyclooctadiene)nickel(0)[8] (8.5 mmoles) and $P(C_6H_5)_3$ (8.5 mmoles) are dissolved at −80 °C in a mixture of toluene (100 ml), alkyne (0.25 mole), and the desired amount of butadiene in a graduated pressure ampoule. The course of the reaction can be followed qualitatively by reference to the volume contraction. Methoxymethyl-, phenyl-, and carboxylate-substituted alkynes sometimes react too violently at 20 °C under these conditions; the reactions should therefore be carried out at temperatures below −10 °C.

Received: July 8, 1969 [Z 53 IE]
German version: Angew. Chem. *81*, 744 (1969)

Table 2. Dependence of yields of mixed oligomers on the substituents [3]. Reaction temperature 20 °C. Molar ratio of butadiene : alkyne at the start of reaction 10 : 1. Ni^0-triphenylphosphine catalyst.

Alkyne used	Product	Yield (%) [a]	Product	Yield (%) [a]
1,4-Dimethoxy-2-butyne	*(3)*, $R^1 = R^2 = CH_2-O-CH_3$ [b]	30	*(6)*, $R^1 = R^2 = CH_2-O-CH_3$ [b]	38
1-Methoxy-2-pentyne	*(3)*, $R^1 = CH_2-O-CH_3$, $R^2 = C_2H_5$ [b]	60	*(6)* [b, c]	29
2-Butyne	*(2)*, $R^1 = R^2 = CH_3$	>90	*(5)*, $R^1-R^2 = CH_3$	≈ 2

[a] Yields referred to reacted alkyne. [b] The compounds of types *(2)* and *(5)* obtained were hydrogenated to *(3)* and *(6)*, respectively, prior to isolation (20 °C/100 atm H_2/Raney Ni). [c] Mixture of *(6a)* + *(6b)*, $R^1 = CH_2-O-CH_3$, $R^2 = C_2H_5$

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Bis(diphenylboryl)diimine [1]

By *N. Wiberg* and *G. Schwenk* [*]

In most cases silicon-nitrogen compounds are readily cleaved by Lewis acids at the Si–N bond [2]. Treatment of bis(trimethylsilyl)diimine [3] should thus lead to a synthesis of new derivatives of diimine, R–N=N–R:

$$(CH_3)_3Si{-}N{=}N{-}Si(CH_3)_3 + 2\ R{-}X \rightarrow 2\ (CH_3)_3Si{-}X + R{-}N{=}N{-}R$$

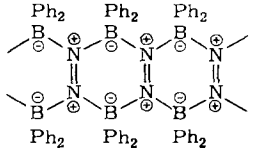
By using chlorodiphenylborane [R–X = $(C_6H_5)_2B$–Cl] in this way we obtained the first pure "azoborane" [4], namely, the brilliant yellow bis(diphenylboryl)diimine *(1)*. This compound completes the series of diimine derivatives R_2N_2 in which the two groups R attached to the diimine residue run from the element of the third to that of the seventh Group of the first short Period:

R_2N_2; R =

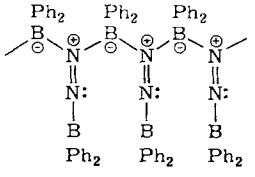
>B	>C	>N	–O	F
yellow	yellow-red	colorless	colorless	colorless

Compound *(1)* is not the sole product; about 70% of the reactants undergo an obscure reaction leading to nitrogen and an oil containing boron-nitrogen compounds of unknown composition.

The diimine *(1)* is polymeric, insoluble in the usual solvents, and extremely unreactive; thermal decomposition occurs only slowly above 400 °C, with loss of all the nitrogen. The compound is stable towards acids, but decomposes in the basic pyridine, giving up half its nitrogen. Two structural formulas *(1a)* and *(1b)* (Ph = C_6H_5) require consideration:



(1a)



(1b)

In *(1a)* the valency requirements of all the nitrogen and boron atoms are fully met; in *(1b)* only half the nitrogen and boron atoms are so satisfied, the other half having a free n-electron pair or an electron deficiency. The findings that organic azo compounds can be only singly protonated and that *(1)* dissolves in pyridine with decomposition are in favor of structure *(1b)*; this formula appears the more probable also because of the color of the compound which, as for other azo compounds, may depend on an n→π* electron transition [5].

Experimental:

Solutions of bis(trimethylsilyl)diimine (15.5 mmoles) and chlorodiphenylborane (31 mmoles) each in methylene dichloride (20 ml) are mixed at −40 °C, the reaction being carried out in the absence of oxygen. The mixture becomes deep blue for a short time and evolves nitrogen. When evolution of nitrogen is complete there is a clear yellowish-orange solution, from which analytically pure *(1)* separates slowly at −25 °C as a yellow precipitate.

Received: July 21, 1969 [Z 54a IE]
German version: Angew. Chem. *81*, 745 (1969)

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[1] Part 2 of Derivatives of Diimine. This work was supported by the Deutsche Forschungsgemeinschaft. – Part 1: [3].

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ESR Spectra of Radical Anions of Aliphatic Azo Compounds: *tert*-Butyl and Trimethylsilyl Derivatives of Diimine [1]

By *U. Krynitz*, *F. Gerson*, *N. Wiberg*, and *M. Veith* [*]

Successive replacement of the tertiary carbon atoms of the relatively stable, pale yellow di(*tert*-butyl)diimine (azoisobutane) *(1)* [2] by the group-homologous silicon atoms leads by way of the less stable, red *tert*-butyl(trimethylsilyl)diimine *(2)* [3] to the extremely unstable, pale blue bis(trimethylsilyl)-diimine *(3)* [4]:

$(CH_3)_3C{-}N{=}N{-}C(CH_3)_3$ *(1)*

$(CH_3)_3C{-}N{=}N{-}Si(CH_3)_3$ *(2)* (α, β)

$(CH_3)_3Si{-}N{=}N{-}Si(CH_3)_3$ *(3)*

In this paper, we report on the radical anions $(1)^{\ominus}$, $(2)^{\ominus}$, and $(3)^{\ominus}$ of these three compounds, which are of theoretical interest as simple π-electron radicals. In contrast to the situation with the known radical anions of aromatic azo compounds [5], the π-spin population in $(1)^{\ominus}$, $(2)^{\ominus}$, and $(3)^{\ominus}$ should be limited mainly to the azo group. This applies particularly to $(1)^{\ominus}$, whereas in the radical anions $(2)^{\ominus}$ and $(3)^{\ominus}$ the unpaired electron can be delocalized to some extent in unoccupied silicon orbitals of suitable symmetry [6].

The radical anions were prepared by reduction of *(1)*, *(2)*, and *(3)* with sodium or potassium in tetrahydrofuran (THF). THF was preferred to 1,2-dimethoxyethane as solvent since it was found that *(2)* and *(3)* are considerably less stable in the latter solvent. However, the radical anions $(1)^{\ominus}$ and $(2)^{\ominus}$ are remarkably stable: after standing for several hours at temperatures below 0 °C their concentration has decreased only slightly. This is only partially true for $(3)^{\ominus}$; although this radical anion is very stable when the counter ion is Na^+, it decomposes even in a few minutes above −50 °C when the counter ion is K^+. The ESR coupling constants for $(1)^{\ominus}$, $(2)^{\ominus}$, and $(3)^{\ominus}$ are listed in Table 1, where the assignments for $a_{N\alpha}$ and $a_{N\beta}$ in the case of $(2)^{\ominus}$ are based on

Table 1. Coupling constants (in gauss) of the magnetic nuclei in $(1)^{\ominus}$, $(2)^{\ominus}$, and $(3)^{\ominus}$. Solvent: THF.

Radical anion	Counter ion/ °C	$a_{N\alpha}$	$a_{N\beta}$	a_H	$a_{^{13}C}$ [a]	$a_{^{29}Si}$
$(1)^{\ominus}$	Na^+/0	8.24 ± 0.05	8.24 ±0.05	0.32 ±0.01	4.7 ±0.5	–
	K^+/0	8.25 ± 0.05	8.25 ±0.05	0.32 ±0.01	4.8 ±0.5	–
$(2)^{\ominus}$	Na^+/0	10.85 [b] ± 0.10	4.28 [b] ±0.05	[c]	[d]	[d]
	K^+/0	10.40 [b] ± 0.10	4.57 [b] ±0.05	[c]	[d]	[d]
$(3)^{\ominus}$	Na^+/0	6.62 ± 0.06	6.62 ±0.06	[c]	–	[d]
	K^+/−80	6.25 ± 0.06	6.25 ±0.06	[c]	–	7.0 ±0.2

[a] Tertiary C atoms. [b] Temperature-dependent coupling constants. [c] Not resolved. [d] Not unambiguously identified.

comparisons with *(1)*$^{\ominus}$ and *(3)*$^{\ominus}$ and on HMO calculations. The characteristic spectra are reproduced in Figures 1a—1d.

Not enough information is presently available for a detailed discussion of the ESR results (Table 1). In the first place, it is questionable whether the parameters that have been proposed for the relations between ^{14}N coupling constants and π-spin populations in other cases [7] may be used here. Secondly, the hybridization state of trimethylsilyl-substituted nitrogen atoms in *(2)* and *(3)* has not been clarified. Even with these limitations the following relations are evident:

1. The sums of the coupling constants $a_{N\alpha} + a_{N\beta}$ decrease along the series *(1)*$^{\ominus}$, *(2)*$^{\ominus}$, and *(3)*$^{\ominus}$: 16.5; 15.2 (15.0); 13.2 (12.5). The decreases correspond to the expectation that trimethylsilyl substituents should have an appreciable share of the π-spin population [6]. It is informative to compare the ^{14}N coupling constants ($a_{N\alpha} = a_{N\beta}$) of the two symmetrical radical anions *(1)*$^{\ominus}$ and *(3)*$^{\ominus}$ with the corresponding values for the radical anion *(4)*$^{\ominus}$ of azobenzene [5]: *(1)*$^{\ominus}$ 8.25; *(3)*$^{\ominus}$ 6.25 (6.62); *(4)*$^{\ominus}$ 4.84 gauss. The capacity of trimethylsilyl substituents for sharing π-spin population is thus intermediate between the capacities of alkyl and of aryl substituents.

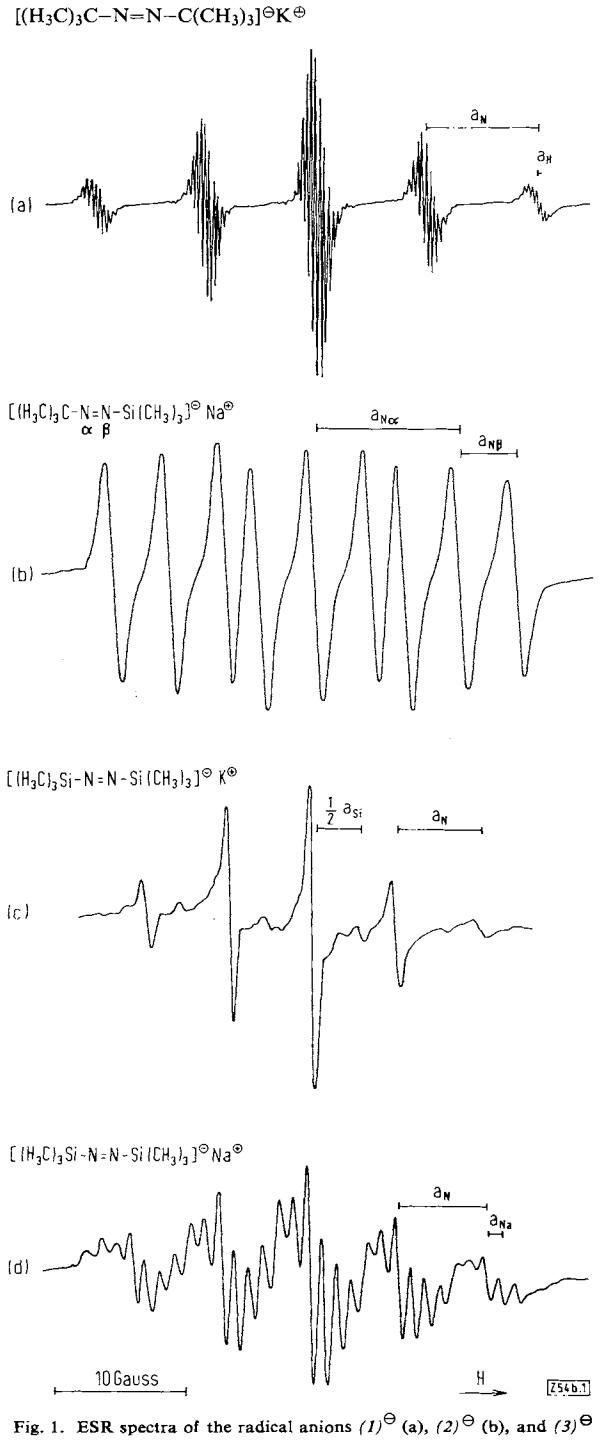


Fig. 1. ESR spectra of the radical anions *(1)*$^{\ominus}$ (a), *(2)*$^{\ominus}$ (b), and *(3)*$^{\ominus}$ (c and d).
Solvent: THF; temperature: 0 °C for a, b, and c, −80 °C for d.

2. In contrast to radical anion *(1)*$^{\ominus}$, where a coupling constant $a_H(C-CH_3) = 0.32$ gauss could be measured (cf. Fig. 1a), the corresponding splittings could not be resolved in the spectra of *(2)*$^{\ominus}$ or *(3)*$^{\ominus}$ (cf. Figs. 1b, c, d). The reason for this probably lies in the small size of $a_H(Si-CH_3)$, which for *(3)*$^{\ominus}$ is likely to be at most 0.1 gauss in view of a line width of 0.6 gauss. This finding cannot yet be interpreted.

3. An additional hyperfine splitting was observed for *(3)*$^{\ominus}$ with Na^+ as counter ion: $a_{Na} = 1.05 \pm 0.05$ gauss (Fig. 1d). The splitting pattern (seven lines of relative intensities 1:2:3:4:3:2:1) corresponds to interaction with two equivalent ^{23}Na nuclei, a phenomenon that has already been found for ketyls in THF with Na^+ or Li^+ as counter ions [8]. Since the electronic structures of the azo and the keto group are related, similar associations might be involved in the two cases. An additional splitting by ^{39}K nuclei of two equivalent K^+ counter ions was not observed either for *(3)*$^{\ominus}$ or for the ketyls mentioned above, probably because of lack of association (larger volume of the K^+ ion) and/or of non-resolution (appreciably lower magnetic moment of the ^{39}K isotope). The former explanation is favored in the case of *(3)*$^{\ominus}$ by the almost identical line widths in the spectra concerned (Figs. 1c and 1d) and also by the stabilization, already indicated, of the radical anion by Na^+ counter ions.

Received: July 21, 1969 [Z 54b IE]
German version: Angew. Chem. *81*, 745 (1969)

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[1] Also Part 3 of Derivatives of Diimines. This work was supported by the Schweizerischer Nationalfonds (Project No. 4651) and by the Deutsche Forschungsgemeinschaft. – Part 2: *N. Wiberg* and *G. Schwenk*, Angew. Chem. *81*, 745 (1969); Angew. Chem. internat. Edit. *8*, 755 (1969).

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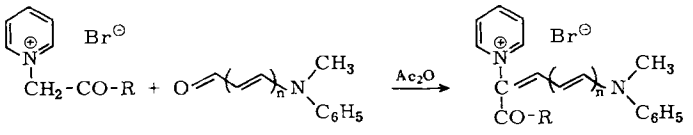
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O-Acylated Vinylogous Amides [1]

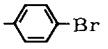
By *H. G. Nordmann* and *F. Kröhnke* [*]

Vinylogous amides (formamides) *(2)* react extremely smoothly with methylene-active compounds such as *N*-(*p*-bromophenacyl)pyridinium bromide *(1)* in acetic anhydride in a kind of vinylogous formylation to give vinylpyridinium salts of the type *(3)* [3].

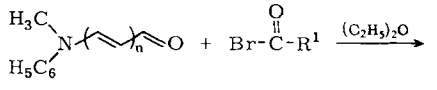
O-Acylated vinylogous amides were assumed to occur as active intermediates in order to explain the unusually high reactivity of vinylogous amides in the above reaction [2, 3]. We have now succeeded in isolating these compounds for the first time [4, 5].



(1) (2) (3)

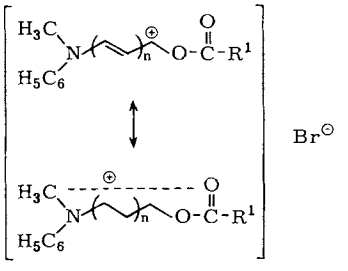
R =  n = 1,2

The amides *(2)* were treated with acetyl and benzoyl bromide *(4)* in anhydrous ether at 0 °C with rigorous exclusion of moisture (baked-out apparatus, argon). The *O*-acylated amides *(5)* were precipitated immediately as analytically pure, pale yellow to yellow substances in 89—98% yield.



(2) (4)

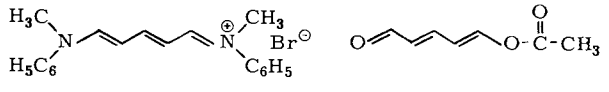
n = 1, 2
R^1 = CH_3; C_6H_5



(5)

The salts *(5)*, which are extremely sensitive to moisture, can be manipulated under argon and stored undecomposed for a considerable time in a Schlenk tube at −20 °C. The results of elemental analysis correspond to the calculated values.

The IR spectrum (nujol) of the compounds *(5)* shows intense, sharp bands in the carbonyl region. The compounds dissociate into *(2)* and acyl bromide *(4)* in inert, non-acylating solvents such as chloroform[6]; they are practically stable in acetic anhydride and acetyl chloride. *(5)*, $n = 2$, $R^1 = CH_3$, is hydrolyzed immediately to the symmetrical vinylogous amidinium salt *(6)* and to *O*-acetylglutaconaldehyde *(7)* by water.

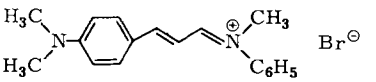


(6) (7)

The formation of *(7)* serves as a proof of the structure of *(5)* since *(7)* can only arise from an *O*-acylated vinylogous amide but not from an *N*-acylated one[7]. The salt *(6)* is formed from the deacylated salt *(5)* and the *N*-methylanilinium bromide that is formed by C—N cleavage on hydrolysis of *(5)*[8]. The surprising formation of symmetrical vinylogous amidinium salts from vinylogous amides in the presence of acylating reagents, which has been observed by other workers[2,9], is doubtless also a "symmetry reaction" of this kind. Compounds *(5)* also react with *N*-methylaniline to give salts of type *(6)*.

We have treated *(5)*, $n = 1$, with *N,N*-dimethylaniline to give the deeply colored immonium salt *(8)*, which affords *p*-dimethylaminocinnamaldehyde on hydrolysis. Compound *(3)*, $n = 1,2$, is formed from *(5)*, $n = 1,2$, and the pyridinium salt *(1)*.

The salts *(5)* could also be identified by UV spectroscopy when moisture was rigidly excluded from the sample: the active intermediate formed from *(2)*, $n = 2$, ("Zincke aldehyde") in acetic anhydride proved identical — apart from the anion — with *(5)*, $n = 2$, $R^1 = CH_3$.



(8)

As highly reactive electrophiles, the *O*-acylated vinylogous amides show a pronounced similarity to the vinylogous "Vilsmeier reagents"[2], the vinylogous formimidyl chlorides[10], and the *O*-alkylated vinylogous amides[11].

Received: July 23, 1969 [Z 55 IE]
German version: Angew. Chem. *81*, 747 (1969)

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[1] Part 7 of Novel Cyanins. — Part 6: ref. [5].

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[6] Cf. *D. E. Horning* and *J. M. Muchowski*, Canad. J. Chem. *45*, 1247 (1967).

[7] Compare the synthesis of β-chlorovinyl aldehydes by hydrolysis of vinylogous formimidyl chlorides: *Z. Arnold* and *J. Žemlička*, Collect. czechoslov. chem. Commun. *24*, 2378 (1959).

[8] *Z. Arnold*, Collect. czechoslov. chem. Commun. *24*, 760 (1959); *S. S. Malhotra* and *M. C. Whiting*, J. chem. Soc. (London) *1960*, 3812.

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[10] *H. E. Nikolajewski*, *S. Dähne*, and *B. Hirsch*, Chem. Ber. *100*, 2616 (1967).

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Electrochemical Oxidation of Aldehydes, Formic Acid, and Carbon Monoxide at Tungsten Carbide Electrodes in 2 N Sulfuric Acid

By *H. Binder*, *A. Köhling*, *W. Kuhn*, and *G. Sandstede*[*]

Because of their stability towards acids the borides, carbides, nitrides, and silicides of the transition metals have been investigated regarding their suitability as electrode materials[1]. Tungsten carbide (WC) has been proved to be electrocatalytically active for the oxidation of hydrogen[2]. We have confirmed that of all the compounds of this type investigated, WC alone exhibits such an activity and, furthermore, we have found that substances other than hydrogen can be oxidized at WC anodes.

For our potentiodynamic and stationary galvanostatic measurements we used the half-cell arrangements described in reference[3].

Various carbonaceous compounds, namely aldehydes, formic acid, and carbon monoxide are converted at WC electrodes at 70 °C. The activity of freshly prepared tungsten carbide is not very high and commercial products are usually not suitable because of their small surface area. However, as for hydrogen[4], the conversion of other fuels significantly increases after anodic loading of the electrodes at 600 to 700 mV (referred to an H_2-electrode in the same electrolyte) over a period of several hours in the presence of reducing agents such as formaldehyde or hydrazine. This is the case not only for electrodes of porous sintered WC but also for plastic bonded hydrophobic electrodes containing WC as catalyst. The current-voltage curves shown in Figure 1 were obtained with formaldehyde and acetaldehyde after such an activation in the presence of hydrazine. The rate of

oxidation of formaldehyde exceeds by far that of acetaldehyde; a current density of up to 50 mA/cm² can be achieved at voltages lower than 300 mV. However, evolution of gases at the electrodes is insignificant and it can be concluded that the current-producing reaction step is the oxidation to formic acid, which can be further oxidized only slowly. The current density increases greatly with the concentration of the aldehyde in the electrolyte.

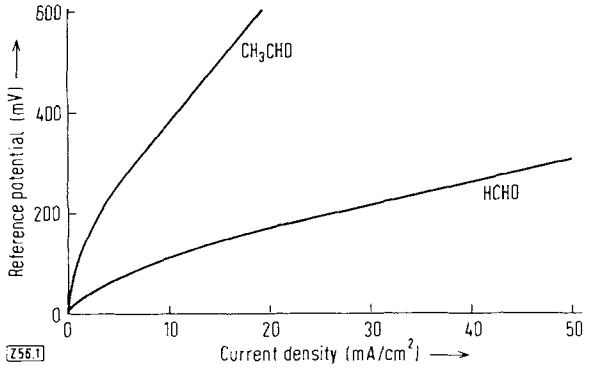


Fig. 1. Stationary galvanostatic current-voltage curves for the oxidation of formaldehyde and acetaldehyde at tungsten carbide in 2 N H_2SO_4 at 70 °C.

The oxidation of acetaldehyde proceeds without evolution of gas, *i.e.* only acetic acid is formed; carboxylic acids, however, cannot be oxidized at WC electrodes. Formic acid is an exception, as it behaves as an hydroxyaldehyde; at sufficiently high temperatures it oxidizes at voltages slightly above 0 mV with evolution of CO_2. Gas is also evolved at the electrode at 90 °C under open circuit conditions, in this case it is probably the evolution of carbon dioxide and hydrogen, which is due to the dehydrogenation of the formic acid (HCOOH → CO_2 + H_2). In the oxidation of formic acid the reaction rate decreases substantially with decreasing temperature (Fig. 2).

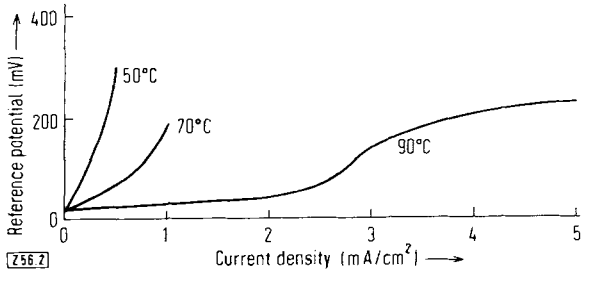


Fig. 2. Stationary galvanostatic current-voltage curves for the oxidation of formic acid at tungsten carbide in 2 N H_2SO_4 at 50, 70, and 90 °C.

At 90 °C and 300 mV the current density is 5 mA/cm² and at 50 °C it decreases to about 10 % of this value. The anomalous character of the curve at 90 °C can easily be explained as follows: At open circuit the hydrogen formed as a result of dehydrogenation of HCOOH determines the potential of the electrode; the rest potential is about 0 mV. At low galvanostatic loading the hydrogen formed by dehydrogenation is first oxidized. At higher current density the formic acid is oxidized directly; this reaction requires a larger overvoltage. Above 300 mV the oxidation reaction is inhibited (clearly recognized in periodic current-voltage curves), and the potential increases rapidly with only a slightly higher loading to about 700 mV; presumably from this point onwards the tungsten carbide itself is attacked.

Several higher aldehydes (*e.g.* propanal, glycolaldehyde, benzaldehyde) can also be oxidized, although in poor yield, to the corresponding carboxylic acids; dark colored condensation products are usually formed at the same time. Alcohols are not converted at WC electrodes under analogous experimental conditions.

At WC gas electrodes even carbon monoxide can be oxidized; however, the current density (3 mA/cm² at 500 mV) is small compared with that reached in the oxidation of hydrogen (150 mA/cm² at 300 mV).

Received: July 21, 1969 [Z 56 IE]
German version: Angew. Chem. *81*, 748 (1969)

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[1] French Pat. 1436504 (1966), Licentia Patentverwertungs GmbH; *W. Kuhn, W. Lindner, G. Sandstede*, French Pat. 1486723 (1967), Robert Bosch GmbH; *F. A. Pohl*, German Pat. Appl. 1496176 (1969), Licentia Patentverwertungs GmbH.

[2] *H. Böhm* and *F. A. Pohl*, Wiss. Ber. AEG-Telefunken *41*, 46 (1968); Lecture 3. Journées int. d'Etude des Piles à Combustible, Brussels, June 1969.

[3] *H. Binder, A. Köhling*, and *G. Sandstede*, Angew. Chem. *79*, 903 (1967); Angew. Chem. internat. Edit. *6*, 884 (1967).

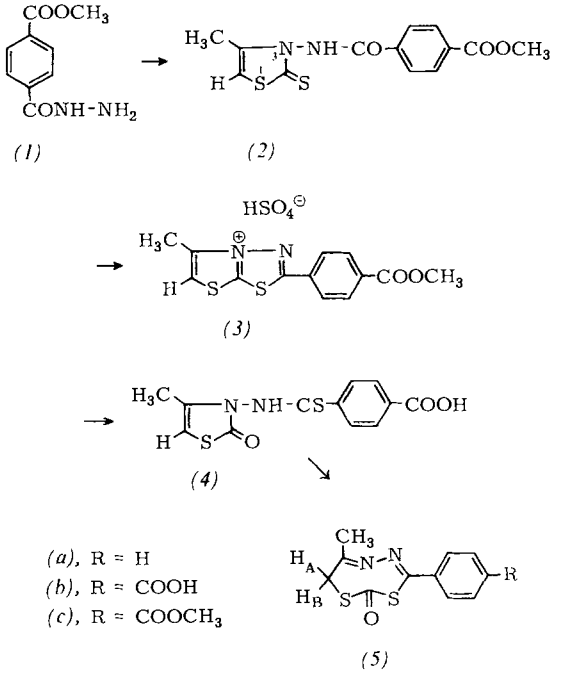
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An Optically Active Heteroocine

By *G. Ege* and *W. Planer* [*]

The ^{1}H—NMR spectrum of 7-methyl-4-phenyl-8*H*-1,3,5,6-dithiadiazocin-2-one *(5a)* shows an AB spectrum for the methylene protons; a chiral conformation was deduced on the basis of this fact [1]. Failure of the signals to coalesce when the sample is heated to 150 °C suggested that the substance can be resolved into optical antipodes.

Optical resolution has now been achieved with the carboxyl derivative *(5b)*. Reaction of dimethyl terephthalate and hydrazine hydrate (molar ratio 2:1) in boiling dioxane for eight days afforded the methyl terephthalate hydrazide *(1)* in 60 % yield [2]. In a series of reactions carried out in a single flask (1. CS_2 + KOH, 2. chloroacetone, 3. HCl), *(1)* gave the thiazolinethione *(2)* [80 %; m.p. 199—201 °C (from methanol); ^{1}H—NMR spectrum (CF_3COOH): δ = 2.44 (3H/d); δ = 4.17 (3H/s); δ = 6.82 (1H/q); δ = 8.12—8.45 (4H/m); $J_{CH_3\text{-}H_5}$ = 1.2 Hz], which is cyclized to the hydro-



gen sulfate *(3)* on treatment with concentrated sulfuric acid[1,3] [85 %; m.p. 259—260 °C (decomposition); ^{1}H-NMR spectrum (CF_3COOH): δ = 2.97 (3H/s); δ = 4.17 (3H/s); δ = 7.90 (1H/s); δ = 8.17—8.51 (4H/m)].

If a solution of *(3)* in aqueous KOH, which has been allowed to stand at room temperature for several hours, is added dropwise to boiling dilute hydrochloric acid, compound *(5b)* is obtained [80 %; m.p. 230 °C (decomposition); ^{1}H—NMR spectrum ([D$_6$]—DMSO): δ = 1.85 (3H/s); AB system: δ_A = 3.76, δ_B = 3.46, J_{AB} = 10 Hz; δ = 7.80—8.20 (4H/m)]. The yellow compound *(4)*, which is precipitated on acidification of a cooled alkaline solution of *(3)*, is formed as intermediate in the above reaction [90 %; m.p. 208—212 °C; UV spectrum (methanol): λ_{max} = 411 (ε = 330), 291 (8040), and 251 nm (18800)]. Compound *(4)* can be converted into *(5b)* both thermally and by the action of acids.

The optical resolution of *(5b)* was carried out with brucine in methanol. After repeated recrystallization from methanol the brucine salt shows a specific rotation of $[\alpha]_{436}^{20}$ = —885 ° (*c* = 0.5; chloroform). Decomposition of this salt with dilute hydrochloric acid gave levorotatory *(5b)* having a specific rotation of $[\alpha]_{436}^{20}$ = —2250 ° (*c* = 0.5; acetone). The ORD curve exhibits the expected Cotton effect. Dextrorotatory *(5b)* was obtained by working up the mother liquor of the brucine salt.

To the best of our knowledge, the heteroocine *(5b)* is the first eight-membered, monocyclic heterocycle not fused to a benzene nucleus whose chirality does not arise from an asymmetric C atom and whose optical resolution has been achieved. Moreover, the activation parameters for ring inversion are exceptionally high. We calculated the following values from the rate of racemization of *(5c)* bearing in mind that $k_{rac} = 2\,k_{inv}$: E_A = 30.6 kcal/mole, log *A* = 12.1, and at 120 °C $\Delta G^{\ddagger}$ = 32.1 kcal/mole, $\Delta H^{\ddagger}$ = 29.8 kcal/mole, and $\Delta S^{\ddagger}$ = —6 e. u.

Attempts to determine the optical purity of levorotatory *(5b)* from the NMR spectra (60 MHz) of a number of diastereomeric derivatives of *(5b)* according to the method of *Raban* and *Mislow*[4] were unsuccessful. Experiments to determine the optical purity by the method of isotopic dilution are in progress.

Received: July 11, 1969; [Z 58 IE]
German version: Angew. Chem. *81*, 749 (1969)

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[1] *G. Ege*, Angew. Chem. *79*, 618 (1967); Angew. Chem. internat. Edit. *6*, 629 (1967).

[2] The hydrazide *(1)* had previously only been obtained in small amounts on reaction of dimethyl isophthalate with hydrazine hydrate; cf. *L. A. Carpino*, J. Amer. chem. Soc. *79*, 96 (1957), particularly p. 98.

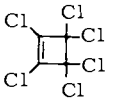
[3] Compare the preparation of thiazolo[2.3-*b*]thiazolium salts: *C. K. Bradsher, D. F. Lohr*, and *W. J. Jones*, Tetrahedron Letters *1965*, 1723.

[4] *M. Raban* and *K. Mislow* in *N. L. Allinger* and *E. L. Eliel*: Topics in Stereochemistry. Vol. *2*, Interscience, New York 1967, p. 199.

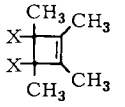
1,2,3,4-Tetrachloro-5,6-dimethyl(Dewar-benzene)

By *R. Criegee* and *R. Huber*[*]

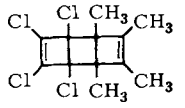
1,2,3,4-Tetrachloro-5,6-dimethyl(Dewar-benzene) (1,2,3,4-tetrachloro-5,6-dimethylbicyclo[2.2.0]hexadiene) *(6)* has been prepared by the following novel route: Treatment of a mixture of hexachlorocyclobutene *(1)*[1] and 3,4-dichloro- and 3,4-dibromo-1,2,3,4-tetramethylcyclobutene *(2)*[2] in boiling ether with lithium amalgam afforded the mixed dimer 1,6,7,8-tetrachloro-2,3,4,5-tetramethylbicyclo[4.2.0.0^{2,5}]-octadiene *(3)* in 15—20% yield, alongside octachlorotricyclo[4.2.0.0^{2,5}]octadiene *(4)*[3]. The products were separated by preparative thin-layer chromatography.



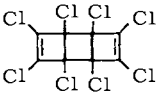
(1)



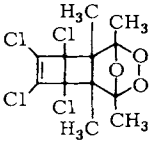
(2a), X = Cl
(2b), X = Br



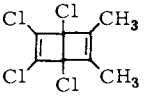
(3)



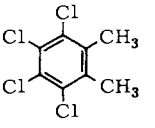
(4)



(5)



(6)



(7)

Only the electron-rich double bond of *(3)* reacts with ozone in pentane at room temperature[4]. On degradation according to the method given by *Story*[5] the ozonide *(5)* loses acetic anhydride, the thermal reaction leading to tetrachloro-*o*-xylene *(7)* whereas the photochemical process (CCl_4, —25 °C, laboratory immersion lamp S-81, 1.4 amp, 15—20 h) gives tetrachloro-*o*-(Dewar-xylene) *(6)* in 82% yield. *(6)* was freed from accompanying *(7)* by vacuum sublimation.

Compound *(6)* undergoes thermal isomerization to *(7)* and has a half-life of 20 min at 120 °C and 9 h at 90 °C.

Compd. [a]	M.p. (°C)	NMR [b]	IR (CCl_4)	UV (λ_{max})
(3)	165—167 (decomp.)	8.41 (s), 8.83 (s) 1:1	1676 [c] 1610 [d]	—
(4)	169—172 (decomp.)		1608 [d]	239 nm (ε = 5200)
(5)	165—166 (decomp.)	8.42 (s), 8.68 (s) 1:1	1610 [d]	
(6)	56—57	8.22 (s)	1680 [c] 1600 [d]	240 nm (ε = 2700)
(7)	225—226	7.55 (s)		

[a] All substances gave satisfactory elemental analyses.
[b] In CCl_4, TMS as internal standard, τ scale.
[c] 1,2-Dimethylcyclobutene stretching vibration.
[d] 1,2-Dichlorocyclobutene stretching vibration.

1,2,3,4-Tetrachloro-5,6-dimethyl(Dewar-benzene) (6)

To a vigorously stirred, refluxing solution of *(2a)* (9.6 g) and *(2b)* (21.2 g) in anhydrous ether (50 ml) are added (i) 0.67% lithium amalgam (528 g) and (ii), dropwise over a period of 3 h, a solution of *(1)* (33.4 g) in anhydrous ether (200 ml). After two further hours the reaction mixture is filtered and the mercury residue washed four times with 100 ml portions of hot chloroform. The solvents are removed from the filtrate and extracts, and the residue obtained is dissolved in cyclohexane (200 ml) and filtered through aluminum oxide (400 g). Washing of the adsorbent with pentane (1.5 l), removal of the solvents, and washing with cold methanol yields a colorless crystalline mixture of *(3)* (8—9 g) and *(4)* (2—3 g). The products can be separated by preparative thin-layer chromatography on silica gel.

A 10-g portion of the mixture of *(3)* and *(4)* in pentane (200 ml) is treated with an excess of ozone at room temperature, whereupon a colorless crystalline precipitate is formed. The precipitate and mother liquor are transferred to a column packed with silica gel (400 g) and eluted with pentane (1 l); 2—3 g of *(4)* can be isolated from the pentane eluate. The ozonide *(5)* is eluted from the column with an ether/

pentane mixture (1:5) and is obtained in the form of leaflets on removal of the solvent (yield 8–9 g).

A solution of *(5)* (917 g) in CCl_4 (7 ml) is irradiated under nitrogen in a glass ampoule at −20 °C for 15–20 h. The contents of the ampoule are chromatographed on silica gel (30 g) and eluted with pentane (500 ml). Evaporation to dryness leaves 578 mg of crystals from which compound *(6)* (534 mg, 82%) is obtained by sublimation at 30 torr (bath temperature 75 °C); compound *(7)* (44 mg, 7%) remains behind as residue.

Received: June 30, 1969 [Z 59 IE]
German version: Angew. Chem. *81*, 750 (1969)

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[1] *W. C. Solomon, L. A. Due*, and *D. W. Schultz*, J. org. Chemistry *31*, 1551 (1966).

[2] The best yield is obtained when a mixture of the dichloro and dibromo compounds is used.

[3] Prepared by *K. O. Scherer* and *T. J. Meyers* [J. Amer. chem. Soc. *90*, 6253 (1968)] by another method.

[4] *(5)* can be obtained directly from the mixture of *(3)* and *(4)* because *(4)* does not react with ozone under the above conditions.

[5] *P. R. Story, W. H. Morrison, T. K. Hall, J. C. Farine*, and *E. E. Bishop*, Tetrahedron Letters *1968*, 3291; *R. P. Story, T. K. Hall, W. H. Morrison*, and *J. C. Farine*, *ibid. 1968*, 5397.

Direct Conversion of Aromatic Nitro Compounds into Isothiocyanates

By *G. Ottmann* and *E. Kober* [*]

Isothiocyanates *(2)* could previously be synthesized from nitro compounds *(1)* only by reduction to the amines and reaction of the latter with, *e.g.*, carbon disulfide and a heavy metal salt or with thiophosgene [1].

We have now been able to accomplish the direct conversion of aromatic nitro compounds (nitrobenzene, dinitrobenzene, and their derivatives) into isothiocyanates by reaction with carbon disulfide or carbonyl sulfide in presence of selected bases.

The reaction is best performed by heating the nitro compound in an autoclave with a) carbon disulfide and alkali metal alkoxide or phenoxide, b) carbon disulfide and an alkyl or aryl sulfide, or c) carbonyl sulfide and an aryl sulfide. Optimum results are obtained at a reaction temperature of between 150 and 170 °C, and by employing carbon disulfide (methods a and b) or carbonyl sulfide (method c) as both reactant *and* solvent. In other solvents, such as benzene, toluene, benzonitrile, *o*-dichlorobenzene, carbon tetrachloride, or 1,1,2-trichloro-1,2,2-trifluoroethane, the reactions result in conversions and yields lower than those reported in the Table.

$RNO_2 \rightarrow RNCS$
(1) *(2)*

R	Base	Meth.	Conversion of *(1)* (%)	Yield of *(2)* (%)
C_6H_5	CH_3ONa	a	66	50
C_6H_5	CH_3SNa	b	34	58
C_6H_5	$S(CH_2CH_2SNa)_2$	b	50	51
C_6H_5	C_6H_5SNa	b	73	61
C_6H_5	*m*-CH_3–C_6H_4SNa	b	93	73
C_6H_5	*m*-CH_3–$C_6H_4SC(S)SNa$	b	53	77
m-CH_3–C_6H_4	CH_3ONa	a	50	66
m-CH_3–C_6H_4	*m*-CH_3–C_6H_4SNa	b	71	87
p-CH_3–C_6H_4	*m*-CH_3–C_6H_4SNa	b	59	75
m-CH_3–C_6H_4	C_6H_5SNa	c	99	55
m-CH_3O–C_6H_4	CH_3ONa	a	41	81
o-CH_3O–C_6H_4	*m*-CH_3–C_6H_4SNa	b	50	88
p-CH_3O–C_6H_4	C_6H_5SNa	c	96	53
m-Br–C_6H_4	CH_3ONa	a	80	58
m-Cl–C_6H_4	*m*-$CH_3C_6H_4SNa$	b	74	84

The conversion of aromatic nitro compounds into isothiocyanates by method a) is accompanied by concomitant formation of anilines in varying amounts. This undesired side reaction is more favored by phenoxides than it is by alkoxides. The formation of anilines is arrested or at least reduced to insignificant levels, and both conversions and yields are increased, when aryl sulfides are employed as base (method b). The aryl sulfides are oxidized predominantly to disulfides, which were isolated. Similar but slightly reduced conversions and yields are achieved when the nitro compounds are treated in CS_2 with a sodium aryl trithiocarbonate, *e.g.* *m*-CH_3–$C_6H_4SC(S)SNa$, formed from sodium *m*-tolyl sulfide and carbon disulfide. Nearly complete conversion of the nitro compounds takes place under the conditions of method c); however, the formation of anilines is not controlled so effectively as in method b).

Extension of the reaction (method b) to aromatic dinitro compounds, *e.g.* *m*-dinitrobenzene, gave 3-nitrophenyl isothiocyanate and small amounts of *m*-phenylene diisothiocyanate. Aliphatic nitro compounds do not react satisfactorily under the above conditions.

m-Tolyl isothiocyanate (method b)

A 300-ml stirring autoclave was charged with 13.7 g of *m*-nitrotoluene, 7.3 g of sodium *m*-tolyl sulfide, and 50 ml of carbon disulfide. The mixture was heated at 160 °C for 3 hours. The crude reaction product was distributed between 100 ml of ether and 75 ml of cold water. The organic layer was dried with $CaCl_2$ and distilled over a spinning band column. Yield 9 g of *m*-tolyl isothiocyanate (87% based on 71% conversion of *m*-nitrotoluene).

Received: June 10, 1969 [Z 65 IE]
German version: Angew. Chem. *81*, 782 (1969)

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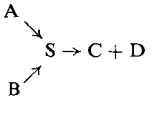
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[1] *Houben-Weyl-Müller*: Methoden der organischen Chemie. Thieme, Stuttgart 1955, Volume IX.

The Carbene/Carbenoid Problem [**]

By *M. Schlosser* and *G. Heinz* [*]

Competitive experiments may afford definitive information about unisolable intermediates in reaction sequences [1]. If a short-lived species S is really the product-forming agent and can be formed from two different starting materials A and B, any reaction products C + D are formed in the same proportions independently of whether the postulated intermediate is derived from A or from B:



In connection with the problem whether "free" carbenes (here C_6H_5–$\ddot{C}H$) or "carbenoids" (carbene-metal salt adducts, here C_6H_5–CHLiX) add to olefins, giving cyclopropane derivatives [2], we have treated the benzyl halides *(1a)*–*(1d)* with butyllithium in the presence of cyclohexene *(2)*, then measuring the proportions in which the products *syn*- and *anti*-7-phenylnorcarane are formed in four solvents (Fig. 1).

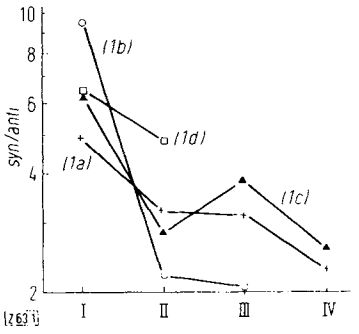
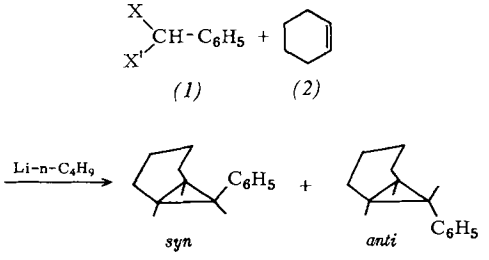


Fig. 1. Proportions of *syn-* and *anti*-7-phenylnorcarane obtained from cyclohexene, butyllithium, and the benzyl halides *(1a)*—*(1d)*.

Conditions: Butyllithium (20 mmoles) in hexane (12.5 ml) was dropped during 1 h into a solution of the halides (40 mmoles) in cyclohexene (6 ml) and a solvent (6 ml) (I = light petroleum, II = diethyl ether; III = tetrahydrofuran, IV = 1,2-dimethoxyethane) at 0 °C. The products were identified by gas chromatography, comparison being with authentic reference samples.



(a), X = H, X′ = F
(b), X = H, X′ = Cl
(c), X = X′ = Br
(d), X = Br, X′ = F

The observed dependence of the *syn/anti* ratios on the preceding step provides only *apparent* confirmation of the carbenoid hypothesis, since the starting materials benzyl fluoride *(1a)* and benzylidene bromide fluoride *(1d)* lead to different proportions of diastereomers, although these must in both cases proceed through the same "carbenoid" C_6H_5—CHLiF. This discrepancy leads to the idea that the product-forming agent — whether it be "free" carbene or a "carbenoid" — may be liberated in differently reactive states according to the mode of its formation.

If the differences in reactivity of these intermediates of differing origins can be ascribed to differing conditions of excitation even in solution[3], then the *syn/anti* ratio should change if the concentration of substrate (here the olefin) and thus the number of collisions before reaction are changed.

We found that under the influence of butyllithium the benzylidene dibromide *(1c)* and cyclohexene give *syn-* and *anti*-7-phenylnorcarane in the ratio 5.7:1. The *syn/anti* ratio increases monotonically to more than 30:1 if the cyclohexene *(2)* is mixed with increasing amounts of light petroleum (I) (to a volume ratio of 1:12). Benzyl chloride *(1b)* behaves similarly (Fig. 2).

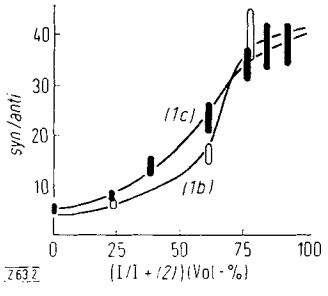


Fig. 2. Dependence of the proportion of *syn-* and *anti*-7-phenylnorcarane on the olefin concentration in reaction of butyllithium on cyclohexene and *(1c)* or *(1b)*.

Conditions: To a solution of the halide (20 mmoles) in a mixture (6 ml) of light petroleum (I) and cyclohexene *(2)* at 0 °C, is added butyllithium (10 mmoles) in the same cyclohexene-light petroleum mixture, dropwise at 0 °C. The products were identified by gas chromatography, comparison being with authentic reference samples.

The increase in stereoselectivity cannot be ascribed to a specific solvation effect: 1-phenyl-2-propylcyclopropane and 7-phenylnorcarane are formed with a *syn/anti* ratio of 3.2:1 and 4.6:1, respectively, in a mixture of pentene, cyclohexene, and light petroleum of composition 20:77:3; if the proportions in the mixture are 20:23:57 the *syn/anti* ratio is 2.9:1 or 26:1 respectively! Further, the *syn/anti* ratio also increases with increasing dilution of the substrate if toluene is used as solvent in place of light petroleum.

The results can be — but need not necessarily be — interpreted as indicating that phenylcarbene C_6H_5-$\ddot{C}$H is the true cyclopropane-forming agent in both cases.

Received: August 1, 1969 [Z 63 IE]
German version: Angew. Chem. *81*, 781 (1969)

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

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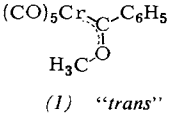
Hindered Rotation about the C—O Bond in Methoxy(methyl)carbene Ligands[1]

By *C. G. Kreiter* and *E. O. Fischer*[*]

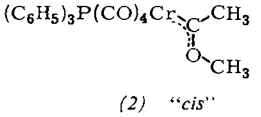
X-Ray structure analyses of pentacarbonyl[methoxy(phenyl)-carbene]chromium(0)[2] *(1)* and *cis*-tetracarbonyl[methoxy-(methyl)carbene]triphenylphosphinechromium(0)[3] *(2)* have shown that the carbene-carbon atom and its three bonds, as well as the carbon atom of the methoxyl group, lie almost in one plane; the carbene-carbon atom is thus sp^2 hybridized and has a "free" p-orbital perpendicular to the bonding plane. The Cr—C distance for the carbene ligands (2.05 and 2.04 Å, respectively) correspond to a bond order[4] of *ca.* 1.2. The electron deficiency on the sp^2 carbon atom is not relieved by the weak metal-carbon back-donation but rather by π-interaction with one of the free electron pairs of the oxygen. Thus the bond lengths between the carbene-carbon and the oxygen atom (1.31 and 1.33 Å, respectively) are much shorter than for C—O single bonds; their partial double-bond character is thus in agreement with the position of the methoxyl group in the sp^2 plane.

The orientation of the methoxyl group is not the same in *(1)* and in *(2)*. If the carbene-carbon/oxygen bond is taken as a "double bond", then the *O*-methyl group is in the *trans-* and *cis*-position to the *C*-phenyl and *C*-methyl group, respectively.

cis-trans Conversions by rotation about a C—O bond should be readily demonstrable by NMR spectroscopy provided



(1) "*trans*"



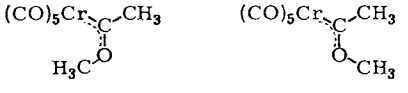
(2) "*cis*"

that the double-bond contribution is not too great[5]. Previous ^{1}H-NMR measurements with methoxy(methyl)carbene complexes were explained on the assumption that one isomer only exists preferentially between −50 and +120 °C[6].

In a more recent study, however, we have found additional information: pentacarbonyl[methoxy(methyl)carbene]chromium(0)[7] *(3)* in [D_6]-acetone at +40 °C shows two sharp signals of equal intensity at τ = 5.32 and 6.97 severally, which can be assigned unambiguously to the *O*-methyl and the *C*-methyl group. When the solution is cooled, these signals first become broader and then each splits into two broad signals of approximately equal intensity, that finally become completely sharp at −40 °C; the phenomenon is reversible.

The spectrum at −40 °C can only be interpreted as being due to a mixture of *cis-trans*-isomers of *(3)*. These isomers differ only in their orientation of the *O*-methyl group towards the *C*-methyl group. It is striking that the signals at τ = 5.11 and 7.00 have the same half-width as have those at τ = 5.61 and 6.83. The half-widths of the first pair are slightly the greater; this is presumably caused by the differing HCOCCH coupling constants of the protons of the two methyl groups in the isomers.

We assigned the signals analogously to those of pentacarbonyl[(methylamino)(methyl)carbene]chromium(0)[8]. An X-ray analysis showed that this complex is formed in the *cis*-form[9]; it is not converted thermally into the *trans*-isomer, but only by base catalysis. Shielding of the *N*-methyl group is greater for the *cis*- than for the *trans*-isomer; the HCNCCH coupling is much greater in the *trans*- than in the *cis*-complex[8]. We assume that in *(3)* also the *O*-methyl group of the *cis*-isomer is more strongly shielded than that in the *trans*-isomer, as is also indicated by the HCOCCH coupling which can be estimated from the line widths.



"*trans*" *(3)* "*cis*"

When the mixture of isomers is warmed the lifetime of both isomers decreases, as shown in broadening, coalescence, and sharpening of the signals. The shapes of the signals permit the lifetimes of the isomers to be calculated[10] at various temperatures; and an activation energy of 12.4 ± 1.0 kcal per mole was determined for conversion of one isomer of *(3)* into the other. The steric findings do not allow any energy difference to be recognized between the *cis*- and the *trans*-form, yet different solvents appear to stabilize the isomers differently. In [D_6]-acetone and [D_4]-methanol the two isomers are present in about equal concentrations, but in [D]-chloroform, chlorobenzene, and fluorobenzene the *trans*-isomer clearly predominates.

Table: Chemical shifts and relative quantities of the *cis-trans*-isomers of pentacarbonyl[methoxy(methyl)carbene]chromium(0) *(3)* at −40 °C in various solvents.

Solvent	τ (OCH_3) *trans*	*cis*	τ (CCH_3) *trans*	*cis*	Relative amounts (%) *trans*	*cis*
[D_6]-Acetone	5.11	5.61	7.00	6.83	50	50
[D]-Chloroform	5.19	5.69	7.03	6.99	90	10
[D_4]-Methanol	5.17	5.66	7.03	6.95	61	39
Chlorobenzene	5.83	6.78	7.49	7.76	84	16
Fluorobenzene	5.77	6.70	7.44	7.69	83	17

Alteration of any of the three substituents on the carbene-carbon atom has a characteristic influence on the rotation around the C—O bond, so that ^{1}H-NMR spectroscopy becomes an important tool for clarification of bonding problems in carbene complexes.

Received: July 24, 1969 [Z 57 IE]
German version: Angew. Chem. *81*, 780 (1969)

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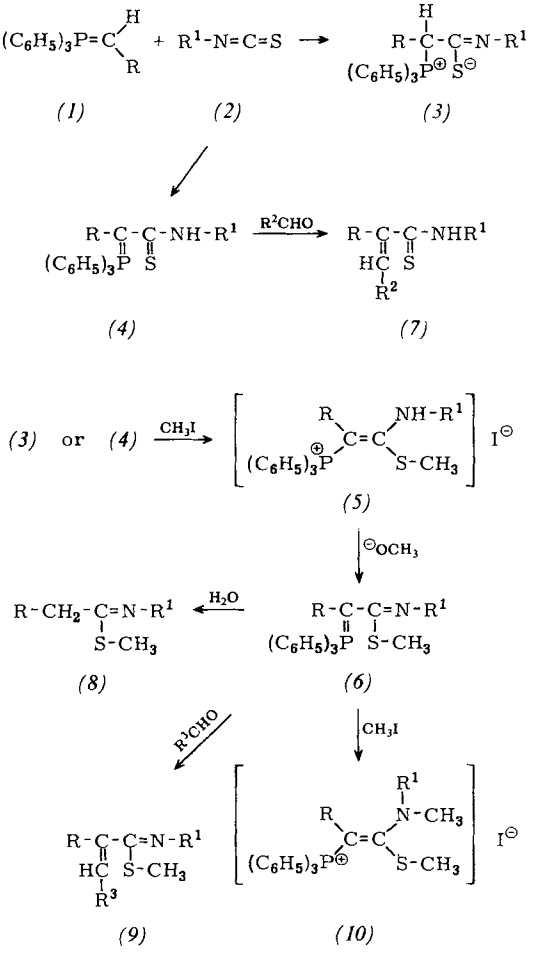
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The Main and Secondary Reactions between Alkylidenetriphenylphosphoranes and Isothiocyanates

By *H. J. Bestmann* and *S. Pfohl*[*]

Reaction of alkylidenetriphenylphosphoranes *(1)* with isothiocyanates *(2)* leads either to betaines *(3)* (when R exerts a +I effect) or to ylides *(4)* (with groups R exhibiting a −I effect and R = H), whose subsequent reactions offer new preparative possibilities.



(1) *(2)* *(3)* *(4)* *(7)* *(5)* *(8)* *(6)* *(9)* *(10)*

R	R^1	*(3)* or *(4)*, m.p. in °C (yield in %)	R^2	*(5)*, m.p. in °C (yield in %)	*(6)*, m.p. in °C (yield in %)	*(7)*, m.p. in °C (yield in %)	*(8)*, b.p. in °C/torr (yield in %)	R^3	*(9)*, b.p. in °C/torr (yield in %)	*(10)*, m.p. in °C (yield in %)
H	C_6H_5	*(4)*, 203 (85)	C_6H_5	215 (98)	162 (71)	136 (73)		C_6H_5	m.p. 89 °C (70)	
			C_6H_5–CH=CH			155 (46)				
			cyclo-C_6H_{11}			104 (33)				
H	CH_3	*(4)*, 203 (80)	C_6H_5	167 (99)		117 (43)		C_6H_5	107/0.01 (51)	185 (45)
			cyclo-C_6H_{11}			66 (45)				
CH_3	C_6H_5	*(3)*, 137 (78)		185 (95)	148 (35)		137/20 (40)	C_6H_5	160/0.2 (53)	
C_6H_5	CH_3	*(4)*, 153 (75)		215 (99)	138 (60)		75/0.1 (30)			252 (75)
C_6H_5	C_6H_5	*(4)*, 140 (80)			181 (90)		m.p. 60 °C (40)			
CO_2CH_3	C_6H_5	*(4)*, 175 (85)		168 (98)	185 (85)					175 (70)

The Wittig reaction of *(4)* with aldehydes affords *N*-substituted thiocarboxamides *(7)* of α,β-unsaturated acids. Both *(3)* and *(4)* undergo *S*-methylation on treatment with methyl iodide; the phosphonium salts *(5)* isolated after this reaction can be converted into the ylides *(6)* by treatment with sodium methoxide. Starting from *(6)*, hydrolysis gives thioimidic acid derivatives *(8)*, Wittig reaction affords the corresponding derivatives of α,β-unsaturated acids *(9)*, and reaction with methyl iodide leads to the substituted vinylphosphonium salts *(10)*.

Thiocinnamanilide

A solution of phenyl isothiocyanate *(2)*, $R^1 = C_6H_5$, (6.75 g, 50 mmoles) in anhydrous benzene (50 ml) is added dropwise and slowly to a salt-free benzene solution of methylenetriphenylphosphorane *(1)*, R = H[1], (50 mmoles). After 12 hours' stirring the initially oily precipitate becomes crystalline. The precipitate is filtered off under vacuum and recrystallized from chloroform/ethyl acetate. M.p. 203 °C, yield 17.0 g (85%) of *(4)*, R = H, $R^1 = C_6H_5$. — To a suspension of this ylide (8.2 g, 20 mmoles) in benzene (150 ml) is added benzaldehyde (2.1 g, 20 mmoles) and the reaction mixture is stirred at room temperature for 48 h, whereupon dissolution occurs. The benzene is subsequently distilled off and the residue recrystallized from isopropanol. M.p. of the thiocinnamanilide *(7)*, R = H, $R^1 = R^2 = C_6H_5$, is 136 °C (value given in literature 128—129 °C[2]), yield 3.5 g (73%).

Received: March 10, 1969;
revised: June 27, 1969 [Z 61a]
German version: Angew. Chem. *81*, 750 (1969)

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[1] *H. J. Bestmann*, Angew. Chem. *77*, 609, 651, 850 (1965); Angew. Chem. internat. Edit. *4*, 583, 645, 830 (1965).

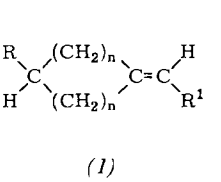
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Partial Asymmetric Synthesis of Substituted Benzylidenecycloalkanes[1]

By *H. J. Bestmann* and *J. Lienert*[*]

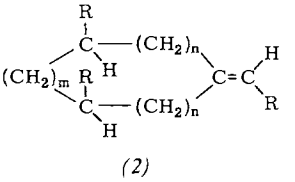
Cycloalkanes having an exocyclic double bond and an even number of C atoms in the ring, which bears a substituent at the greatest possible distance from the double bond, are chiral molecules [type *(1)*]. The same applies to all *cis*-disubstituted cycloalkanes with a exocyclic double bond having two identical substituents at equal distances from the double bond [type *(2)*]. In both cases it is essential that R and $R^1 \neq H$, although $R = R^1$ is possible.

We have found that optically active molecules of types *(1)* and *(2)* can be obtained by partial asymmetric synthesis, the route selected being a Wittig reaction of the corresponding ketones with optically active alkylidenephosphoranes. We chose benzylidenemethylphenyl-*n*-propylphosphorane *(3)* as the optically active ylide since the absolute configuration of the phosphonium bromide obtained from *(2)* on liberation of HBr by sodamide is known[2].



(1)

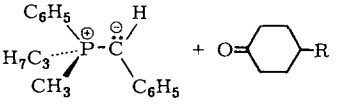
$n = 0, 1, 2, 3 \ldots .$
$n = 0$ = allene



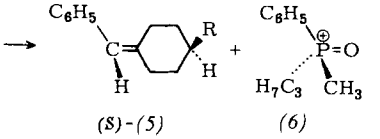
(2)

$n = 0, 1, 2, 3 \ldots .$
$m = 0, 1, 2, 3 \ldots .$

The reaction of *(3)* with 4-substituted cyclohexanones *(4)* leads to optically active 4-substituted benzylidenecyclohexanes *(5)*, belonging to type *(1)*. The absolute configuration of *(5a)* has already been determined[3]. It was found that reaction of the (*R*)-ylide *(3)* [configuration as shown in *(3)*], which is obtained from (*S*)-(+)-benzylmethylphenylpropylphosphonium bromide[4], with 4-methylcyclohexanone *(4a)* affords (*S*)-(+)-benzylidene-4-methylcyclohexane *(5a)* in an optical yield of 43%.



(R)-(3) *(4)*



(S)-(5) *(6)*

(a), R = CH_3 *(c)*, R = $C(CH_3)_3$ *(e)*, R = OC_2H_5
(b), R = C_2H_5 *(d)*, R = OCH_3

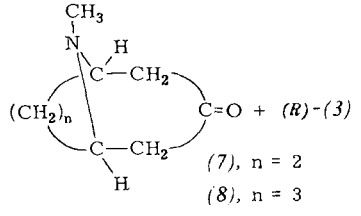
Ylide	Product	$[\alpha]_D$ of *(5)* (°)
(*R*)-*(3)*	(*S*)-*(5a)*	+25.8
(*S*)-*(3)*	(*R*)-*(5a)*	−25.4
(*R*)-*(3)*	(*S*)-*(5b)*	+20.1
(*S*)-*(3)*	(*R*)-*(5b)*	−19.9
(*R*)-*(3)*	(*S*)-*(5c)*	+21.8
(*S*)-*(3)*	(*R*)-*(5c)*	−21.1
(*R*)-*(3)*	(*S*)-*(5d)*	+ 4.5
(*R*)-*(3)*	(*S*)-*(5e)*	+ 5.9

All compounds *(5)* obtained from (*R*)-*(3)* show a negative Cotton effect in the ORD curves. The form of the CD curves is also similar. We therefore conclude that all these compounds possess the (*S*) configuration, whereas the (*R*) enantiomers of *(5)* are formed preferentially on reaction of (*S*)-*(3)* with the cyclohexanones *(4)*.

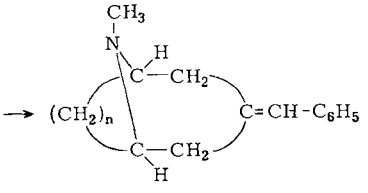
In all the reactions the ylides *(3)* were obtained from the optically pure phosphonium salts. Since the compounds *(5b)*—*(5e)* have not yet been obtained in optically pure form, and since attempts to resolve them into the pure enantiomers have so far been unsuccessful, no optical yield can be given for their preparation.

The (*R*)-(+)-methylphenylpropylphosphine oxide *(6)*, whose absolute configuration is known[5,6], is formed alongside *(5)* in all reactions in which the (*S*)-(+)-phosphonium salt is used as starting material. The specific rotation $[\alpha]_D = 18.4°$ to 18.8° found for *(6)* indicates that the Wittig reaction proceeds in the usual way, *i.e.* with complete retention of configuration at the phosphorus atom[6,7].

Reaction of tropinone *(7)* and pseudopelletierine *(8)* with (*R*)-*(3)* affords the optically active compounds *(9)* and *(10)*, respectively, which belong to type *(2)*.



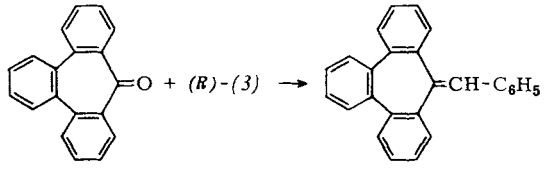
(7), n = 2
(8), n = 3



(9), n = 2 $[\alpha]_D = -89.5°$
(10), n = 3 $[\alpha]_D = -51.40°$

Nothing can be said about the optical yield of *(9)* and *(10)*, or about their absolute configurations. Mention should be made of the fact that these molecules cannot be described by the Cahn-Ingold-Prelog rules[8].

Tribenzocycloheptene derivatives having an exocyclic double bond are chiral[9]. We obtained the optically active compound *(12)* from the ketone *(11)*[10] and (*R*)-*(3)*. As for compounds *(9)* and *(10)*, no statement can be made regarding the optical yield, absolute configuration, and assignment of compound *(12)* to the (*R*) or the (*S*) series.



(11) *(12)* $[\alpha]_D = -8.6°$

Received: July 2, 1969 [Z 61b IE]
German version: Angew. Chem. *81*, 751 (1969)

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3-Nitrophthalic Anhydride as Blocking Agent in Merrifield Polypeptide Syntheses[1]

By *Th. Wieland, Chr. Birr*, and *H. Wissenbach*[*]

In stepwise synthesis of peptides by the Merrifield method[2] each incomplete reaction step decreases the homogeneity of the final product. The greatest effect is seen in the coupling steps in which a small part of the free amino ends of the peptide chain may escape reaction with the attaching *tert*-butoxycarbonyl (BOC) amino acid and can thus lead at the following step to formation of a false sequence. Our object was to block the undesired faulty peptide at its free amino end after each coupling step, and to do this in such a way that after removal of the finished peptide from the resin all the compounds formed from the false peptides could be separated easily and simply from the desired polypeptide.

We found 3-nitrophthalic anhydride to be a suitable blocking agent for this purpose. It is an energetic acylating agent, attacking even relatively unreactive amino groups; the resulting 2-carboxy-3-nitrobenzoyl derivatives are such strong acids owing to the "*ortho*-effect" of the nitro group (*o*-nitrobenzoic acid has $pK \approx 2.3$) that they can be readily separated even from acid peptides by chromatography on an anion exchanger.

To demonstrate the utility of this blocking agent we have built up the plastein-active[3] pentapeptide L-tyrosyl-L-leucylglycyl-L-glutamyl-L-phenylalanine on a polystyrene carrier. 5 g of polystyrene was chloromethylated and then esterified with BOC-phenylalanine (4 mmoles); after removal of the BOC group[2], the next BOC-amino acid was condensed on by dicyclohexylcarbodiimide in methylene dichloride, but the latter acid was used, not in three-fold molar excess, but only in equimolar amount so as to simulate unsuitable conditions. Glutamic acid was used as its BOC-γ-benzyl ester. Contrary to previous procedures, after each condensation the resin was washed three times with 35 ml each of methylene dichloride, ethanol, and dimethylformamide (DMF), then reacted with a solution of 3-nitrophthalic anhydride (870 mg, 4.5 mmoles) in DMF (20 ml) for 3 min, and shaken with a solution of triethylamine (1 ml) in DMF (5 ml) for 30 min. It was then washed with 35 ml of DMF, dioxane, ethanol, and glacial acetic acid three times each, and the BOC group of the last BOC-amino acid added was removed[2].

Subsequent debenzylation and removal of the products from the resin by HBr in trifluoroacetic acid gave a mixture (*ca.* 2 g) which was digested with ether and then separated by chromatography on Dowex 1 × 2 in an acetic acid gradient (water → 50% acetic acid). This eluted first unknown by-products (*ca.* 200 mg) then the desired pentapeptide (980 mg) after a small, easily separable fore-fraction, and much later the mixture of blocked acidic intermediate peptides (100 mg).

The pentapeptide was electrophoretically and chromatographically homogeneous and on total hydrolysis gave the amino acids Phe, Glu, Gly, Leu, and Tyr in the proportions 0.98 : 1.13 : 1.00 : 1.07 : 0.89 (*D. Georgopoulos*). In the plastein reaction[3] with pepsin, a 25-mg sample gave 14 mg (60%) of water-insoluble polypeptide mixture.

Paper electrophoresis at pH 6.5 separated the blocked intermediate peptides into the four expected constituents (2-carboxy-3-nitrobenzoyl derivatives of Phe, Glu-Phe, Gly-Glu-Phe, and Leu-Gly-Glu-Phe), which appeared with approximately equal intensity on development with the *tert*-butyl hypochlorite-tolidine reagent[4].

Received: August 4, 1969 [Z 67 IE]
German version: Angew. Chem. *81*, 782 (1969)

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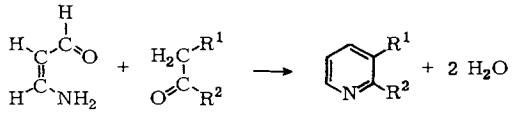
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Single-step Synthesis of Pyridines from 3-Aminoacrolein and Carbonyl Compounds

By *E. Breitmaier* and *E. Bayer*[*]

3-Aminoacrolein *(1)*[1,2] cyclocondenses with carbonyl compounds of type *(2)* to give pyridine derivatives of type *(3)*; R^1 and R^2 may also be part of the ring.



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

	R^1	R^2	Pyridine derivative	B.p. (°C/ 12 Torr)	Yield (%)	Ref.
(a)	$COOC_2H_5$	CH_3	Ethyl 2-methyl-3-pyridine-carboxylate	107–108	50	[3]
(b)	$COCH_3$	CH_3	3-Acetyl-2-methylpyridine	104–105	55	[4]
(c)	$-(CH_2)_4-$		5,6,7,8-Tetra-hydroquinoline	98– 99	20	[5]

The cyclocondensation proceeds *via* a Schiff base – formed between the amino group of *(1)* and the carbonyl group of *(2)* – combined with a Knoevenagel reaction between the formyl group of *(1)* and the methyl group of *(2)*.

General procedure:

Ammonium acetate (50 mg) is added to a mixture of 3-aminoacrolein *(1)*[1,2] (0.05 mole) and a carbonyl compound *(2)* (0.06 mole) and the mixture is stirred under reflux for 12 hours at an oil-bath temperature of 110 °C. The oily reaction mixture is then poured into ether (100 ml) and the resulting ether solution is dried with magnesium sulfate and filtered under vacuum. The ether is evaporated off and the residue is fractionated at 12 torr.

The structure of the pyridines *(3a)*–*(3c)* can be established on the basis of their ^{1}H-NMR spectra.

Received: August 8, 1969 [Z 69 IE]
German version: Angew. Chem. *81*, 785 (1969)

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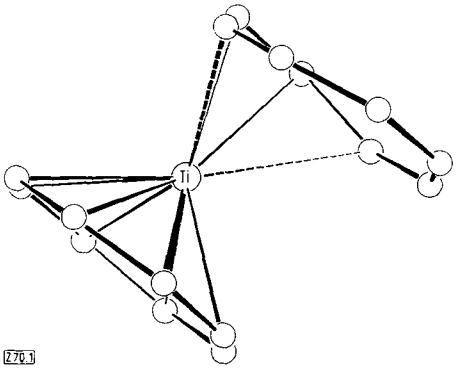
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Crystal Structure of Bis(cyclooctatetraene)titanium

By *H. Dietrich* and *M. Soltwisch*[*]

The violet π complex bis(cyclooctatetraene)titanium synthesized by *Breil* and *Wilke*[1] crystallizes monoclinically in the space group $Pb(C_s^2)$ with $a = 7.00$, $b = 12.26$, $c = 7.92$ Å, $\gamma = -114.85°$, $V = 617$ Å^3; $Z = 2$, $d_{x\text{-ray}} = 1.378$ gm/cm^3. The crystal structure was determined from X-ray diffraction data recorded on a counting-tube diffractometer using filtered $Cu_{K\alpha}$ radiation.



The molecule contains one planar and one boat shaped cyclooctatetraene ring. The planar one (C–C bond length 1.41 ± 0.02 Å[2]) is symmetrically attached to the titanium atom (all Ti–C bond lengths 2.32 ± 0.02 Å[2]), while the nonplanar ring is bonded to the titanium atom *via* four carbon atoms only. In the Figure the two shorter Ti–C bond lengths (2.2 Å each) are marked by full lines, the two longer ones (2.5 Å each) by broken lines. The coordination of the titanium is thus very similar to that in tris(cyclooctatetraene)-dititanium[1,3], in which, however, the two shortest Ti–C bonds to the non planar ring are about 0.1 Å longer.

The crystal is partially disordered. Apparently another molecular form exists in which the nonplanar ring interacts with the titanium atom *via* three carbon atoms only (shortest Ti–C bond length 2.2 Å). At present the discrepancy factor is $R = 10\%$.

Received: July 31, 1969 [Z 70 IE]
German version: Angew. Chem. *81*, 785 (1969)

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Proton Magnetic Resonance Studies on Polysaccharide Derivatives

By *H. Friebolin, G. Keilich,* and *E. Siefert*[*]

Proton magnetic resonance studies on synthetic polymers such as polystyrene, PVC, poly-α-methylstyrene are generally complicated by the broad signals of the individual protons. The line broadening arises mainly from conformative and configurative factors, and in the case of copolymers from composition factors. Once a degree of polymerization of 20 has been exceeded, the ^{1}H-NMR spectra of these polymers remain almost unchanged and differ considerably from the spectra of the monomers.

The acetyl and benzoyl derivatives of polysaccharides exhibit a quite different behavior. We have conducted measurements on a large number of different tri-*O*-acetyl- and tri-*O*-benzoyl-polysaccharides having degrees of polymerization from about 30 to 3000 (molecular weights ranging from 9000 to 900000) in $CDCl_3$ with the aid of a 220 MHz spectrometer. Figure 1

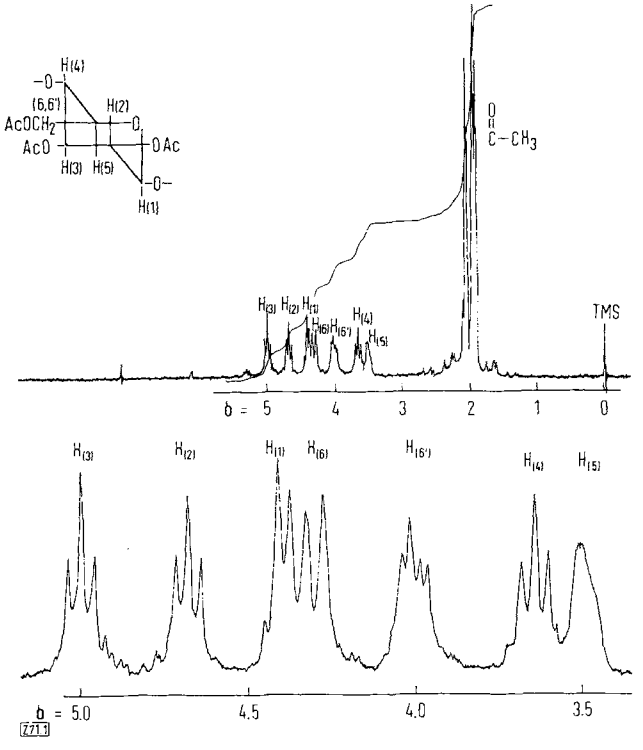


Fig. 1. ^{1}H-NMR spectra of 2,3,6-tri-*O*-acetylcellulose having a degree of polymerization of ≈200 (mol. wt. *ca.* 60000). Measuring frequency: 220 MHz; solvent: $CDCl_3$ (TMS); T = +60 °C.

shows the ^{1}H-NMR spectrum of a 2,3,6-tri-*O*-acetylcellulose having a degree of polymerization of *ca.* 200 (mol. wt. *ca.* 60000). The signals of all seven ring protons are seen individually between δ = 3.5 and 5 ppm alongside the separate signals belonging to the three methyl groups of the acyl substituents in positions 2, 3, and 6. The width of the lines is only about double that occurring in the monosubstituted monosaccharide. The signals can therefore be assigned to the various ring protons by means of the spin-spin coupling constants, and the configuration of the substituents and the nature of the glycosidic bond between the monomers can be determined unequivocally. The coupling constant J_{12} = 8 Hz corresponds to an axial-axial coupling between H(1) and H(2), *i.e.* H(1) is in an axial position; it therefore follows that the monomer units are joined by β-glycosidic linkages. The configuration of the monomer units corresponds to that of glucose since, according to the magnitude of the coupling constants, the protons on C-2, C-3, and C-4 are axial. The spectrum is thus in accord with the generally recognized structure of cellulose.

We also hope to be able to assign the signals of the acetyl-substituents in order that we may use this method, *e.g.*, to elucidate the structure of partially acetylated celluloses possessing industrial interest.

As a second example we shall give the 220-MHz spectrum of 2,3,6-tri-*O*-acetylamylose having a degree of polymerization of *ca.* 100 (mol. wt. *ca.* 30000) together with assignments (see Figure 2). The coupling constant for this compound J_{12}

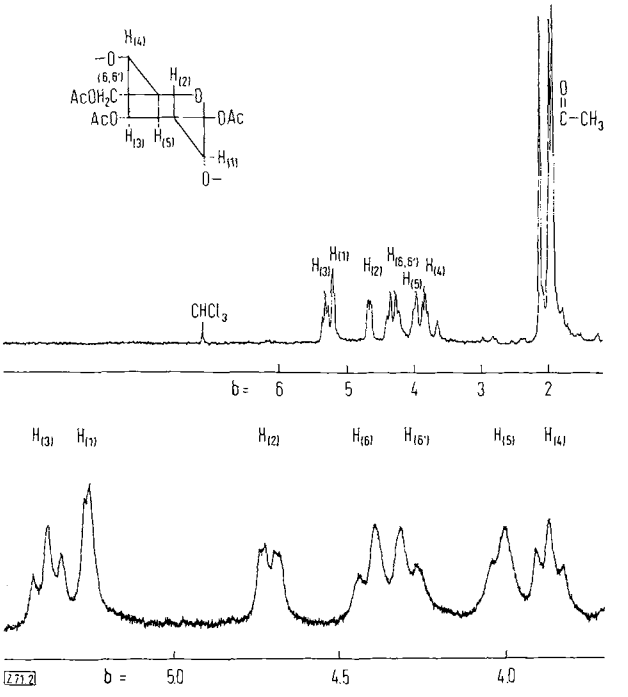


Fig. 2. ^{1}H-NMR spectra of 2,3,6-tri-*O*-acetylamylose having a degree of polymerization of ≈100 (mol. wt. *ca.* 30000). Measuring frequency 220 MHz; solvent: $CDCl_3$ (TMS); T = +20 °C.

is only about 3 Hz. This value, which was deduced from the splitting of the H(1) signal, corresponds to a coupling between axial and equatorial protons. Since the magnitude of the coupling constant J_{23} reveals that the proton on C-2 is in the axial position, H(1) must be equatorial. The magnitudes of the other coupling constants indicate that the protons on C-3 and C-4 are axial. The methyl signals of the three *O*-acetyl groups occur separately as in tri-*O*-acetylcellulose; the signals have not yet been assigned. Thus the structure hitherto assumed for amylose – α-glycosidically linked glucose units – is confirmed by the ^{1}H-NMR spectrum.

We obtained ^{1}H-NMR spectra showing the same excellent resolution and proving similarly amenable to analysis with 2,3,6-tri-*O*-benzoylcellulose and -amylose having degrees of polymerization from 100 to 200.

For all such polysaccharide derivatives the signals of all the ring protons are still separate at degrees of polymerization in excess of 1000 (mol. wt. > 500000); they are, however, broadened to such an extent that the individual coupling constants can no longer be determined.

The ^{1}H-NMR spectra of other polysaccharide derivatives — such as those of dextran, mannan, and pullulan — can be analyzed in a similar fashion. The spectrum of tri-*O*-benzoyl-pullulan (α-1,4 : α-1,6 linkages in the ratio 2 : 1) can be interpreted, *e.g.*, directly as a superposition of the spectra of the corresponding amylose(α-1,4) and dextran(α-1,6) derivatives.

Since the development of this method of spectral analysis we have been able to identify an unknown polysaccharide (*ca.* 2—3 mg), isolated from biological material, as cellulose by comparison of the spectrum of the tri-*O*-benzoyl derivative with that of an authentic sample. ^{1}H-NMR studies have thus

proved to be a useful tool for the structural elucidation of polysaccharides.

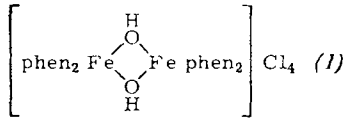
Received: July 30, 1969 [Z 71 IE]
German version: Angew. Chem. 81, 791 (1969)

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Radiochemical Investigation of the Coordination State of Iron in the Dinuclear Iron(III)-1,10-Phenanthroline Complex Ion

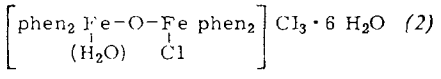
By *P. Gütlich*[*] and *B. W. Fitzsimmons*[**]

In aqueous solution iron(III) chloride and 1,10-phenanthroline (phen) form a dinuclear complex which, on the basis of chemical analyses and its behavior in solution, was originally formulated as

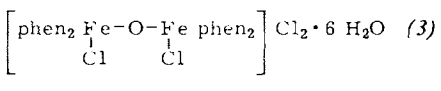


(1)

with a double OH bridge[1]. Results of magnetic[2–7] and potentiometric measurements[1,6] are in accord with a dinuclear structure for the complex compound, in which iron has the oxidation number +3. Recent studies on magnetic behavior[8] lend support to a high-spin iron(III) model with $S = 5/2$ and $g = 2.00$ and without any contribution by temperature-independent paramagnetism (TIP). Moreover, these results, together with IR spectroscopic findings[9], strongly suggest a single oxo bridge between the two iron atoms (formula *(2)* or *(3)*).



(2)

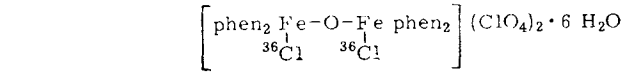


(3)

The number of chlorine atoms directly coordinated to iron was hitherto uncertain.

We have now been able to confirm unequivocally the proposed structure *(3)* by radiochemical methods.

The iron(III)-1,10-phenanthroline complex was prepared, in the presence of $^{36}Cl^-$ ions (Cl-36: $t_{1/2} = 3.1 \times 10^5$ a; 0.7 MeV β^-), according to the method given by *Gaines et al.*[1]. The results of elemental analysis were in good agreement with the values calculated for the empirical formula $Fe_2O(phen)_4Cl_4 \cdot 6H_2O$. The IR spectrum (700—900 cm^{-1}) corresponded with previously recorded data[8]. The count rate i_1 of an aliquot of the solution of the ^{36}Cl-labeled compound in methanol was measured with a scintillation counter. Another aliquot was cooled in a Dry Ice/acetone bath and treated with a methanolic solution of $LiClO_4$; the resulting precipitate, the sparingly soluble perchlorate of the iron(III)-1,10-phenanthroline complex ion, was centrifuged off and its count rate i_2 determined. The ratio $i_2 : i_1$ obtained from five experiments conducted under identical conditions was found to be 0.497 ± 0.005. This means that 49.7% of the total ^{36}Cl activity of the starting compound $Fe_2O(phen)_4Cl_4 \cdot 6H_2O$ was present in the cationic complex of the sparingly soluble perchlorate after precipitation. This finding is explicable only if the perchlorate has the structure:



and the labeled starting material the structure *(3)*.

Received: August 5, 1969 [Z 75 IE]
German version: Angew. Chem. 81, 788 (1969)

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B. W. F. wishes to thank the Akademisches Auslandsamt of the Technische Hochschule Darmstadt for financial support of his research in Darmstadt.

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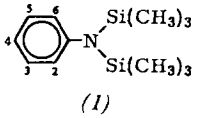
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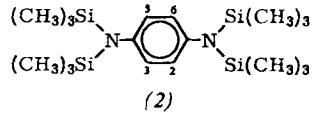
ESR Spectra of the Radical Anions of *N*-Trimethylsilyl Derivatives of Aniline and *p*-Phenylenediamine[11]

By *F. Gerson, U. Krynitz*, and *H. Bock*[*]

Amino substituents, as electron donors, lower the electron affinity of aromatic compounds. For this reason radical anions can be prepared neither from aniline and *p*-phenylenediamine nor from their *N*-alkyl derivatives. If the *N*-hydrogen atoms or *N*-alkyl groups are replaced by trimethylsilyl groups two effects are to be expected: A) interaction between the lone electron pair of the nitrogen and unoccupied silicon orbitals of suitable symmetry; B) twisting of the bis(trimethylsilyl)amino substituent out of the benzene π-plane due to the large spatial demands of the bulky trimethylsilyl residues[2]. As shown for example by the ionization energies[3], both effects impair the conjugation of the nitrogen lone pair with the aromatic π-electron system and consequently lower the donor character of the amine substituents.



(1)



(2)

N,N-Bis(trimethylsilyl)aniline *(1)* and *N,N,N',N'*-tetrakis(trimethylsilyl)-*p*-phenylenediamine *(2)*[3] ought, therefore, to exhibit a stronger tendency to accept an additional π-electron than the corresponding *N*—H- and *N*-alkyl compounds. In fact, both corresponding radical anions $(1)^{\ominus}$ and $(2)^{\ominus}$ are accessible from *(1)* and *(2)* respectively by reduction with potassium in 1,2-dimethoxyethane (DME) at low temperatures.

The ESR spectra (Fig. 1a and 1b) are very similar to each other; they exhibit five main components, which correspond

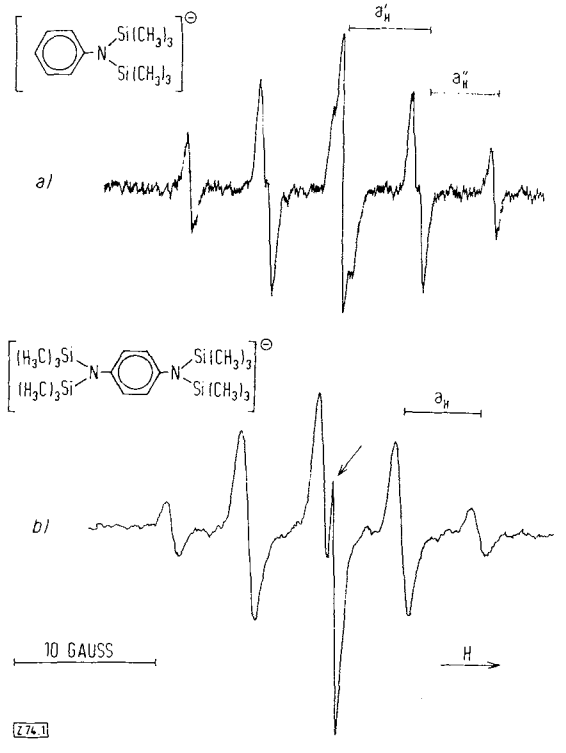


Fig. 1. ESR spectra of the radical anions *(1)*$^{\ominus}$(a) and *(2)*$^{\ominus}$(b). Solvent: DME; counterions: K^+; T: −90 °C. The upper arrow in b) shows the signal of the solvated electron.

to the splitting patterns of the radical anions of mono- and *para*-disubstituted alkylbenzenes[4]. This proves that despite the above mentioned effects A and B, the bis(trimethylsilyl)-amino substituent still clearly functions as an electron donor. Consequently, in *(1)*$^{\ominus}$ and *(2)*$^{\ominus}$ — as in the radical anions of mono- and *para*-disubstituted alkyl derivatives — the symmetrical orbital of benzene

$$\Psi_{a^+} = 0.577\,(\Phi_1 + \Phi_4) - 0.289\,(\Phi_2 + \Phi_3 + \Phi_5 + \Phi_6)$$

is more strongly destabilized than its antisymmetrical counterpart

$$\Psi_{a^-} = 0.500\,(\Phi_2 - \Phi_3 + \Phi_5 - \Phi_6)$$

(The two lowest antibonding orbitals Ψ_{a^+} and Ψ_{a^-} are degenerate in unsubstituted benzene.)

In *(1)*$^{\ominus}$ and *(2)*$^{\ominus}$ the unpaired electron thus occupies the orbital Ψ_{a^-}, which leads to the π spin population being distributed almost exclusively among the four centers 2, 3, 5, and 6.

The coupling constants for both pairs of equivalent ring protons in *(1)*$^{\ominus}$ are $a_{H'} = 5.7 \pm 0.1$ and $a_{H''} = 5.1 \pm 0.1$ gauss. For the four equivalent ring protons in *(2)*$^{\ominus}$ a coupling constant of $a_H = 5.43 \pm 0.05$ gauss has been recorded. These values are comparable with the corresponding data for the radical anions of toluene ($a_{H'} = 5.45$ and $a_{H''} = 5.12$ gauss) and *p*-xylene ($a_H = 5.34$ gauss) respectively[4]. If an HMO model similar to that for the toluene radical anion is used for the interpretation of the coupling constants of the ring protons in *(1)*$^{\ominus}$ then $a_{H'}$ can be assigned to the ring protons on the centers 3 and 5, and $a_{H''}$ to those on centers 2 and 6. The coupling constants of the ^{14}N nuclei in *(1)*$^{\ominus}$ and *(2)*$^{\ominus}$ and of the *p*-proton in *(1)*$^{\ominus}$ could not be measured directly since the unresolved small splitting due to the large sets of equivalent trimethylsilyl protons results in additional line broadening. From the observed widths of the hyperfine components (0.6 gauss for *(1)*$^{\ominus}$ and 0.8 gauss for *(2)*$^{\ominus}$), these coupling constants can be approximately derived: a_H (4) and $a_N \leqslant 0.5$; $a_H(Si{-}CH_3) \leqslant 0.1$ gauss.

The electron donor effect of bis(trimethylsilyl)amino substituents is also confirmed by the observation that under the same conditions the signal of the solvated electrons occurs in the spectrum of *(2)*$^{\ominus}$ (Fig. 1b) but not in that of *(1)*$^{\ominus}$ (Fig. 1a). The equilibrium[5]

$$\text{Amine} + e^{\ominus}_{solv} \qquad \text{Amine}^{\ominus} + \text{DME}$$

must accordingly be shifted less strongly to the right in the case of the disubstituted compound *(2)* than in the case of the monosubstituted *(1)*.

Received: August 5, 1969 [Z 74 IE]
German version: Angew. Chem. *81*, 786 (1969)

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Tetrafluoroorthoperiodic Acid and Iodine Dioxide Trifluoride

By *A. Engelbrecht* and *P. Peterfy*[*]

If, as in the preparation of pentafluoroorthotelluric acid from an orthotellurate and fluorosulfonic acid[1,2], $Ba_3H_4(IO_6)_2$[3] is allowed to react with a 20-fold excess of HSO_3F and the reaction mixture then distilled under reduced pressure a fraction is obtained which contains tetrafluoroorthoperiodic acid, $HOIOF_4$, and HSO_3F in the ratio 2 : 1.

$$Ba_3H_4(IO_6)_2 + 14\,HSO_3F \rightarrow 2\,HOIOF_4 + 8\,H_2SO_4 + 3\,Ba(SO_3F)_2$$

The ^{19}F-NMR spectrum shows that both the *cis* (C_{2v}) and the *trans* form (D_{4h}) of the pseudooctahedral ion $[OIOF_4]^-$ are present in a ratio of about 3 : 1 in the mixture at 20 °C. The spectrum contains two triplets (with slight intensity perturbations of the second order) due to the ion with C_{2v} symmetry, and, superimposed on the triplet at higher field strength, a singlet which we assign to the isomer having D_{4h} symmetry. We have not, as yet, been able to separate the isomers from the excess of fluorosulfonic acid or the isomers from each other.

On addition of SO_3 (60% oleum) the mixture turns yellow; yellow needle-like crystals having the composition IO_2F_3 (mol. wt., mass spectrometrically, 216), m.p. 41 ± 0.5 °C, sublime *in vacuo* from the resulting mixture.

$$HOIOF_4 + SO_3 \rightarrow IO_2F_3 + HSO_3F$$

The ^{19}F-NMR spectrum of molten IO_2F_3 contains two doublet-triplet systems (AB_2 spin systems) in the ratio ≈ 3 : 1. This indicates also (assuming the fundamental structure of IO_2F_3 to be trigonal bipyramidal) the presence of two isomers (C_{2v} and C_s). Assignment of the different doublet-triplet combinations to the two isomers is possible from the results of investigations on alkyl- and arylfluorophospho-

ranes[4]; the signals of the axial F atoms always appear at lower field strengths than those of the equatorial atoms. The same reasoning is used in the case of isomers of SF_4 derivatives[5]. The relative positions of the multiplets are also in accord with the rule that the axial positions are occupied by the most electronegative ligands. As shown in Table 1, the chemical shifts of each of the axial and equatorial fluorine atoms agree very well even in the case of the two isomers of $HOIOF_4$; all these resonance lines lie between those of IFI[6] and IF_5[7] and very close to the resonance lines of OIF_5[6].

Chemical shifts and coupling constants (56.4 MHz).

		Sym.	Type	$\delta^{19}F$ (ppm) [a] axial	equatorial	J_{FF} (Hz)
IF_5 [b]	pure	C_{4v}	AB_4	−138.4	− 89.8	85
IF_7 [b]	pure	—	—	−251		—
IOF_5 [b]	2:1 in IF_5	C_{4v}	AB_4	−189	−153	280
IO_2F_3	pure	C_{2v}	AB_2	−184	−146	180
IO_2F_3	pure	C_s	AB_2	−165	−147	210
$HOIOF_4$	1:2 in HSO_3F	D_{4h}	A_4	—	−146	—
$HOIOF_4$	3:2 in HSO_3F	C_{2v}	A_2B_2	−167	−145	221

[a] External standard CF_3COOH.
[b] Measured against SiF_4 as internal standard (SiF_4: 83.8 ppm against CF_3COOH) [6].

Procedure

$Ba_3H_4(IO_6)_2$ (86 g) is added slowly with ice-cooling to HSO_3F (200 g), and $HOIOF_4$ (30 g) in admixture with HSO_3F is distilled from the reaction mixture (b.p. 46 °C/≈1 torr; yield 64%). For conversion into IO_2F_3, 60% oleum is added in small portions and the IO_2F_3 thus formed is immediately sublimed off at 30 °C/≈1 torr. Yield of IO_2F_3 about 24 g (80%).

IO_2F_3 ignites on contact with inflammable organic substances, is wetted only slowly by water, and hydrolyzed to HF and H_5IO_6. On exposure to direct sunlight, it decomposes with liberation of oxygen.

$$IO_2F_3 \xrightarrow{h\nu} IOF_3 + {}^1/_2O_2$$

partly in the form of ozone.

Received: July 14, 1969 [Z 60 IE]
German version: Angew. Chem. *81*, 753 (1969)

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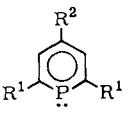
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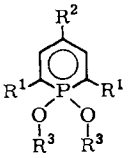
Crystal and Molecular Structure of 1,1-Dimethoxy-2,4,6-triphenylphosphorin

By *U. Thewalt*[*]

Dimroth and *Städe*[1] have been able to obtain 1,1-dialkoxy- and 1,1-diaryloxyphosphorins *(2)* by oxidation of 2,4,6-trisubstituted phosphorins *(1)* with mercury(II) acetate in the presence of alcohols or phenols.



(1)



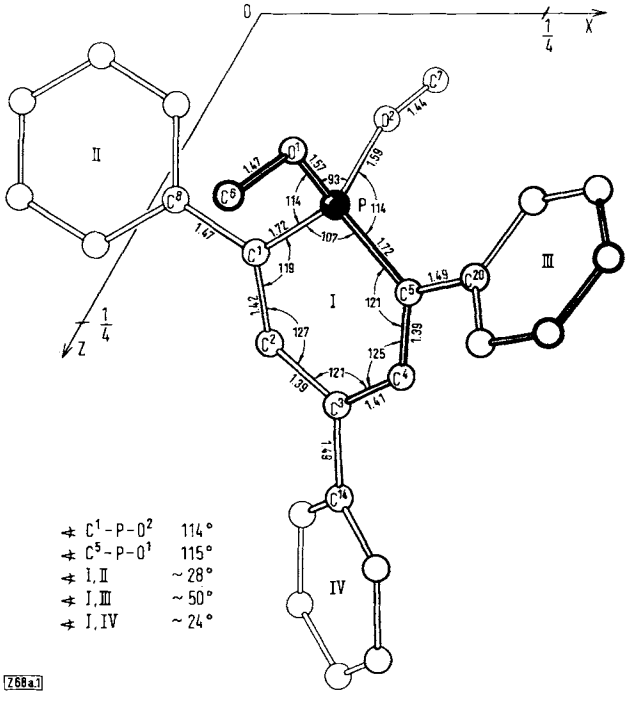
(2)

The compounds *(2)*, like phosphorins themselves, are characterized by their unusual stability. Since X-ray structure analyses[2,3] on two compounds of type *(1)* show that the six π electrons in the C_5P rings are delocalized (planar form of the ring, equal C—P bond distances of about 1.74 Å, aromatic C—C bond lengths), the molecular geometry of a compound of type *(2)* having tetracoordinate phosphorus seems of interest.

Monoclinic prismatic crystals of 1,1-dimethoxy-2,4,6-triphenylphosphorin *[(2)*: $R^1 = R^2 = C_6H_5$; $R^3 = CH_3$], which fluoresce yellow-green, were obtained by cooling a benzene/ethanol solution[4].

Crystal data: space group $P2_1/c$; $Z = 4$; $a = 16.53$, $b = 7.01$, $c = 20.98$ Å, $\beta = 119.8°$; $d_{X\text{-ray}} = 1.22$, $d_{exp} = 1.22$ g/cm³. The intensities of the strong X-ray reflections were measured with an automatic two-circle diffractometer; those of the weaker ones were estimated visually from Weissenberg photographs (all with $Cu_{K\alpha}$ radiation). From a total of 4161 independent reflections, 953 were unobserved.

The structure determination was carried out by means of the symbolic addition method[5] using 333 reflections with $E \geqslant 1.7$. The positional and isotropic temperature parameters of the atoms other than hydrogen were refined by the least squares method. The conventional R value for the 3208 observed reflections is 15.5%. Localization of the hydrogen atoms was not performed. The molecular structure and main bond lengths and angles are given in the figure.



Z68a.1

Projection along the *b* axis of a 1,1-dimethoxy-2,4,6-triphenylphosphorin molecule. The estimated standard deviations of the bond lengths (Å) and angles (°) are 0.01—0.02 Å and 1—2° resp.

The C—P bond lengths (1.72 and 1.72 Å) lie between the value for the C—P single bond and that for the C=P double bond of tetracoordinate phosphorus (*e.g.* in $(C_6H_5)_3P{=}CH_2$[6], C—P distance = 1.82 Å; C=P distance = 1.66 Å); similar distances (1.73—1.75 Å) were also observed in com-

pounds *(1)* [2,3]. The C—C bond lengths in the phosphorin ring (I) agree, within experimental error, both mutually and with the C—C bond lengths in benzene. The C_5P ring deviates slightly but significantly from planarity (deviations from the C^2PC^4 plane: C^1, −0.11; C^3, 0.07; C^5, −0.02 Å).

The three bonds to the phenyl rings project out a little from the C^2PC^4 plane (C^8, −0.33; C^{14}, 0.17; C^{20}, −0.20 Å). The C—P—C bond angle, like that in the phosphorins *(1)* [2,3], is relatively small, having a value of 107°; the symmetrical variation of the remaining inner angles of the central ring is worthy of note.

The O^1PO^2 plane is perpendicular to the C^1PC^5 plane; the O^1PO^2 angle of 93° is surprisingly small. The P—OCH_3 bond lengths (1.57 and 1.59 Å) are comparable with the P—OR distances found in phosphoric esters.

The observed P—C bond distances suggest participation of the d orbitals of phosphorus in these bonds. The aromaticity of the central ring I can be deduced from its near planarity and from the bond lengths. The three bonds between the rings have a length corresponding to that of a $C(sp^2)$—$C(sp^2)$ single bond. The phenyl rings are twisted with respect to the plane of the central ring; the configuration is not propeller-like. The C—C distances in rings II and III are, within the limits of error, the same as those of normal aromatic bond lengths. In ring IV, on the other hand, unrealistic distances (1.28 to 1.45 Å) — due to extensive thermal motion of this ring — are observed.

Received: July 25, 1969 [Z 68a IE]
German version: Angew. Chem. *81*, 783 (1969)

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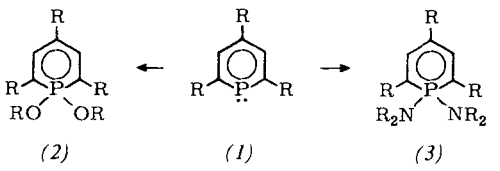
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New Free-Radical Reactions with Phosphorins

By *K. Dimroth, A. Hettche, W. Städe*, and *F. W. Steuber* [*]

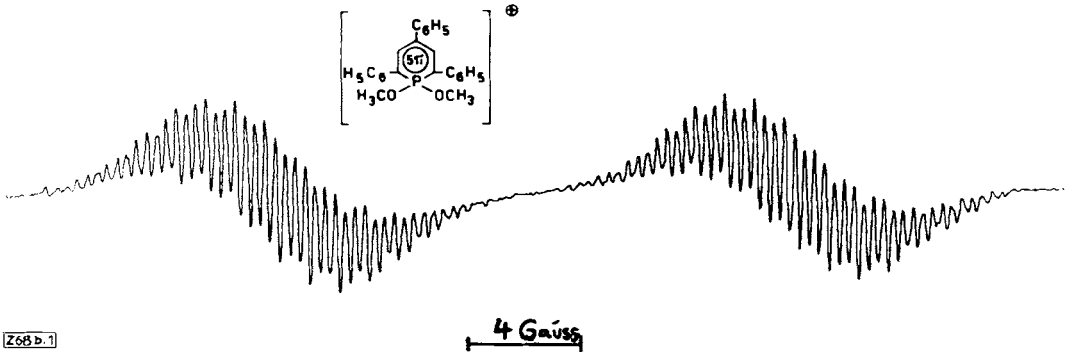
Oxidation of 2,4,6-trisubstituted phosphorins *(1)* with mercury(II) acetate in the presence of alcohols or phenols leads to the formation of compounds containing tetravalent phosphorus, *i.e.* to 1,1-dialkoxy- or 1,1-diaryloxyphosphorins *(2)* respectively [1]. In our opinion, this reaction proceeds in the first step *via* the phosphorin radical cation [2,3].

We have now been able to prepare 1,1-diaryloxyphosphorins using 2,4,6-triphenylphenoxyl as oxidizing agent and the phenoxide from this reaction as reaction partner; thus, reaction of 2,4,6-triphenylphosphorin with 2,4,6-triphenylphenoxyl in the molar ratio 1 : 2 leads to formation of 1,1-bis-(2,4,6-triphenylphenoxy)-2,4,6-triphenylphosphorin.



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

A further reaction of this type is that of phosphorins with tetraphenylhydrazine. When 2,4,6-triphenylphosphorin was allowed to react with the diphenylaminyl radical formed on heating the hydrazine the first representative of a new class of compounds *(3)* was formed, namely 1,1-bis(diphenylamino)-2,4,6-triphenylphosphorin (yellow fluorescing crystals, m.p. 179 °C; ^{31}P-NMR: δ −29.5 ppm (δH_3PO_4 = 0), $J_{PH^3,5}$ = 36 Hz in pyridine as solvent; UV: λ_{max} (ε): 439 (8.45×10^3) 330 nm (1.9×10^4) in cyclohexane as solvent). The phosphorin radical cation can be detected by ESR spectroscopy in this reaction too.



The compounds of type *(2)* and *(3)* must — as crystal structure analysis shows [4] — contain an aromatic system with spd hybridization at the tetravalent phosphorus.

Also in agreement with this assumption is the fact that compounds *(2)* and *(3)* can be readily oxidized both electrolytically and by lead(IV) benzoate to give a new class of stable radical cations. The ESR spectrum of the 1,1-dimethoxy-2,4,6-triphenylphosphorin radical cation ($|a_P|$ = 18.4 gauss) is shown in Figure 1. The radical cation of 1,1-bis(trideuteriomethoxy)-2,4,6-triphenylphosphorin gives exactly the same spectrum.

This indicates that the delocalization of the unpaired electrons is mainly limited to the aromatic system.

1,1-Bis(2,4,6-triphenylphenoxy)-2,4,6-triphenylphosphorin

A solution of 2,4,6-triphenylphenoxyl (2.2 g, 6.8 mmoles) in benzene (20 ml) is added dropwise at room temperature to a solution of 2,4,6-triphenylphosphorin (1.1 g, 3.4 mmoles) in benzene (20 ml). The mixture is stirred for 2 hours. Yield 1.6 g (48 %) of yellow crystals having m.p. 249–251 °C; UV: λ_{max}(ε): 425 (1.32×10^4), 323 (1.70×10^4), 251 nm (9.20×10^4) in cyclohexane.

1,1-Bis(diphenylamino)-2,4,6-triphenylphosphorin

A mixture of 2,4,6-triphenylphosphorin (324 mg, 1 mmole) and tetraphenylhydrazine (390 mg, 1.16 mmole) in 30 ml dry benzene is heated for 2 hours. The benzene is then evaporated and the dark green fluorescing, viscous residue is taken up in a little benzene/*n*-hexane and chromatographed on an SiO_2 column. The product thus obtained can be recrystallized from ethanol/acetone; m.p. 179 °C (decomp); yield: 340 mg (52 %).

Received: July 28, 1969 [Z 68b IE]
German version: Angew. Chem. *81*, 784 (1969)

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Electron Transfer from an Excited Electron Donor in the Triplet State to an Acceptor Molecule

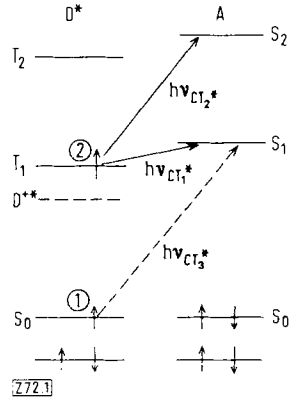
By *G. Briegleb* and *H. Schuster*[*]

We have investigated the influence of electron donor-acceptor (EDA) complex formation on the triplet-triplet (TT) absorption spectrum of the electron donors (D) naphthalene *(1)* and phenanthrene *(2)* in complexes with the electron acceptors (A) tetrachlorophthalic anhydride *(3)* and pyromellitic dianhydride *(4)*. The TT absorption spectra were recorded in *n*-propyl ether glass at $T = 96$ to 118 °K by flash spectrophotometry[1]. The triplet state of *(1)* and *(2)* in the complex $|DA|$ with *(3)* or *(4)* was excited by irradiation within the frequency of the charge transfer (CT) absorption bands *via* the singlet excited state $|\dot{D}^+\dot{A}^-|_S^*$ of the complex with subsequent "intersystem crossing" energy transfer $|\dot{D}^+\dot{A}^-|_S^* \rightarrow |D_T^*A|$. This excitation mechanism was possible since the condition $E_{|\dot{D}^+\dot{A}^-|_S^*} > E_{|D_T^*A|}$, or in the case of complexes with donor-triplet excimers $E_{D\cdot\cdot|\dot{D}^+\dot{A}^-|_S^*} > E_{|DD_T^*A|}$, was fulfilled. The triplet state had to be excited *via* the CT singlet state in order to prevent a triplet excitation of the free donor molecules not bonded in the complex.

The TT absorption spectra of complexed *(1)* and *(2)* in the frequency range 20 to 25 × 10^3 cm^{-1} exhibit characteristic changes compared to the TT absorption spectra of the free donors *(1)* and *(2)*[2]. The triplet lifetime is also reduced by complex formation, *i.e.* the probability of the $T \rightarrow S_0$ transition is increased. The TT spectrum of complexed triplet excimers of *(1)* and *(2)* was measured at slightly higher temperatures (106—113 °K) and/or in the presence of an excess of donor. It was also possible to detect the excimers in the phosphorescence spectrum by irradiation within the frequency of the CT band at $T = 100$ to 120 °K and in the presence of an excess of the donor[2].

The ionization energy of the triplet excited donor bonded in the complex $|D_T^*A|$ is reduced by the energy required for $T_1 \leftarrow S_0$ excitation. Hence CT* absorption bands corresponding to *transition of an electron from the triplet excited donor to an unoccupied energy level of the acceptor* in frequency ranges of relatively long wavelength could be expected. We first found CT* bands of this kind in complexes $|D_T^*A|$ of triplet excited *(1)* and *(2)* with *(3)* and *(4)* after the population of $|D_T^*A|$ had been increased by flash excitation in the frequency range of the CT bands of the complexes $|DA|$ in the *ground state* in solutions in *n*-propyl ether glass at 96 to 118 °K.

The experimentally determined CT* frequencies of the CT* band maxima are given in the Table, as are the CT* frequencies $\tilde{\nu}_{CT_1^*}$, $\tilde{\nu}_{CT_2^*}$, and $\tilde{\nu}_{CT_3^*}$ for a transition of the D_T^* electron 1 or 2 of the T_1-excited donor to various energy levels of the acceptor calculated[3] assuming the various



possibilities of electron transition (energy level scheme, see Figure). Comparison of the observed and estimated $\tilde{\nu}_{CT^*}$ values shows that $\tilde{\nu}_{CT_1^*}$ does not correspond to the measured CT*-absorption bands. No distinction can be made between $\tilde{\nu}_{CT_2^*}$ and $\tilde{\nu}_{CT_3^*}$ within the limits of accuracy of estimation. A superposition of both transitions is conceivable, thus providing a possible explanation *inter alia* for a diffuse broadening of the CT* band in the case of the phenanthrene complex *(2)—(3)*.

Received: July 28, 1969 [Z 72 IE]
German version: Angew. Chem. *81*, 790 (1969)

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N-Halogenoimidosulfur Difluorides and *N,N'*-Dihalogenosulfur Diimides

By *K. Seppelt* and *W. Sundermeyer*[*]

N-Halogenoimidosulfur difluorides *(2)* have previously been prepared by reaction of halogens with *N*-fluoroformylimidosulfur difluoride[1], $FC(O)NSF_2$, in the presence of cesium fluoride or by reaction of halogens with bis(difluorosulfur(IV)imido)mercury[2], $Hg(NSF_2)_2$.

We have recently investigated the cleavage of *N*-halogenobis(trimethylsilyl)amines *(1)* with non-metallic halides[3] and have found a further route to compounds *(2)* by reaction of *(1)* (X = Cl, Br) with sulfur tetrafluoride.

$$\underset{(1a),\ X = Cl}{X{-}N[Si(CH_3)_3]_2} + SF_4 \rightarrow \underset{(2)}{X{-}N{=}SF_2} + 2\,(CH_3)_3SiF$$
$$(1b),\ X = Br$$

	Tetrachlorophthalic anhydride *(3)*				Pyromellitic dianhydride *(4)*			
	$\tilde{\nu}_{CT^*_{exp}}$	$\tilde{\nu}_{CT_1^*}$ [a]	$\tilde{\nu}_{CT_2^*}$ [a]	$\tilde{\nu}_{CT_3^*}$ [a]	$\tilde{\nu}_{CT^*_{exp}}$	$\tilde{\nu}_{CT_1^*}$ [a]	$\tilde{\nu}_{CT_2^*}$ [a]	$\tilde{\nu}_{CT_3^*}$ [a]
$[Naphthalene]_T^*$	19—20	6.5	18.4	18.5	16.5	3.7	15.7	15.7
$[Phenanthrene]_T^*$	[b]	6.4	18.4	15.4	16.0	3.4	15.4	12.4

$\tilde{\nu}$ in 10^3 cm^{-1}.

[a] Calculated [3] (cf. energy-level diagram).
[b] The position of $\tilde{\nu}_{CT^*}$ could not be determined accurately (no clear maximum).

The physical and spectroscopic data found for the products *(2)* are identical with those found by earlier workers[1,2]. This new method of preparation of *(2)* confirms the assumption that these compounds are *N*-halogenoimidosulfur difluorides and not the isomeric difluoronitridosulfur halides, $N \equiv SF_2X$. Previous evidence for the structure *(2)* was based mainly on the occurrence of nitrogen-halogen fragments in the mass spectrum; however, the possibility of these fragments arising from recombination could not be ruled out.

The analogous reaction of *N*-iodobis(trimethylsilyl)amine *(1c)* with sulfur tetrafluoride does not lead to the still unknown *N*-iodoimidosulfur difluoride (cf.[2]) but (presumably *via* this compound as unstable intermediate) to *N,N'*-diiodosulfur diimide *(3)*.

$$\underset{(1c)}{2\,I{-}N[Si(CH_3)_3]_2} + SF_4 \rightarrow \underset{(3)}{I{-}N{=}S{=}N{-}I} + 4\,(CH_3)_3SiF$$

A solution of SF_4 in 1,2-dichloroperfluoroethane is added dropwise at about 0 °C to a solution of *(1c)* in the same solvent. An orange-red crystalline precipitate forms that can be recrystallized from methylene chloride. Compound *(3)* melts and simultaneously explodes at 106 °C. Similarly to S_4N_4, it explodes on impact and a distinct smell of SO_2 is noticeable; on ignition it deflagrates with simultaneous emission of violet iodine vapor. The crystals are almost insensitive to hydrolysis and are only slightly soluble in organic solvents such as methylene chloride, carbon tetrachloride, and benzene. Compound *(3)* was identified by elemental analysis and by mass spectrometry[4] [*m/e* = 314 (INSNI 100%), 187 (INSN 6%), 173 (INS 4%), 141 (IN 2.5%), 127 (I 11%), 60 (NSN 3.5%), 46 (SN 7.5%), and 32 (S 2%) together with a few recombination fragments such as I_2 and IS; 13 eV]. The IR spectrum (KBr) contains bands at 1094 (s), 1047 (vs), 950 (s), 631 (s), 465 (m), 327 (m), and 297 cm^{-1} (m).

N,N'-Dibromosulfur diimide Br—N=S=N—Br *(4)* can be prepared under the same experimental conditions. Compound *(4)* is much more soluble in the above mentioned solvents than is *(3)*. The pale yellow crystals of *(4)* melt at +0.5 °C with partial decomposition; they are more sensitive to impact than the crystals of *(3)*.

The mass spectrum [*m/e* = 218, 220, 222 (BrNSNBr 33%), 139, 141 (BrNSN 3%), 125, 127 (BrNS 12%), 93, 95 (BrN 14%), 79, 81 (Br 38%), 60 (NSN 2%), 46 (SN 100%), and 32 (S 39%); 70 eV], the IR spectrum (nujol) [1127 (s), 1035 (vs), 921 (s), 657 (s), 603 (m), 519 (m), 417 (m), and 370 (w)], and the Raman spectrum[5] [1133 (w), 926 (vs), 662 (m), 608 (m), 533 (s), 426 (w), 379 (m), 198 (m), and 88 (w)] are in agreement with the assumed structure *(4)*. Attempts to prepare the homologous chlorine derivative of *(3)* and *(4)* have so far failed.

Received: August 5, 1969 [Z 73 IE]
German version: Angew. Chem. *81*, 785 (1969)

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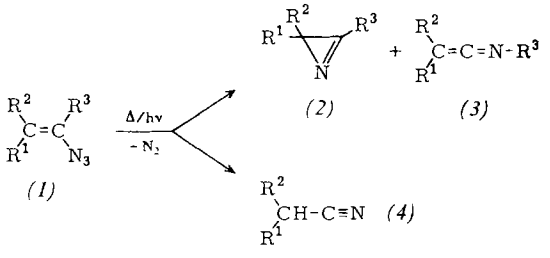
[4] We thank Dr *H. Seidl*, Badische Anilin- und Soda-Fabrik, for the recording and discussion of the mass spectrum.

[5] We are grateful to Dr. *H. Eysel*, Universität Heidelberg, for the recording and discussion of the Raman spectrum.

Synthesis and Reactions of a 2*H*-Azirine Unsubstituted on C—3

By *W. Bauer* and *K. Hafner*[*]

Thermolysis[1] or photolysis[2] of 1-alkyl or 1-aryl-vinyl azides *(1)* (R^1 = R^2 = H, aryl, alkyl; R^3 = aryl, alkyl)[3] leads to the formation of 2*H*-azirines with a substituent at C-3 *(2)* and to ketenimines *(3)*. However, the decomposition of "terminal" vinyl azides *(1)* (R^1 = R^2 = H, aryl, alkyl; R^3 = H) gives only the nitriles *(4)*[4] and none of the expected, and formerly unknown, 2*H*-azirines which lack a substituent at the 3-position.

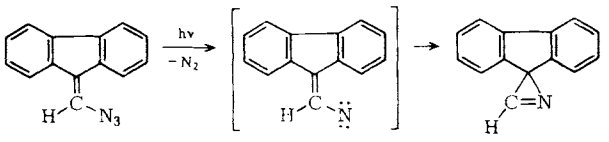


(1) *(2)* *(3)* *(4)*

Using the reaction scheme which is generally used for the synthesis of substituted fulvenes from 6-fulvenyl tosylates we have been able to prepare the "terminal" vinyl azide 9-(azidomethylene)fluorene *(5)*[5] from 9-fluorenylidenemethyl tosylate and sodium azide[6] and to study its reactions. Whilst *(5)* reacts with triphenylphosphine to give the corresponding iminophosphorane[7] (yield 77%, yellow prisms, m.p. 206—207 °C), the thermally rather unstable spiro[2*H*-azirine-2,9'-fluorene] *(7)* could be prepared as the first C-3 unsubstituted 2*H*-azirine by photochemical decomposition of *(5)* in anhydrous diethyl ether at −15 ° (UV lamp Type Q 81, Original Hanau, Duran glass, irradiation time 1 h) and careful work-up (isolation at −70 °C, recrystallization at −50 °C). Presumably the initial formation of the nitrene *(6)*

Comp.	Yield (%)	M.p. (°C)	UV λ_{max} (nm) (log ε)	NMR (τ) [a]	IR (cm^{-1})
(7)	74	83—85 (decomp.) yellowish needles (*n*-hexane)	234 (4.31), 260 (4.19), 270 (4.43), 284 (4.10) (dioxane)	−0.35 (1 H/s), 2.11—3.17 (8 H/m) ($CDCl_3$)	1665 [13] (C=N) (CCl_4)
9-Isocyano-fluorene	10	113—115 (subl.) colorless needles (petroleum ether)	224 (4.34), 231 (4.18), 267 (4.28), 279 (4.15), 292 (3.44), 302 (3.16) (dioxane)	2.17—2.9 (8 H/m), 4.47 (1 H/s) ($CDCl_3$)	2140 (−N≡C) (KBr)
(9)	21	325—327 red needles (ethyl acetate)	237 (4.72), 263 (4.71), 304 (4.06), 332 (4.18), 439 (4.27), 453 (4.28) (dioxane)		1600 (C=N) (KBr)
(10)	36	215—217 colorless needles (ethyl acetate)	227 (4.28), 236 (4.12), 270 (4.21), 293 (3.66), 305 (3.67) (dioxane)	1.3 (1 H/broad), 1.61 (1H/m), 2.31—2.83 (8 H/m), 3.91 (1 H/d) ([D_6]-DMSO)	3280 (N—H), 1665 (C=O), (KBr)
(11)	21	139—141 yellow platelets (methanol)	225 (4.35), 233 (4.16), 270 (4.24), 293 (3.72), 305 (3.74) (dioxane)	1.99 (1 H/s), 2.18—2.9 (8 H/m), 4.82 (1 H/s), 6.28 (3 H/s) ($CDCl_3$)	1650 (C=N), (KBr)

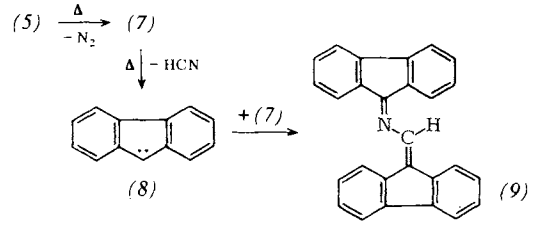
[a] TMS as internal standard.



(5) (6) (7)

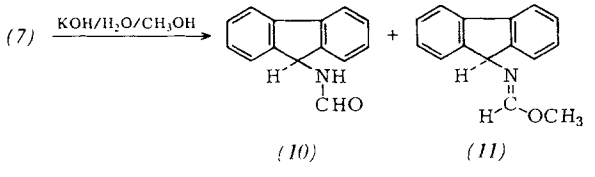
is followed by intramolecular cyclization to give *(7)*. Irradiation of *(7)* in anhydrous diethyl ether at −15 °C (UV lamp Type Q 81, Original Hanau, quartz glass, irradiation time 6 h) leads to the formation of a mixture of 9-cyano-[8] and 9-isocyanofluorene[9], which can be separated by layer chromatography (Silica gel PF_{254}, petroleum ether/ether 4 : 1). Under the same conditions compound *(5)*, like *(7)*, can also be converted into these two compounds (yields 38% and 8% resp.) — presumably *via* intermediate formation of *(7)*.

Thermolysis of *(5)* and of *(7)* in anhydrous petroleum ether in the presence of atmospheric oxygen and absence of moisture yields *N*-(9-fluorenylidene)-9-fluorenylidenemethylamine *(9)*[6] in addition to 9-fluorenone (24%).



(8) (9)

That fluorenone and *(9)* are formed both from the azide *(5)* and from the azirine *(7)* suggests that thermal decomposition of *(5)* also involves the formation of *(7)* as an intermediate. The products are presumably formed by reaction of 9-fluorenylidene *(8)*, produced by elimination of HCN from *(7)*, either with oxygen[10] or with *(7)*. It is perhaps surprising that neither alkaline nor acidic hydrolysis of *(7)* gives a dihydropyrazine derivative[11]. On the other hand, *(7)* reacts with KOH in methanol-water to yield a mixture of *N*-(9-fluorenyl)formamide *(10)*[11] and methyl *N*-(9-fluorenyl)-imidoformate *(11)*[12].



(10) (11)

Received: August 1, 1969 [Z 76 IE]
German version: Angew. Chem. *81*, 787 (1969)

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[8] The compound is identical with the 9-cyanofluorene synthesized from 9-fluorenylaldoxime and thionyl chloride; *W. Wislicenus* and *K. Russ*, Ber. dtsch. chem. Ges. *43*, 2719 (1910).

[9] 9-Isocyanofluorene was synthesized independently by reaction of *(10)* (obtained from 9-fluorenylamine and ethyl formate in 92% yield) with tosyl chloride/pyridine.

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[11] *(10)* is identical with a sample synthesized from 9-fluorenylamine and ethyl formate.

[12] Reaction of *(7)* with methanolic-aqueous HCl also affords *(10)* (12%) along with 9-fluorenone (15%) and 9-fluorenol (8%).

[13] The discrepancy between the C=N absorption in the IR spectrum of *(7)* and the C=N absorption of 2*H*-azirines substituted on C-3 (1740–1780 cm^{-1}) [2] cannot, as yet, be explained.

Trifluoromethylfluorosulfane and 1,2-Bis(trifluoromethyl)disulfane 1,1′-Difluoride

By *F. Seel* and *W. Gombler*[*]

The existence of sulfenyl fluorides RS—F has hitherto been established only in a limited number of cases by NMR spectroscopy: R = $(CF_3)_2CF$[1] and CF_nCl_{3-n} (n = 0 to 3)[2]. We have now been able to convert trifluoromethylchlorosulfane *(1)* quantitatively into trifluoromethylfluorosulfane (trifluoromethanesulfenyl fluoride, "perfluoromethyl mercaptan") *(2)* by reaction with mercury(II) fluoride and to study the physical and chemical properties of the sulfenyl fluoride.

The gaseous compound CF_3SF is characterized unequivocally by its mass spectrum (CF_3^+ 100, CF_3SF^+ 90.5, CF_2S^+ 29.2, CF_3S^+ 23.8, SF^+ 17.2) and by its extremely simple IR spectrum which demonstrates the extensive independence of the CF stretching vibrations (1190 and 1152 cm^{-1}) and the SF stretching vibration (808 cm^{-1}). Surprisingly, the NMR spectrum of the liquid compound was much more complicated than expected (cf. Figure and Table). It contains not only a signal characteristic of sulfenyl fluorides at extremely high δ values, with a 1,3,3,1 quadruplet splitting owing to spin coupling with the CF_3 group and an associated doublet that is to be assigned to the CF_3 group, but also the very intense signals (two triplets having a quartet fine structure, four superposed quadruplets) due to a more complicated compound. The positions of the signals and their fine structure show the compound to be a dimer of *(2)*, 1,2-bis(trifluoromethyl)disulfane 1,1′-difluoride *(3)*. The fact that addition of potassium fluoride increases the sharpness of the signals suggests that exchange processes are occurring *via* hydrogen fluoride which is inevitably formed in small amounts during the preparation of *(2)* and *(3)*. NMR studies also showed that the equilibrium between *(2)* and *(3)* is established only slowly below 0 °C. In the liquid phase it lies mainly on the side of *(3)*. Whereas the sulfenyl chloride *(1)* boils at −1 °C[3], the vapor pressure above the dimer of *(2)* amounts to only 300 torr at 0 °C. (Exact vapor pressure measurements are difficult owing to the slow equilibration and readiness with which the substance decomposes.)

Compounds *(2)* and *(3)* are converted quantitatively into hexafluorodimethyldisulfane *(4)* and trifluoromethylsulfur trifluoride *(5)* within the course of several hours at room temperature, particularly in the presence of potassium fluoride; the stoichiometry of the disproportionation

$$3\,CF_3SF \rightarrow \underset{(2)}{CF_3SF_2SCF_3} + \underset{(3)}{CF_3SF} \rightarrow \underset{(4)}{CF_3SSCF_3} + \underset{(5)}{CF_3SF_3}$$

could be established by integration of the areas under the NMR signals.

(2) and *(3)* react rapidly with base metals (*e.g.* Mg) and relatively noble metals (such as Cu and Hg) to give the metal fluoride and *(4)*. The walls of pure nickel vessels that have been rendered passive with SF_4 are comparatively resistant

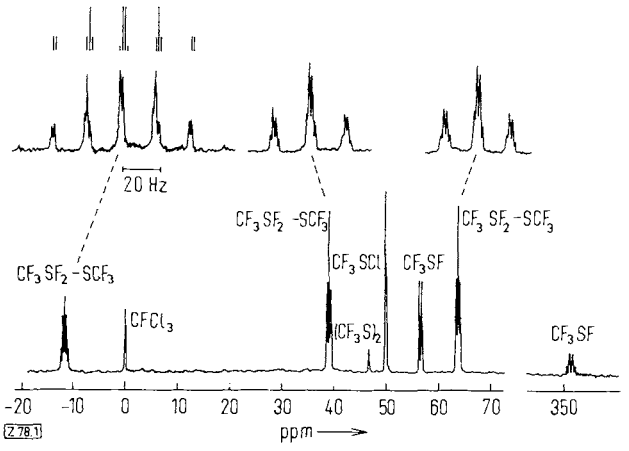


Figure: ^{19}F-NMR spectrum of a mixture of the compounds *(1)*, *(2)*, *(3)*, and *(4)*.

(The decomposition products *(4)* to *(7)* were identified by NMR and mass spectrometry. No indication was found for a hydrolysis product $CF_3S(O)SCF_3$ corresponding to *(3)*.)

Procedure:

The preparation of *(2)* and *(3)* was carried out in a vacuum apparatus consisting of a glass U-tube and two pure-nickel or platinum U-tubes that are separated from one another by nickel or stainless-steel valves and can be closed to the atmosphere by means of taps made of the corresponding material (glass or metal). HgF_2 (an approximately five-fold excess is used) must form a 5-cm layer in the central U-tube. Prior to reaction the sulfenyl chloride is condensed into the glass U-tube and frozen with liquid nitrogen. Transport of the diluted gas through the HgF_2 layer, which is heated externally to 130 °C, is effected by heating the first U-tube to −80 °C and cooling the third one with liquid nitrogen. Compound *(1)* should not contain any HCl, and the HgF_2 should be completely free from oxide; the apparatus must also be previously purged with SF_4 to remove layers of water and oxide.

Table: ^{19}F-NMR data ($CFCl_3$ as internal standard) for trifluoromethylsulfur compounds at −50 °C. F_a = equatorial, F_b = axial fluorine atom bonded to sulfur; F_c = fluorine atoms of the trifluoromethylthio group, F_d = fluorine atoms of the other CF_3 group.

	CF_3SCl *(1)*	CF_3SF *(2)*	$CF_3SF_2SCF_3$ *(3)*	CF_3SSCF_3 *(4)*	CF_3SF_3 *(5)*	CF_3SFO *(6)*	$CF_3SO_2SCF_3$ *(7)*
δF_a (ppm)		+351.5			+48.8	+22.1	
δF_b			−12.6		−51.2		
δF_c	+49.9	+56.6	+39.1	+46.8			+34.8
δF_d			+63.7		+70.0	+83.6	+70.2
$^JF_aF_b$ (Hz)					63.9		
$^JF_aF_c$		24.5					
$^JF_aF_d$					1.3	4.7	
$^JF_bF_c$			19.4				
$^JF_bF_d$			17.9		22.3		
$^JF_cF_d$			1.5				1.3

to attack. *(3)* reacts with the walls of glass vessels to give the disulfane *(4)*, trifluoromethanesulfinyl fluoride *(6)*, and 1,2-bis(trifluoromethyl)disulfane 1,1'-dioxide (*S*-trifluoromethyl trifluoromethanethiolsulfonate) *(7)*, which has already been detected as a hydrolysis product of *(1)* [4]. *(7)* is also formed on hydrolysis of *(2)* and *(3)* on moist potassium fluoride. The formation of *(6)* can be interpreted by

$$CF_3SF_3 + O^{2-} \rightarrow CF_3SOF + 2\,F^- \quad (O^{2-} \text{ from } H_2O \text{ or } -SiO_3^{2-})$$
(6)

and that of *(4)* and *(7)* by the series of reactions

$$CF_3SF \xrightarrow[-F^-]{+O^{2-}} CF_3SO^- \xrightarrow{\times 2} CF_3S^- + CF_3SO_2^-$$

$$CF_3S^- + CF_3SF \rightarrow CF_3SSCF_3 + F^-$$

$$CF_3SO_2^- + CF_3SF \rightarrow CF_3SO_2SCF_3 + F^-$$

Received: August 11, 1969 [Z 78 IE]
German version: Angew. Chem. *81*, 789 (1969)

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CONFERENCE REPORTS

Rare Earth Organometallic Sandwich Complexes

By *A. Streitwieser jr.* [*]

It is convenient to consider the important bonding in ferrocene $(\pi\text{-}C_5H_5)_2Fe$ as derived from the overlap of the highest occupied molecular orbital of two parallel cyclopentadienyl rings with a vacant atomic orbital at the central metal. There are two such degenerate orbitals in each of which a vertical nodal plane divides the wave function into four parts whose symmetry permit overlap with the corresponding d_{xz} and d_{yz} atomic orbitals of iron.

If this approach is applied to the next higher homolog, the cyclic 10-electron π-rings, the highest occupied molecular orbitals now have two orthogonal vertical nodal planes that require an eight-lobed f_{xyz} or $f_{z(x^2-y^2)}$ atomic orbital of a central metal for appropriate symmetry-permitted overlap. Such accessible f-atomic orbitals are to be found in the rare-earth elements and particularly in the actinide rare-earths; for example, uranium. A suitable cyclic 10-π electron system to test this concept is cyclooctatetraene dianion. *R. D. Fischer* [1] has previously discussed the possibility that the sandwich complex $U(C_8H_8)_2$ may derive stability from the involvement of f-orbitals.

The reaction of cyclooctatetraene dianion with uranium tetrachloride in THF produces blue-green crystals that are stable to water and to aqueous acid or alkali. The compound can be sublimed or recrystallized from benzene or toluene. The compound is pyrophoric but controlled air oxidation yields uranium oxides and cyclooctatetraene. Mass spectral analysis gives a parent peak for $U(C_8H_8)_2$ and the fragmentation pattern indicates a ferrocene-like sandwich structure. X-ray analysis [2] confirms the sandwich structure with planar 8-membered rings in a D_{8h}-configuration. An inspection of the possible electronic structures shows that all of the appropriate molecular orbitals of the two π-rings have symmetry that permits overlap with suitable atomic orbitals of the uranium. The relative stability of the complex to hydrolysis compared with similar sandwich complexes of cyclooctatetraene dianion with several transition elements prepared by *Breil* and *Wilke* [3] suggests that additional bonding is involved in the uranium compound such as that involving the f-orbitals.

Lecture at Darmstadt on June 30, 1969 [VB 208 IE]
German version: Angew. Chem. *81*, 754 (1969)

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Internal Oxidation and Related Phenomena in Alloys

By *J. L. Meijering* [*]

Oxygen is soluble to some extent in certain metals such as Ag, Cu, Ni, and Fe. If such a metal A contains in solid solution a small amount of an element B with a stronger oxygen affinity, then oxygen often diffuses inward more rapidly than element B diffuses outward, and the oxide of B is then formed not on the surface, but in the interior of the sample. There is generally a fairly sharp boundary between the zone of internal oxidation (A—BO) and the zone without it (A—B). The depth of this boundary increases with the square root of time.

Both external and internal oxidations occur when *e.g.* nickel containing 1 % of Al is heated. The internally oxidized zone is under a surface layer, which consists mostly of NiO. In some alloys, *e.g.* Pd with 70 atom-% of Cu, the same oxide (here Cu_2O) may form both in this surface layer and in the interior of the sample [1]. This is partly because the solubility product of Cu_2O in Pd is relatively high, so that the boundary becomes very blurred.

The solubility product of the oxide is very important for the degree of dispersion. The smaller the difference between A and B in affinity for oxygen, the higher the solubility of the oxide, and the more it can agglomerate. In silver, the stable oxides MgO, BeO, and Al_2O_3 are almost molecular dispersions, as indicated by the lattice parameters, the electrical resistance [2], and electron microscopy [3].

In the internal oxidation of *e.g.* Ag—Mg and Cu—Be alloys, the finely dispersed oxide causes considerable hardening. The precipitation hardening or the cold rolling of silver alloys and copper alloys bring about a comparable hardening, but this is destroyed by subsequent heating to 400 °C, while oxidation hardening is performed even at 800—950 °C. Practical applications lie in the field of electrical contacts [4].

When element B is present in a fairly high concentration, internal oxide films are often formed between the oxide particles. Regular variations in the oxide concentration can come about by disturbances in the reaction balance at the oxidation boundary. These disturbances may be caused by changes in the oxygen pressure or the temperature, or also by a special geometry of the sample [5].

Phenomena analogous to internal oxidation occur *e.g.* with nitrogen, carbon, and hydrogen. The internal auridization of Mg-containing lead is a recent example [6]. It is based on the rapid diffusion of gold through the lead lattice, and on the relatively high affinity of lead for strongly electropositive metals.

Lecture at Münster on June 30, 1969 [VB 211 IE]
German version: Angew. Chem. *81*, 792 (1969)

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Recent Investigations of Psychotropic Compounds

By *J. Th. Hackmann* [*]

It is well known that environment and upbringing are very important for the individual. It is much more difficult to study the influence of neurohormones, and therefore less is known about it, although their significance is now better understood owing to the study of psychotropic compounds. It has been found that psychotropic compounds are often chemically related to neurohormones, as, for instance, psilocine, but in many cases, such as the active ingredient of hashish (cannabidiol), the corresponding neurohormone is not yet known.

The importance of the indole nucleus in psychotropic compounds has been repeatedly indicated. However, more attention should be paid to the presence of the 1-methylpiperidine ring (cf. scopolamine and 1-piperidyl glycolates) since this in particular is responsible for the apparent reality of hallucinations. The results often approach forms of mental disease and without doubt they are caused by biochemical disturbances in the brain (transmethylation).

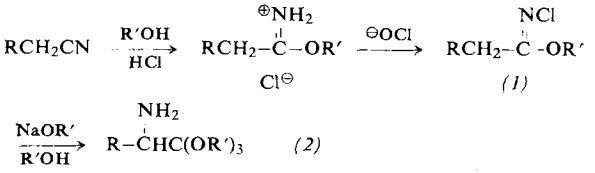
Chemical compounds can influence, not only instincts, but also emotions, the source of which lies in the hypothalamus. It is of great importance to learn which compounds can cause the emotions by electrical stimulation of the selected region of the brain. Effects of this type can be achieved in all vertebrates; it is only necessary that the respective equivalent regions be stimulated electrically. Several plants are known whose extracts cause interesting effects; the organic chemist is recommended to study the constituents of *Solanum gayanum*, *Myrothamnus moschatus*, *Cineraria aspera*, *Latua venenosa*, *Hydnocarpus venenata*, *etc.*

It is remarkable that the drugs of Indian folk medicine have not been more intensively studied in spite of the success of *Rauwolfia serpentina*, for these drugs include, for instance, products that are claimed to increase memory and are thus used on mentally retarded children. Testing some of these products in rats has shown that these claims are indeed justified. A large and important field is thus open to study.

Lecture at Aachen on June 24, 1969 [VB 210 IE]
German version: Angew. Chem. *81*, 753 (1969)

[*] Prof. Dr. J. Th. Hackmann
Twente University of Technology
P.O. box 217
Enschede (Netherlands)

A general synthesis for α-amino acid ortho esters *(2)* is given by *W. H. Graham*: The nitrile is converted, *via* the imino ether, to the α-chloro imino ether *(1)*, which yields the α-amino acid ortho ester *(2)*:



The yields are good. The reaction temperature depends upon the acidity of the α-methylene proton. When R = C_6H_5, the reaction takes place at room temperature, and otherwise at 60—70 °C. With α-disubstituted acetonitriles the synthesis fails. The reaction is probably closely related to the Neber reaction. / Tetrahedron Letters *1969*, 2223 / —Ma.

[Rd 71 IE]

Tetracyanomethane *(1)* has been synthesized for the first time by *E. Mayer* by reaction of tricyanomethylsilver with cyanogen chloride in a bomb tube at 100 °C:

$$AgC(CN)_3 + ClCN \rightarrow \underset{(1)}{C(CN)_4} + AgCl$$

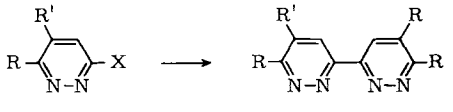
The crystalline compound *(1)* is readily soluble in aprotic solvents, sublimes at 60 °C, and decomposes at temperatures above 160 °C. As shown by the IR spectrum, *(1)* bears three equivalent CN groups (point group T_d). On alkaline hydrolysis, *(1)* behaves similarly to ClCN, which contains a positively charged CN group, to form the tricyanomethyl anion *(2)* and cyanate:

$$C(CN)_4 + 2\,OH^- \rightarrow \underset{(2)}{C(CN)_3^-} + OCN^- + H_2O$$

Compound *(2)* is also the main product of acid hydrolysis. Reaction of *(1)* with LiCl in acetonitrile gives tricyanomethyl-Li and ClCN, and should therefore prove useful as a cyanation agent. / Mh. Chem. *100*, 462 (1969) / —Ma.

[Rd 72 IE]

The synthesis of 3,3'-bipyridazine derivatives *(1)* has been accomplished by *H. Igeta, T. Tsuchiya, M. Nakajima,* and *H. Yokogawa*, by reaction of 3-halogenopyridazine derivatives with hydrazine hydrate (5—12 h) at room temperature in 5% ethanolic NaOH or KOH solution in the presence of $Pd/CaCO_3$ with vigorous stirring. 3-Chloropyridazine gives somewhat better yields than the bromine compound. Small amounts of by-products occur, which are formed by exchange of halogen for alkoxy or H. The dimeric compound

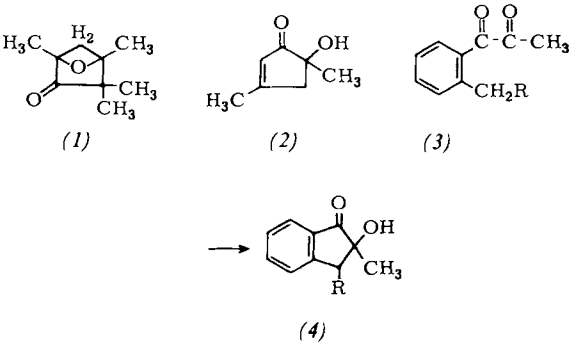


(1)

X = Cl, Br
R = H, CH_3, OCH_3, NH_2
R' = H, CH_3

cannot be obtained from 3-chloro-4-methylpyridazine. Compound *(1)* forms chelate compounds with Fe^{II}, Co^{II}, and Ni^{II}. / Tetrahedron Letters *1969*, 2359 / —Ma. [Rd 74 IE]

The photochemical conversion of unsaturated 1,2-diketones into cyclic compounds has been studied by *R. Bishop* and *N. K. Hamer*. Photolysis of β,γ- and γ,δ-unsaturated acyclic 1,2-diketones in pentane solution under an N_2 atmosphere with light of wavelength $\lambda > 380$ nm afforded 5-oxabicyclo-[2.1.1]hexan-2-ones, the double bond initially migrating over a cyclobutanol intermediate. For example, 4,4,5-trimethyl-5-hexene-2,3-dione yields 1,3,3,4-tetramethyl-5-oxabicyclo-[2.1.1]hexan-2-one *(1)* quantitatively. α,β-Unsaturated 1,2-diketones gave high yields of hydroxycyclopentenone derivatives. The irradiation of 5-methyl-4-hexene-2,3-dione in



(1) *(2)* *(3)* *(4)*

pentane with sunlight led to 3,5-dimethyl-5-hydroxy-2-cyclopenten-1-one *(2)*. *o*-Alkyl-substituted aryl-1,2-diketones such as *(3)* afforded 2-hydroxyindanones *(4)* in a similar way. / Chem. Commun. *1969*, 804 / —Ma. [Rd 75 IE]

The rate of association of lactams *(1)* in carbon tetrachloride has been investigated by *C. Y. S. Chen* and *C. A. Swenson* by measurement of the extinction of the N—H stretching vibrations in the region 3000—3500 cm^{-1}. The lactams *(1)*, $n = 1$—4, in a *cis*-configuration with reference to the peptide bond form cyclic dimers. The dissociation enthalpies of the dimers were found to be:



(1)

n	1	2	3	4
ΔH (kcal/mole)	6.37	5.90	5.52	6.33

The higher enthalpies for *(1)*, $n = 1$ and 4, are explained by the lower and higher polarity of the carbonyl bond than in *(1)*, $n = 2$ and 3, which follows from the position of the CO stretching vibrations. These factors lead to a considerable energy gain during the dimerization. The lactam *(1)*, $n = 5$, exists both in the *cis*- and in the *trans*-form; the predominantly associated form is the cyclic dimer of the *cis*-form having a dissociation enthalpy of about 6 kcal/mole. / J. physic. Chem. *73*, 1363 (1969) / —Hz. [Rd 79 IE]

The kinetics of some reactions of difluorocarbene in the gas phase have been investigated by *W. J. R. Tyerman* by spectroscopic measurements in the absorption band of CF_2 at 249 nm. CF_2 was prepared by flash photolysis of $C_2F_4/NO_2/N_2$ mixtures. The molar decadic extinction coefficient of CF_2 at 249 nm is 7620 ± 400 l $mole^{-1}$ cm^{-1} at 298 °K. The dimerization of CF_2 in C_2F_4/N_2 and CF_2CFCl/N_2 mixtures was followed; the rate constant defined by

$$d[CF_2]/dt = -2\,k_1\,[CF_2]^2$$

for the dimerization of CF_2 can be represented by $k_1 = (2.5 \pm 0.5) \times 10^6\ T^{1/2} \exp(-200 \pm 50)/T$ l mole^{-1} sec^{-1} in the temperature region 298–446 °K. At 298 °K the rate constant for the reaction of CF_2 with CFCl is about $(6 \pm 5) \times 10^8$ l mole^{-1} sec^{-1}. The rate constant expression $k_2 = 8.7 \times 10^4\ T^{1/2} \exp(-3200 \pm 625)/T$ l mole^{-1} sec^{-1} has been found for the formation of hexafluorocyclopropane from reaction of CF_2 with C_2F_4. / Trans. Faraday Soc. *65*, 1188 (1969) / —Hz. [Rd 80 IE]

The structure of dimethylgermane has been determined by *E. C. Thomas* and *V. W. Laurie* from the microwave spectrum in the region 8–35 GHz. All rotation transitions of the molecule are split into quartets by the internal rotation of the methyl groups; from the magnitude of the splitting the height of the potential well of the internal rotation was found to be 1182 ± 40 cal/mole. The C—Ge bond length is 1.950 ± 0.003 Å, the C—Ge—C angle has a value of 110.0 ± 0.5 °. Comparison of this almost tetrahedral angle with the angles in dimethylsilane (111.0 °) and propane (112.4 °) indicates that the interaction between the methyl groups practically disappears in the dimethyl compounds of the heavier elements of the fourth main group. The dipole moment of dimethylgermane is 0.616 ± 0.006 D. / J. chem. Physics *50*, 3512 (1969) / —Hz. [Rd 81 IE]

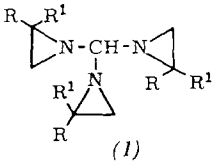
The polarographic behavior of cinnamaldehyde has been investigated by *D. Barnes* and *P. Zuman*. It can be established from the experimental results that the double bond is first hydrogenated and then the aldehyde is reduced, the cleavage of water from the aldehyde hydrate being the rate determining step for the second reaction. At intermediate pH values the hydrogenation of the C=C double bond can be resolved into several partial steps: in weakly acid solutions protonated cinnamaldehyde is reduced to a radical; in moderately alkaline solutions non-protonated aldehyde is reduced to a radical anion. These radicals can react (i) with each other with dimerization, (ii) with the starting material undergoing polymerization, and (iii) with mercury to form organomercury compounds. With monovalent cations in the range Li to tetraalkylammonium increasing amounts of adducts can be detected, which give rise to characteristic polarographic waves. / Trans. Faraday Soc. *65*, 1668, 1681 (1969) / —Hz. [Rd 83 IE]

Lithium peroxide, LiO_2, has been prepared by *L. Andrews* by reaction of Li atoms with oxygen in matrices of inert gases or oxygen at about 15 °K. The IR spectra of LiO_2 species of various isotopic compositions show that the geometric structure of the molecule is an isosceles triangle with O—O = 1.33 Å, Li—O = 1.77 Å, and the angle O—Li—O = 44.1 °. The force constant of the O—O bond is 5.59 ± 0.05 mdyne/Å and thus corresponds with that in the O_2^- ion. Therefore, LiO_2 can also be considered as an isolated essentially ionic molecule $Li^+O_2^-$. At higher lithium concentrations Li_2O_2 is also formed in the matrix by addition of Li to LiO_2; a rhombic structure containing two equivalent Li and two equivalent O atoms can be ascribed to Li_2O_2. / J. chem. Physics *50*, 4288 (1969) / —Hz. [Rd 84 IE]

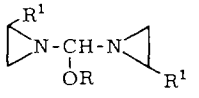
A Ti atom having coordination number 7 in a pentagonal-bipyramidal environment is present in the dinuclear complex μ-oxalatobis(oxalato)hexaquodititanium(III) · 4 H_2O, according to an X-ray structure analysis carried out by *M. G. B. Drew*, *G. W. A. Fowles*, and *D. F. Lewis*. The brown complex, which crystallizes in the space group $P\bar{1}$, has an almost pentagonal-bipyramidal configuration at the Ti atoms: the terminal bidentate C_2O_4 group (*d* TiO 2.08 to 2.09 Å), the bridging quadridentate C_2O_4 group (*d* TiO 2.16 to 2.19 Å), and one H_2O molecule (*d* TiO 2.08 Å) occupy the five equatorial positions, and two further H_2O molecules (*d* TiO 2.04–2.08 Å) are in the axial positions. The bridging C_2O_4 group is planar, while the terminal TiC_2O_4 unit deviates markedly from planarity. / Chem. Commun. *1969*, 876 / —HB. [Rd 89 IE]

Fibrous, pressure-induced sulfur is probably identical with the Ψ-sulfur investigated by *Prins*. According to an X-ray structure analysis carried out by *M. D. Lind* and *S. Geller*, it possesses a helix structure in which eight alternately left- and right-handed spirals are arranged along the *c* axis of the monoclinic unit cell ($a = 17.6$, $b = 9.25$, $c = 13.8$ Å, $\beta = 113$ °) in such a manner that ten S atoms in three turns form a period 13.8 Å long. All the spirals have a radius of 0.95 ± 0.003 Å and are close-packed. The crystals are yellow, and remain undecomposed for years when kept in air at room temperature. Crystal twinning gives the impression of an orthorhombic unit cell of twice the actual size. / J. chem. Physics *51*, 348 (1969) / —HB. [Rd 90 IE]

A simple synthesis of tris(aziridino)methane *(1)* is reported by *W. Funke*. Reaction of aziridines with dichlorocarbene, which is produced from chloroform and NaOH powder in benzene, affords *(1)*. The yields of tris(aziridino)-, tris(2-methylaziridino)-, and tris(2,2-dimethylaziridino)methane are 65, 43, and 30%, respectively. Compounds *(1)*, which are stable in the absence of air and moisture, polymerize in the presence of acids or alkylating agents. Bis(aziridino)alkoxymethanes *(2)* can be prepared by reaction of dichloromethyl methyl ether with aziridine in a suspension of NaOH in ether. Examples: *(2)*, R = CH_3, R^1 = H, 70% yield; C_2H_5, H, 50%; isopentyl, H, 82%; CH_3, CH_3, 57%. Compounds *(2)* are stable liquids exhibiting a less pronounced tendency to polymerize than *(1)*. Reaction of aziridine with chloroform-$NaOCH_3$ affords a mixture of tris(aziridino)methane, bis-



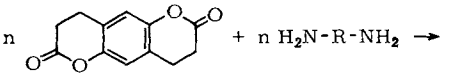
(1)



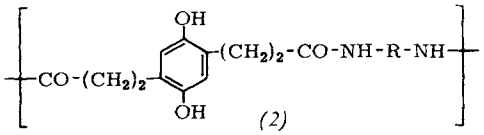
(2)

(aziridino)methoxymethane, and aziridinodimethoxymethane (25, 29, 12%). / Liebigs Ann. Chem. *725*, 15 (1969) / —Ma. [Rd 91 IE]

Redox polyamides *(2)* have been synthesized by *N. Nakabayashi* and *H. G. Cassidy* by condensation of the bislactone *(1)* with diamines such as hexamethylenediamine, piperazine, 4-aminoethylpiperidine, or 1,3-bis(4-piperidinyl)propane. The lactone function protects the OH groups until the onset



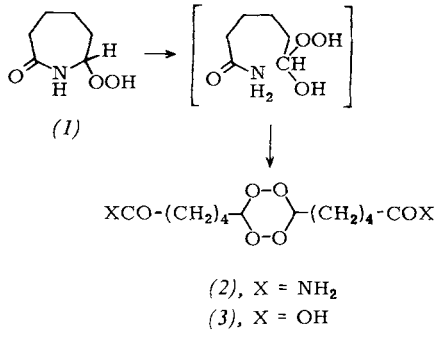
(1)



(2)

of polymerization, whereupon free hydroquinone hydroxyl groups appear. The polymer formed is oxidizable. / J. Polymer Sci. *7*, A-1, No. 5, 1275 (1969) / —Ma. [Rd 93 IE]

1,2,4,5-Tetroxane derivatives from ε-caprolactam hydroperoxide *(1)* have been obtained by *E. Höft, A. Rieche,* and *W. Schön.* Rapid treatment of *(1)* with 70—80% H_2SO_4 at room temperature and dilution with water leads to 3,6-bis-(carbamoylbutyl)-1,2,4,5-tetroxane *(2)*, m.p. 213—215 °C, in 88% yield. Reaction of *(2)* with hot 10% H_2SO_4 gives the dicarboxylic acid *(3)*, which can be converted into esters and



(1)

(2), X = NH_2
(3), X = OH

amides *via* the dichloride. The tetroxanes do not explode on impact or on overheating. They are suitable for use as polymerization initiators. / Liebigs Ann. Chem. *725*, 241 (1969) / —Ma. [Rd 92 IE]

The rotational isomerism of *m*-halogenobenzaldehydes has been studied by *G. A. Crowder* and *F. Northam* on the basis of the IR spectra. In the pure liquid compounds, the *cis*-O- and *trans*-O-isomers are present alongside each other; in the solid state, the chloro and bromo compound are present only as the lower-energy *cis*-O-isomer. *m*-Iodobenzaldehyde exists as the *trans*-O-isomer in the solid state; in the liquid state the energy difference between the rotamers is low. The greater stability of the *cis*-O-form of the chloro and bromo compounds is attributed to the inductive effect of the halogen: the H atom lying between the substituents carries a partial positive charge, thus leading to stabilization of the *cis*-O-form. / J. chem. Physics *50*, 4865 (1969) / —Hz. [Rd 94 IE]

The structure of B_2Cl_4 in the gas phase has been determined by *R. R. Ryan* and *K. Hedberg* by electron diffraction. In contrast to the solid state, in which the molecule is planar, the two BCl_2 planes are perpendicular to each other at equilibrium in the gas phase (symmetry D_{2d}). Structural data (at 251 °K): B—Cl = 1.750 Å; B—B = 1.702 Å; Cl—B—Cl = 118.65 °. Comparison of the diffraction maxima corresponding to the interatomic distances, which change on internal rotation about the B—B axis, with calculated values yielded a potential threshold $V_0 = 1.85$ kcal/mole for internal rotation according to the equation

$$V = {}^1/_2\, V_0\,(1 - \cos 2\Theta)$$

J. chem. Physics *50*, 4986 (1969) / —Hz. [Rd 95 IE]

Formation and reactions of the ozonide ion in aqueous alkaline H_2O_2 have been studied by *V. R. Landi* and *L. J. Heidt* by flash photolysis. The O_3^- ion is recognized by an absorption maximum at 430 nm. In all cases the O_3^- absorption decayed by a first order process; the rate constant of the decay increases with the concentration of H_2O_2 and decreases with the concentration of OH^- and dissolved O_2. During the decay of O_3^- a relatively long-lived intermediate is formed, which was identified as ozone. The following reactions take place:

$$O_3^- = O_2 + O^- \quad k = (2.81 \pm 0.14) \times 10^3\ \mathrm{sec}^{-1}$$
$$O_2 + O^- = O_3^- \ (k_2) \quad k_2/k_3 = 3.6 \pm 0.3$$
$$O^- + HO_2^- = O_2^- + OH^- \ (k_3)$$
$$O_3^- + O_2^- + H_2O = O_3 + HO_2^- + OH^-$$

The increased stability of O_3^- at higher NaOH concentration is rationalized in terms of formation of the ion pair NaO_3, an equilibrium constant of 2.24±0.11 $mole^{-1}$ having been determined for this process. / J. Physic. Chem. *73*, 2361 (1969) / —Hz. [Rd 96 IE]

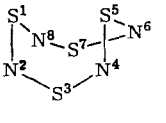
The solubility of Al_2O_3 in rutile has been studied at 1200 to 1426 °C on the basis of changes in the lattice constant *c* by *R. A. Slepetys* and *P. A. Vaughan.* The solubility increased with the temperature of annealing from 0.62 wt.-% Al_2O_3 at 1200 °C to 1.97% at 1426 °C. At temperatures below 1240 °C the dissolved phase in equilibrium is corundum and above this temperature it is Al_2TiO_5. The solubility of Al_2O_3 also increased on addition of Nb_2O_5. The density of a sample of rutile annealed at 1426 °C and containing 1.6% Al_2O_3 was 4.199 g cm^{-3} (pure rutile: 4.202 g cm^{-3}). These data are in accord with a solution model in which Al^{3+} and O^{2-} are incorporated into rutile lattice sites in the ratio of 1 : 2 and the excess of Al^{3+} occupy interstitial sites. Values of the enthalpy of solution of 35 kcal $mole^{-1}$ for Al_2TiO_5 and 100 kcal $mole^{-1}$ for Al_2O_3 were calculated from the temperature dependence of the solubility. The enthalpy of formation of Al_2TiO_5 in the temperature range around 1240 °C is thus calculated as —599 kcal $mole^{-1}$. / J. physic. Chem. *73*, 2156 (1969) / —Hz. [Rd 97 IE]

The vapor pressure and the crystal structure of metallic curium have been investigated by *P. K. Smith, W. H. Hale,* and *M. C. Thompson.* In the temperature range 1179 to 2068 °K and at pressures of 10^{-7} to 10^{-1} torr the vapor pressure equation

$$^{10}\log P\,(\mathrm{atm}) = (4.74 \pm 0.37) - (18060 \pm 590)/T\,(^\circ\mathrm{K})$$

was determined by an effusion method. The boiling point extrapolated to atmospheric pressure is 3540 °K. A hitherto unknown form of the metal having a face-centered cubic structure, the lattice constants 4.382 Å, and a density of 19.26 g cm^{-3} was identified. Comparison of these data with those found for related metals indicated that curium has a valence of 4 in this form. The entropy of melting of Cm is low (no figure can be given); this is a consequence of the relatively high entropy of solid Cm which contains contributions from transformations of several electronic configurations ($5f^6\ 6d^2\ 7s^3$ and $5f^7\ 6d\ 7s^2$). / J. chem. Physics *50*, 5066 (1969) / —Hz. [Rd 98 IE]

The vibrational spectra of S_4N_4 and S_2N_2 have been studied by *J. Bragin* and *M. V. Evans.* All the frequencies found in the case of S_4N_4 *(1)* could be assigned; the molecule has a cradle-like structure with the following bond lengths (in Å): S^1N^2 = 1.62; S^1S^5 = 2.58; S^1S^3 = 2.69, and the angles $N^2S^1N^8$ = 105 °; $S^1N^2S^3$ = 113 °; $S^1S^5N^4$ = 90 °. The four nitrogen



(1)

atoms form a plane. The calculated force constants show that repulsions between non-bonded atoms play a large role in S_4N_4. A planar rhomboidal structure with alternate S and N atoms is suggested for S_2N_2. Raman-active S—N frequency

of the class B_1g is not available for calculation of force constants in the case of S_2N_2 since the substance is too unstable to furnish interpretable spectra. / J. chem. Physics *51*, 268 (1969) / —Hz. [Rd 99 IE]

The electrical conductivity of CuCl at high pressure, as determined for tablets at 370—670 °K and 10—55 kbar is reported by *R. S. Bradley, D. C. Munroe,* and *P. N. Spencer.* A plot of the logarithm of the conductivity against $1/T$ at constant pressure is a straight line which changes its slope at 220 ± 20 °C. The slope, which can be regarded as a measure of the activation energy of the conduction process, falls in the low temperature range and rises in the high temperature region with increasing pressure, from which it may be concluded that electronic conduction predominates at lower temperatures and ionic conduction at higher temperatures. Doping with $CdCl_2$ up to 1 mole-% has little effect on the conductivity; doping with $CuCl_2$, on the other hand, causes a considerable increase in the conductivity; at higher pressures (40 kbar) electronic conductivity predominates in the whole range of temperatures investigated. Similar studies were carried out with CuCN, AgCN, AuCN. / Trans. Faraday Soc. *65*, 1912, 1920 (1969) / —Hz. [Rd 100 IE]

Solvent effects in the fluorescence and phosphorescence of indole are discussed by *C. M. Chopin* and *J. H. Wharton.* The relative quantum yields for fluorescence and phosphorescence change considerably on going from nonpolar to polar solvents, without any corresponding changes becoming apparent in the absorption spectrum. The authors assume, deviating from earlier interpretations, that isomerization from the first excited singlet state of indole to the corresponding state of 2*H*-indole can take place relatively easily; the triplet states of the two molecules also lie at very similar energies. Varying solvent stabilization of the excited states then affords a ready explanation of the observed anomalies in the emission spectra. / Chem. Physics Letters *3*, 552 (1969) / —Hz. [Rd 101 IE]

BOOK REVIEWS

Electrochemische Stromerzeugung (Electrochemical Production of Current). By *F. von Sturm.* Vol. 5 of "Chemische Taschenbücher", edited by *W. Foerst* and *H. Grünewald.* Verlag Chemie GmbH, Weinheim/Bergstrasse 1969. 1st Edit., ix + 189 pp., 83 illustrations, paper DM. 16.—.

The direct conversion of chemical into electrical energy has aroused much interest in the last decade because of the manifold requirements of our present technology and civilization. Although the thermodynamic and technical advantages of this type of energy production have been general knowledge for a very long time, there are still great difficulties preventing its realization in an economically rational manner. This has stimulated research into the use of new methods intended to supplement the classical established systems for conversion of electrochemical energy or to replace them by more efficient systems.

The pocketbook under review gives an excellent introduction to this type of problem. It begins with a brief sketch of the mode of action, construction, and limitations of classical primary and secondary batteries; this section also treats modern, alternative systems for such purposes. The main weight, however, is placed on the problems of fuel cells (about 2/3 of the text); the author attempts to delineate the trend of their development, placing the main emphasis on successful methods but without forgetting interesting sidelines even when there is no present prospect of their realization.

The presentation is clear and stimulating, and this well written introduction can be very warmly recommended.

H. Gerischer [NB 838 IE]

Statistische Elektrizität als Gefahr (The Dangers of Static Electricity). By *K. Haase.* Verlag Chemie GmbH., Weinheim/Bergstr. 1967. 1st Edit., 124 pp., 21 illustrations, DM 14.—.

Most of us have at one time or another picked up a static charge from a modern floor-covering, and were unpleasantly surprised by the resulting powerful sparks. Some of us may also have tried to use this phenomenon to ignite a gas burner or perhaps ether, and have found that this technique works all too readily.

Static may be encountered in industry with transmission belts and with spinning machines. Pneumatically conveyed materials can collect a high charge, as can insulating dusts on drying and unloading. Static electricity also builds up whenever insulating liquids or gases leave grounded equipment. It is therefore laudable that *K. Haase* should have written this readily understandable book on the dangers of static, a book that will be welcomed especially by process engineers and by those concerned with the design of new production plant.

The first section, occupying about a third of the book, describes the physical principles: electrostatics, charging up by charge separation, physics of the ignition of explosive mixtures. The second section deals with measurement techniques, including some specific methods of measurement for floors, shoe soles, and drive belts. In the last two sections the author discusses the ways of eliminating static electricity as a source of danger. This part is illustrated by 19 practical examples. The book ends with a bibliography, a formula index, and an alphabetical index.

K. J. Euler [NB 817 IE]

Dreiringe mit zwei Heteroatomen. Oxaziridine – Diaziridine – Cyclische Diazoverbindungen (Three-membered Rings containing Two Hetero Atoms. Oxaziridines, Diaziridines, Cyclic Diazo Compounds). By *E. Schmitz.* Vol. 9 in the series "Organische Chemie in Einzeldarstellungen". Springer-Verlag, Berlin-Heidelberg-New York 1967. 1st Edit., xii + 179 pp., 5 illustr., bound DM 58.— / $ 14.50.

Since three-membered rings containing two hetero atoms were first synthesized in the 1950's, this monograph treats a very young area of organic chemistry, one, by the way, to whose rapid development the author has himself contributed decisive material. It is true that nitrones, hydrazones, diazomethane, and certain peroxides were earlier formulated as three-membered ring compounds, but all such structures were finally abandoned in favor of acyclic ones.

Each chapter is developed in accord with the historical course of discovery of its three-membered ring system. Treatment begins with the oxaziridines, the proof of whose structure was so important because, after a whole series of faulty interpretations, this provided the first certain occurrence of a three-membered hetero ring system. Oxaziridines are among the strongest organic oxidizing agents although they are themselves oxidized by peracids, a reaction from which an elegant synthesis of nitrosoalkanes in good yield has been developed.

This section is followed by one on diaziridines, whose ready accessibility and unusually varied modes of reaction do not merely make them interesting to the preparative organic chemist but have attracted general attention as having been developed in several directions for industrial production of hydrazine. The book closes with a description of diazirines, first prepared in 1960 and whose parent compound, cyclodiazomethane, was first obtained by *E. Schmitz* and *R. Ohme*. Reading this chapter, which contains a wealth of preparative and theoretical aspects (concerning, for example, the thermal decomposition or ring expansion) gives the impression also that here we are still quite at the beginning of promising developments. The theoretician will be particularly interested in a detailed analysis of the electron configurations and transitions of diazirines. The clarity of the writing and the intelligibility of this book are very welcome; it deals with the literature up to the middle of 1966; and it contains many UV, IR, and NMR spectroscopic data, as well as tables giving yields for most of the three-membered ring systems synthesized.

This book can be highly recommended and will doubtless take an important place in the library of the organic chemist.

J. Gosselck [NB 833 IE]

Steroid Reaction Mechanism. By *D. N. Kirk* and *M. P. Hartshorn*. Vol. 7 in the series "Reaction Mechanism in Organic Chemistry". Elsevier Publishing Company, Amsterdam-London-New York 1968. 1st Edit., xii + 474 pp., 57 illustrations, 31 tables, bound, Dfl. 85.—.

This book is a very useful adjunct to the well-known steroid monographs, *e.g. Fieser* and *Fieser*'s "Steroids" or *Djerassi*'s "Steroid Reactions".

After an introduction to conformational analysis a total of eleven chapters provide a comprehensive review of the manifold steroid reactions of present knowledge from the viewpoint of reaction mechanism, namely: 1, Steroids, Reaction Mechanisms and Conformational Analysis; 2, Reactions of Alcohols and Halides; 3, Steroid Olefins; 4, Steroid Ketones; 5, Solvolytic Reactions and Rearrangements of Steroid Derivatives; 6, Steroid Amines; 7, Reactions of Derivatives of Steroid Ketones; 8, Rearrangements of Epoxides; 9, Rearrangements involving Functional Groups; 10, Functionalization of Non-Activated Carbon Atoms; 11, Photochemical Reactions.

In addition to *ca.* 1300 references inclusive up to 1967, there is an appendix containing supplementary literature up to 1968. An alphabetic index of functional groups provides for rapid recovery of material on a desired subject.

The clear text, instructive formulas, and intelligible tables make understanding of the material easy even for the reader who is not familiar with the field. Since steroid examples are didactically excellent for treatment of much mechanistic organic chemistry, this book can be recommended also to the more advanced student. With few exceptions, *e.g.* Birch reduction of aromatic compounds, the reader will obtain an excellent and almost complete survey of the present state of steroid chemistry. The book fills a real gap; its publication is welcome and it is to be hoped that it attains wide circulation amongst those interested in this area.

R. Wiechert [NB 832 IE]

Rodd's Chemistry of Carbon Compounds, Vol. II: Alicyclic Compounds, Part C: Polycyclic Compounds Excluding Steroids. Edited by *S. Coffey*. Elsevier Publishing Company, Amsterdam-London-New York 1969. 2nd Edit., xvi, 481 pp., 155 figures, 64 tables, bound Dfl. 90.—[1].

The compilers of the new edition of Rodd's Chemistry of Carbon Compounds were faced with the problem of presenting the subject matter, which has grown immensely since the first edition was published in 1953, as concisely and as clearly as possible in the new edition. This problem has been brilliantly solved, though Volume II has unavoidably expanded from its original two parts to four. The present Part C corresponds roughly to the earlier part B, but no longer contains the steroids or the monocyclic and acyclic terpenoids. This is regrettable, since chemists working in the isoprenoid field will no longer have available to them a single reference book that covers the whole field.

Each of the six chapters begins with a brief discussion of the nomenclature of the class of compounds in question. This is followed by descriptions of general synthetic routes and occurrence, and sometimes the proof of the structure in the case of natural products. The individual substances are then discussed in the order hydrocarbons, alcohols, ketones, acids, *etc.* The literature is taken into account up to the beginning of 1966, and in some cases even up to 1968. The extended formulas are much better than in the first edition. A very welcome addition to the chapter on bicyclic monoterpenes is a section on the absolute configurations of these compounds. The book begins with the description of polycarbocyclic systems with separate rings and spiro compounds. This is followed by condensed cyclic systems and bridged ring compounds. The bicyclic monoterpenes of the thujane, carane, and pinane groups and the norbornane system are discussed at some length. Rapid development in the sesquiterpenoid field has entailed expansion of this chapter by almost 100% in relation to the first edition. A similar situation is found in the final chapter on di-, sester-, and triterpenoids. A four-page section on physical methods for the determination of the structure and configuration of natural products must necessarily be incomplete. A careful examination of this work will convince any reader that the best possible solution to the problem of a modern reference book has been found.

The volume can be wholeheartedly recommended, and should find a place in every library. *E. Klein* [NB 825 IE]

[1] Cf. Angew. Chem. *79*, 912 (1967); Angew. Chem. internat. Edit. *6*, 894 (1967).

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 4 50 75, Telex 46 1855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors**: *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 11
NOVEMBER 1969
PAGES 781–932

The Conservation of Orbital Symmetry [***]

By R. B. Woodward [*] and Roald Hoffmann [**]

1. Introduction

Of the various ways in which the phenomena of chemical bonding have been treated from the theoretical point of view, the molecular orbital method may fairly be deemed to have been the most fruitful in the hands of the organic chemist, and most adaptable to his needs. None the less, the method, with a few conspicuous exceptions, has been used mainly in the study of the static properties of molecules – in ground and excited states – and only rarely have its potentialities been explored in relation to reacting systems.

In 1965, in a series of preliminary communications [1–3], we laid down some fundamental bases for the theoretical treatment of all concerted reactions. The history of the genesis of these ideas has been described elsewhere [4]. The basic principle enunciated was that reactions occur readily when there is congruence between orbital symmetry characteristics of reactants and products, and only with difficulty when that congruence does not obtain – or to put it more succinctly, *orbital symmetry is conserved in concerted reactions.* This principle has met with widespread interest; the applications made of it, the tests which it has survived, and the corollary predictions which have been verified are already impressive. In this paper we develop our views at some length, survey some of the developments – in our hands and those of others – of the three years just past, and make some new projections.

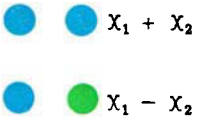
2. Orbitals and Bonding

It is worth while to review the elementary aspects of the molecular orbital theory of bonding [5]. Molecular orbitals are constructed as combinations of atomic orbitals, and are then populated by electron pairs. When two equivalent atomic orbitals, χ_1 and χ_2, combine, they always yield a bonding combination and a corresponding antibonding orbital *(1)*.



(1)

The bonding combination is characterized by positive overlap, and by concentration of electron density in the region between the nuclei. By contrast, the antibonding combination exhibits negative overlap, and a nodal surface in the region between the nuclei. When χ_1 and χ_2 are *s* orbitals, the bonding combination is $\chi_1+\chi_2$, and the antibonding one $\chi_1-\chi_2$.



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[***] This memoir will also be published as a separate brochure, copies of which can be ordered from Verlag Chemie GmbH, D-694 Weinheim, Postfach 129/149 (Germany), Academic Press Inc., 111 Fifth Avenue, New York, N.Y. 10003 (USA), or Academic Press Inc. Ltd., Berkeley Square House, Berkeley Square, London W. 1 (England), at a price of *ca.* DM 16.– or $ 4.40. A German version is also available from Verlag Chemie GmbH.

[1] *R. B. Woodward* and *Roald Hoffmann*, J. Amer. chem. Soc. *87*, 395 (1965).

[2] *Roald Hoffmann* and *R. B. Woodward*, J. Amer. chem. Soc. *87*, 2046 (1965).

[3] *R. B. Woodward* and *Roald Hoffmann*, J. Amer. chem. Soc. *87*, 2511 (1965).

[4] *R. B. Woodward:* Aromaticity. Special Publication No. 21. The Chemical Society, London 1967, p. 217.

[5] In addition to the classical text by *C. A. Coulson* (Valence. 2nd ed., Oxford University Press, London 1961), we recommend: *C. A. Coulson* and *E. T. Stewart* in *S. Patai:* The Chemistry of Alkenes. Wiley-Interscience, New York 1964, *E. Heilbronner* and *H. Bock:* Das HMO-Modell und seine Anwendung. Verlag Chemie, Weinheim 1968, and *R. S. Mulliken*, Science *157*, 13 (1967); Angew. Chem. *79*, 541 (1967).

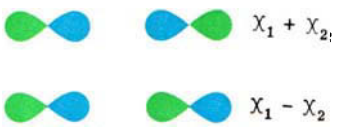
When χ_1 and χ_2 are p orbitals interacting in a σ manner, and oriented as shown in *(2)*



(2)

Throughout this paper, the phases of wave-functions are color-coded: positive = blue, negative = green. When phase relationships are not relevant, the orbitals are presented in solid gray.

the bonding combination is again $\chi_1+\chi_2$ and the antibonding combination $\chi_1-\chi_2$.



It is important to realize, however, that were the basis orbitals initially arbitrarily oriented in some other



(3)

fashion, such as *(3)*, then, since $\chi_2=-\chi_2$, the bonding combination would be $\chi_1-\chi_2'$, and the antibonding one $\chi_1+\chi_2'$. It should also be kept in mind that multiplying an entire wave function by -1 does not affect its energy. Thus, overlap of minus with minus lobes is precisely equivalent to plus with plus lobes, and $-\chi_1-\chi_2$ is the *same* bonding orbital as $\chi_1+\chi_2$.

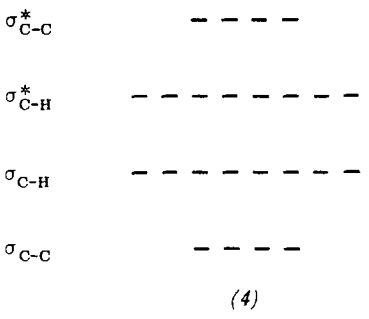


The description of σ bonds in hydrocarbons is simple. Each formal chemical bond engenders a σ and a σ^* orbital. The C–H and C–C cases are:



The molecular orbitals are represented in our drawings as the overlap of two hybrids of unspecified hybridization. It should be emphasized that this is only intended as an artistic mnemonic device: the only essential features of a σ orbital are that it is approximately cylindrically symmetrical around the bond axis, that it concentrates electron density in the region between the nuclei, and that there is no nodal plane between the atoms.

Our simple picture of bonding in, say, cyclobutane, shows four C–C σ levels, and eight C–H σ levels, each with a matching σ^* level *(4)*. The carbon 1*s* orbitals are not considered. Each of the σ levels is occupied by

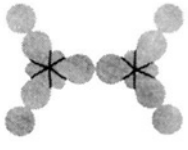


(4)

two electrons. Spectroscopic studies indicate that the gap between occupied and unoccupied levels must be of the order of 10 electron volts.

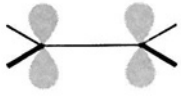
The orbitals we have constructed are semi-localized. They are delocalized over only two atoms. Such orbitals are satisfactory for an analysis of some properties of the molecules – those which depend on all of the occupied molecular orbitals: bond lengths, energies, dipole moments. They are not the proper molecular orbitals of the molecule. The latter are completely delocalized, subject to the full symmetry of the molecule. For a discussion of physical properties depending on one or two specific molecular orbitals, such as spectra or ionization, it is absolutely necessary to construct these equivalent delocalized orbitals. The mechanics of delocalization will be described in Section 3.

In addition to σ bonds, the molecules of organic chemistry contain delocalized π orbitals. Thus, the electronic structure of ethylene is described as follows: There are four σ C–H bonds and a σ C–C bond *(5)*. Each



(5)

generates a σ and a σ^* level, and five pairs of electrons are placed in the σ levels. There remain two electrons and two atomic p orbitals perpendicular to the plane of the molecule *(6)*. These combine to give π and π^* orbit-



(6)

als, differentiated by the absence or presence of a node between the atoms (Figure 1).

There are two independent symmetry operations which may be used to classify these orbitals; the mirror plane m, perpendicular to the molecular plane and bisecting the molecule, and the two-fold rotation axis C_2, passing through the center of the carbon-carbon bond. It should be noted carefully that the symmetry properties

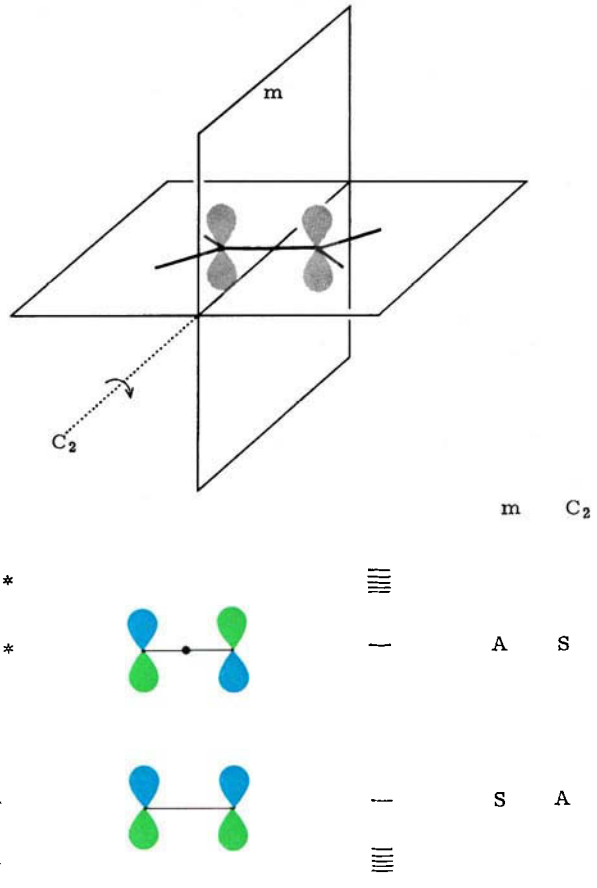


Figure 1. Molecular orbitals of ethylene and symmetry properties of the π and π^* orbitals. A = antisymmetric, S = symmetric. The horizontal bars indicate the relative orbital energies.

of the ethylene orbitals under each of the above operations are precisely opposite. Thus, the π orbital is symmetric (S) with respect to the mirror plane m, and antisymmetric (A) with respect to the rotation axis C_2.

The overlap between the two $2p_z$ orbitals is significantly less than that involved in σ interactions, and so the π bond is weaker than a σ bond, and the π and π^* levels are raised and lowered, respectively, from the sea of σ and σ^* levels (Figure 1).

The π molecular orbitals of the three-orbital allyl system are shown in Figure 2. Their nodal structure should be carefully noted. By virtue of their character as π orbitals, they all are antisymmetric under reflection in the plane of the allyl system. The lowest orbital, doubly occupied in the allyl cation, has no additional nodes. The middle, nonbonding orbital, which is singly occupied in the allyl radical, and doubly occupied in the anion, has a single nodal plane which precludes any contribution of the $2p$ orbital at the central carbon atom. The orbital of highest energy has two nodes.

The molecular orbitals of the four-orbital butadiene system are shown in Figure 3 for an *s-cis* arrange-

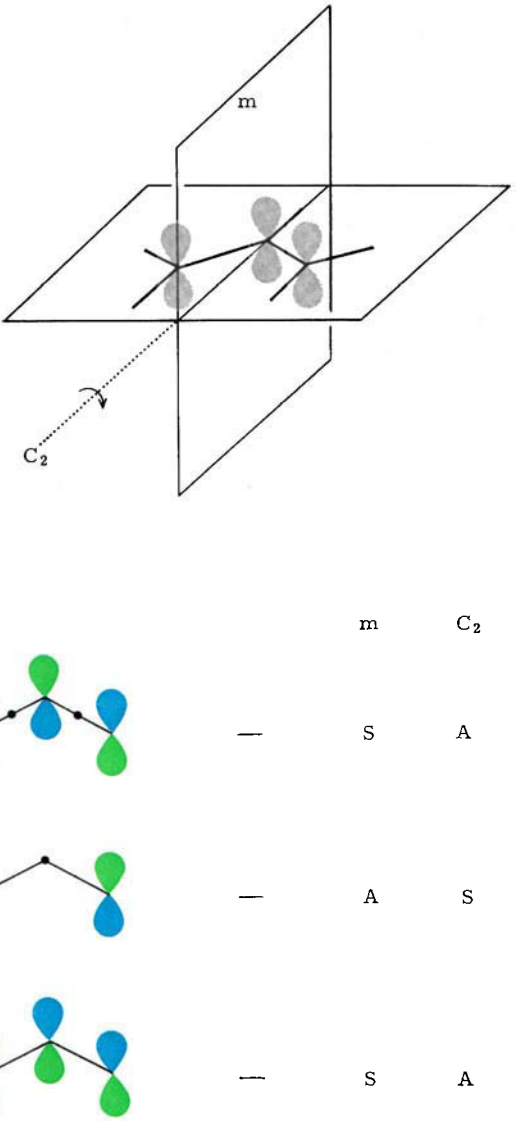
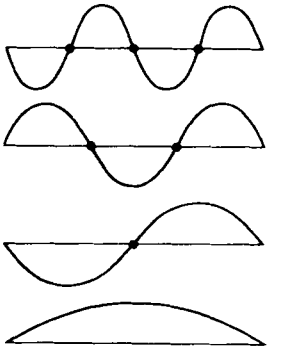


Figure 2. π molecular orbitals of the allyl system. A = antisymmetric, S = symmetric.

ment [6,7]. Note once again the nodal structure and the alternating symmetry properties. The correlation of higher energy with an increasing number of nodes is



(7)

[6] Throughout this paper molecular orbitals are symbolized in terms of the atomic orbitals whose interaction gives the actual molecular orbital; since we are in general interested only in nodal properties, we ignore the fact that the coefficients – and thus the relative sizes – of the resultant atomic orbital contributions are not all identical.

[7] The electronic structure of polyenes is perhaps the most highly developed branch of semi-empirical molecular orbital theory. A very good survey of the field is given in *L. Salem:* The Molecular Orbital Theory of Conjugated Systems. Benjamin, New York 1966. See also *A. Streitwieser:* Molecular Orbital Theory for Organic Chemists. Wiley, New York 1961.

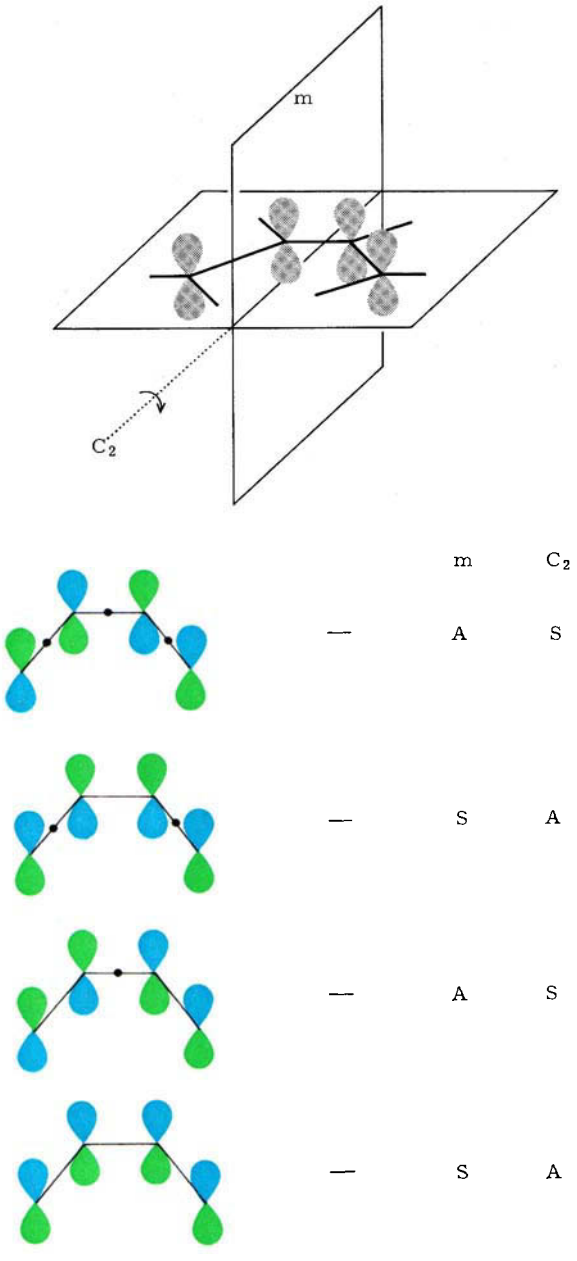


Figure 3. π molecular orbitals of *s-cis*-butadiene. A = antisymmetric, S = symmetric.

not an accident, but rather a general consequence of either classical or quantum mechanics. The envelopes of polyene orbitals coincide with the curve of the wave function of a particle in a one-dimensional box *(7)*. The lowest orbital has no nodes, the next higher one has one node, the next two, and so on until the highest orbital has the maximum number of nodes possible. The general expression for the k^{th} molecular orbital of a polyene or polyenyl system with n carbon atoms is

$$\Psi_k = \sum_{i=1}^{n} C_{ki}\,\Phi_i$$

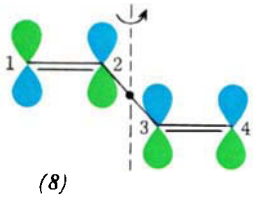
where the Φ_i are the atomic orbitals numbered consecutively from one end. The coefficients are given by the expression [7]

$$C_{ki} = \sqrt{\frac{2}{n+1}}\sin\frac{\pi ki}{n+1}$$

The orbitals alternate in symmetry with increasing energy.

If n is even, there are $n/2$ bonding π orbitals and $n/2$ antibonding. If n is odd, there are $(n-1)/2$ bonding, $(n-1)/2$ antibonding, and one nonbonding orbital.

A final point of much importance is that no molecular orbital may be at the same time symmetric and antisymmetric with respect to any existing molecular symmetry element. Thus, the orbital *(8)* is symmetric un-



(8)

der rotation by 180 ° if atoms 2 and 3 are viewed, but antisymmetric if 1 and 4 are considered; it is not an acceptable molecular orbital of butadiene.

3. Correlation Diagrams

The united atom-separated atoms diatomic correlation diagrams first drawn in the early nineteen-thirties by *Hund* and *Mulliken* have an important place in theoretical chemistry [8]. In constructing such a diagram, one imagined the process of two atoms approaching each other from infinity. The energy levels of the separated atoms were placed in approximate order of energy on one side of the diagram. One then imagined the approach of the atoms through the physically realistic molecular region into the physically impossible process of nuclear coalescence. The energy levels of the resulting united atom were once again known. They were placed on the other side of the diagram. One then proceeded to classify the initial separated and the final united atom orbitals with respect to the symmetry maintained throughout the hypothetical reaction. Levels of like symmetry were connected, paying due attention to the quantum mechanical noncrossing rule – that is, only levels of unlike symmetry are allowed to cross (Figure 4).

In this way, from the relatively well-known level structures of the separated atoms and the united atom valuable information was obtained about the level structure of the intermediate region corresponding to the molecule. It was this kind of diagram which provided a

[8] *F. Hund*, Z. Phys. *40*, 742 (1927); *42*, 93 (1927); *51*, 759 (1928); *R. S. Mulliken*, Phys. Rev. *32*, 186 (1928); Rev. Mod. Phys. *4*, 1 (1932). See also *G. Herzberg*: The Electronic Structure of Diatomic Molecules. 2nd edition, Van Nostrand, Princeton 1950.

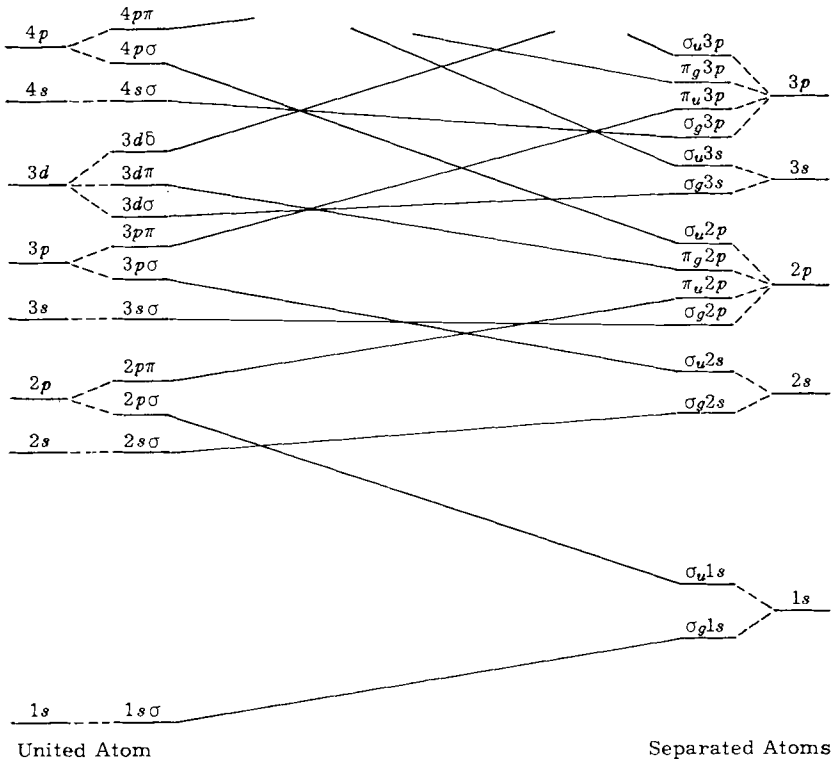


Figure 4. A typical atomic correlation diagram.

rationalization for the existence of the oxygen molecule as a ground-state triplet.

In an exactly analogous manner a correlation diagram may be drawn for a concerted reaction such as cycloaddition. On one side one writes down the approximately known energy levels of the reactants, on the other side those of the product. Assuming a certain geometry of approach one can classify levels on both sides with respect to the symmetry maintained throughout the approach, and then connect levels of like symmetry. Such a molecular correlation diagram yields valuable information about the intermediate region, which represents in this case the transition state for the reaction.

We would like to illustrate in some detail the construction of a molecular correlation diagram. The first example we choose is the maximum-symmetry approach of two ethylene molecules, leading to cyclobutane (Figure 5). As usual in theoretical discussions, maximum insight into the problem at hand is gained by simplifying the case as much as possible, while maintaining the essential physical features. In this instance we treat in the correlation diagram *only four* orbitals – the four π orbitals of the two ethylenes. In the course of the reaction these four π orbitals are transformed into four σ orbitals of cyclobutane. We may safely omit the C–H and the C–C σ bonds of the ethylene skeleton from the correlation diagram because, while they undergo hybridization changes in the course of the reaction, their number, their approximate positions in energy, and in particular their symmetry properties are unchanged.

The first step in the construction of a correlation diagram involves isolating the essential bonds and placing them at their approximate energy levels in reactants and products; the result is shown for the case at hand in Figure 6, in which the dashed horizontal line is the

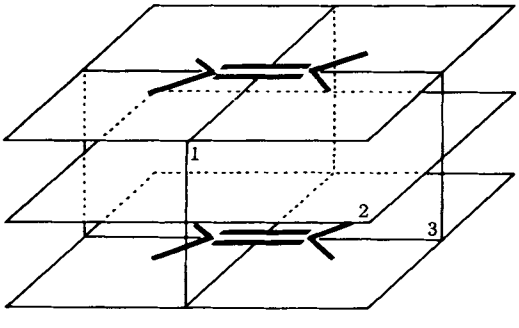


Figure 5. Parallel approach of two ethylene molecules.

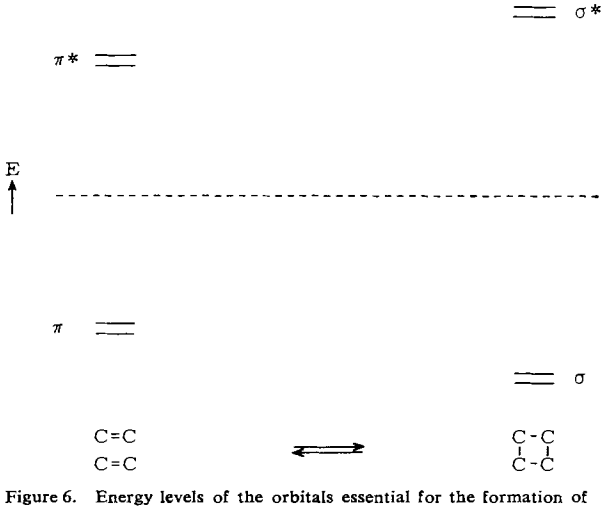
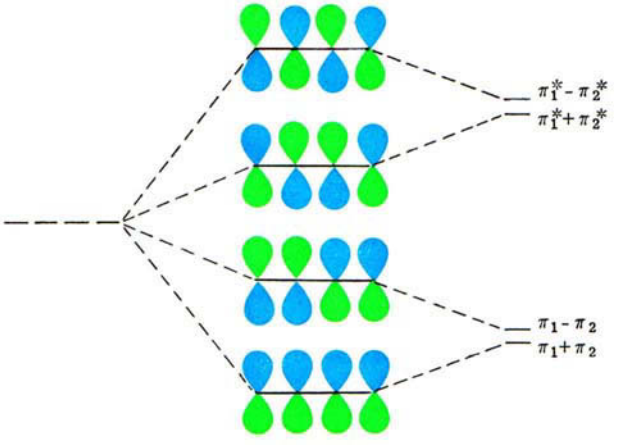


Figure 6. Energy levels of the orbitals essential for the formation of cyclobutane from two ethylene molecules in the geometry shown in Figure 5.

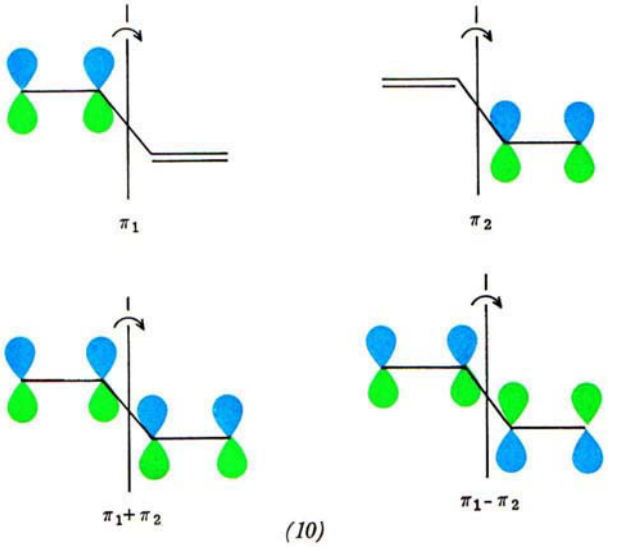
nonbonding level – approximately the energy of an electron in a free carbon 2*p* orbital. We have separated σ and σ^* by an energy greater than that between π and π^*; although there is little reason to question this assignment, it is important to emphasize that it is in no way essential to the subsequent argument. To assign an order of magnitude to the vertical energy scale we may take the distance between π and π^* as approximately 5 electron volts [7].

In the next step the proper molecular orbitals for the reactants and products are written down. A digression on constructing molecular orbitals for interacting systems is in order at this point. Consider an *s-trans*-butadiene. One way to derive the four molecular orbitals of butadiene is to allow all of the four atomic orbitals to interact as illustrated at left in *(9)*.



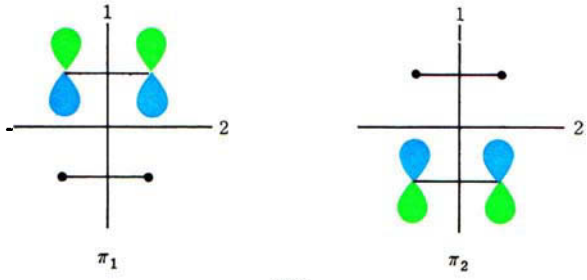
(9)

Yet another way is to view butadiene as arising from the interaction of two semi-localized double bonds. Consider the bonding π orbitals of the two ethylenes. While π_1 and π_2 are entirely satisfactory for a description of the isolated double bonds, they are not the proper combinations to use as molecular orbitals for butadiene. Molecular orbitals must be symmetric or antisymmetric with respect to any molecular symmetry element which may be present. In the case at hand the crucial symmetry operation is a 180° rotation around the two-fold axis. The obvious combinations to use, and ones which do satisfy the symmetry conditions, are $\pi_1 \pm \pi_2$ *(10)*. These, of course, turn out to be topologically identical with the two lowest-energy butadiene orbitals which were constructed by considering direct interaction of all four atomic orbitals.

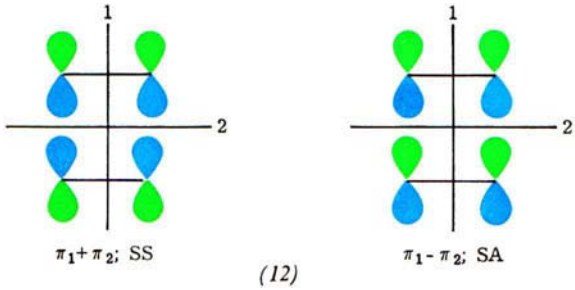


(10)

We are now prepared to treat the analogous problem of the molecular orbitals of two ethylenes approaching each other. Drawing orbital cross-sections in plane 3 (*cf.* Figure 5), diagram *(11)* represents localized π bonds of the two ethylenes. These are not the proper combinations to choose for a discussion of the orbitals of the complex of two ethylenes; they are not symmetric or antisymmetric under reflection in plane 2. Again the obvious combinations are $\pi_1+\pi_2$ and $\pi_1-\pi_2$ *(12)*.



(11)

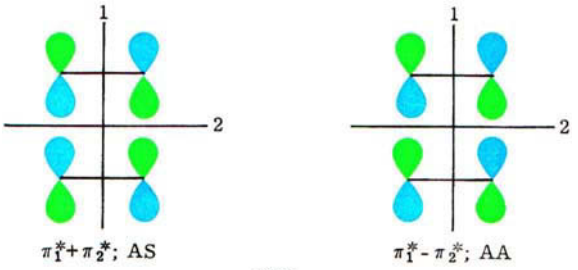


(12)

The first of these is symmetric with respect to reflection in both planes 1 and 2 (abbreviated as S_1S_2 or simply SS); the second is symmetric under reflection in plane 1, and antisymmetric under reflection in plane 2 (S_1A_2 or SA) [9]. Both orbitals, of course, are symmetric with respect to reflection in plane 3, and this trivial information need not be explicitly specified. At large separation between the ethylenes, $\pi_1+\pi_2$ and $\pi_1-\pi_2$ will be

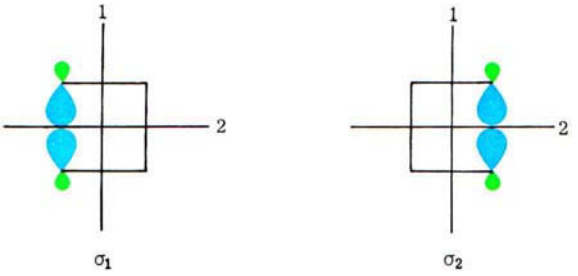
[9] We could, of course, label the levels with their proper symmetry designations, appropriate to the D_{2h} symmetry of the approach. We deliberately use the symmetric (S) and antisymmetric (A) labels since the nodal properties of the orbitals are then most clearly discernible.

degenerate, but at small separations $\pi_1+\pi_2$ will be at lower energy than $\pi_1-\pi_2$ since the former has fewer nodes. Similar combinations of antibonding molecular orbitals for the complex are shown in *(13)*.

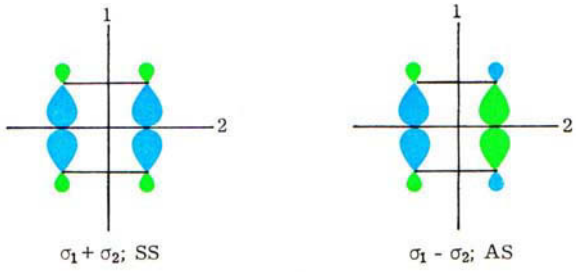


(13)

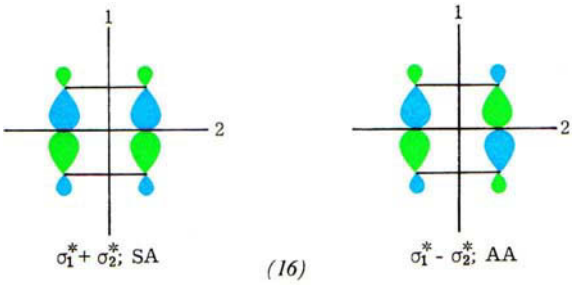
One must next analyze the situation in cyclobutane in an entirely analogous way. Consider the localized σ bonds *(14)*. Again these do not satisfy all the symmetry operations of the cyclobutane molecule, and one must take the two combinations $\sigma_1\pm\sigma_2$ *(15)*; a similar procedure must be followed for the antibonding σ^* orbitals *(16)*.



(14)



(15)



(16)

We are now equipped to examine the correlation of the orbitals of reactants with those of the product (Figure 7). The direction in which the various levels will move may be obtained without detailed calcula-

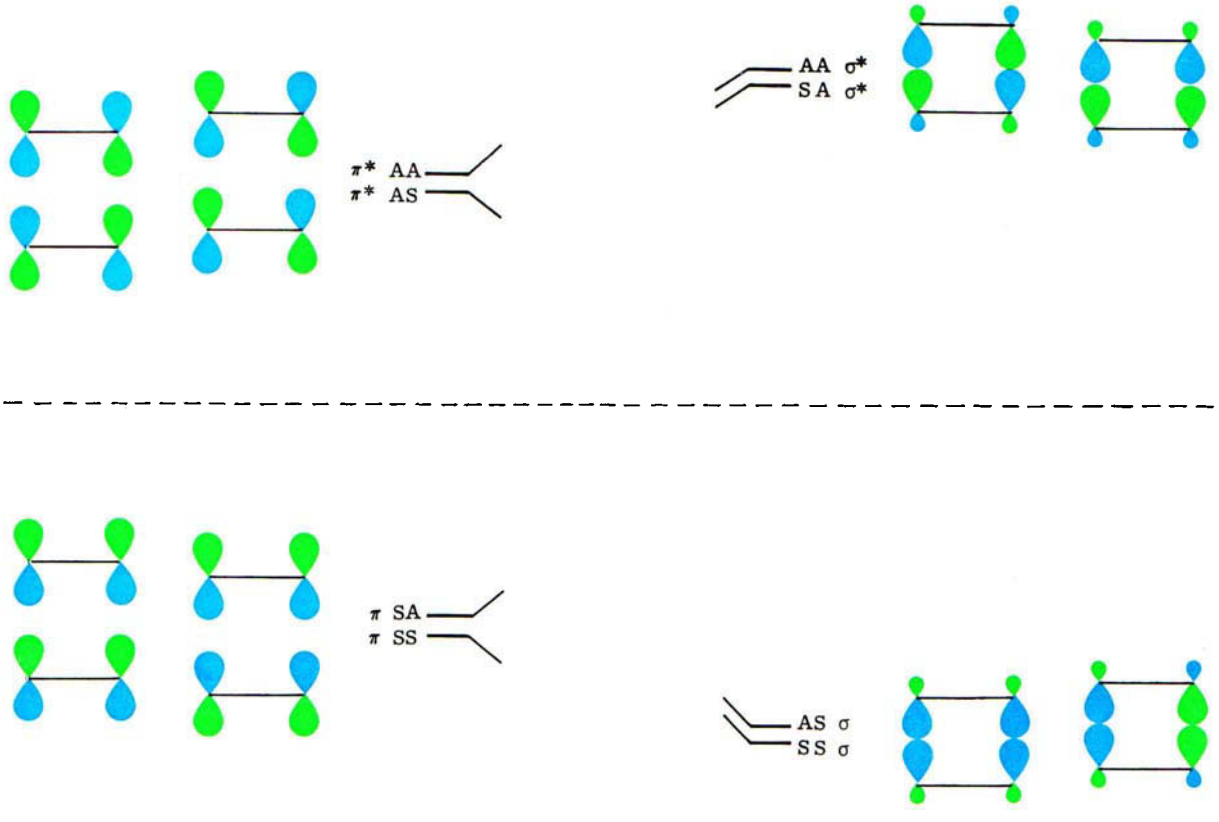


Figure 7. Initial displacements of orbital energy levels in the reaction: 2 ethylenes $\rightleftarrows$ cyclobutane.

tion, by examining in each case whether any level is bonding or antibonding along the reaction coordinate; in doing this one should keep in mind the definition of bonding or antibonding. Consider the two molecular orbitals for the hydrogen molecule, formed from two 1*s* orbitals (Figure 8). σ_g is bonding because electrons

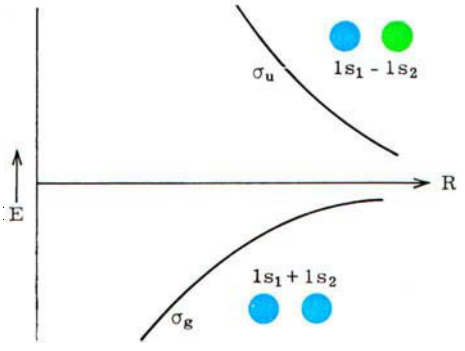


Figure 8. Formation of the bonding (σ_g) and antibonding (σ_u) molecular orbitals of the hydrogen molecule from two atomic 1*s* orbitals.

occupying it lie in the region between and are shared by the nuclei; σ_u is antibonding and at higher energy because the presence of a node between the nuclei isolates electrons populating the orbital in the regions of the individual terminal nuclei. There is another aspect of bonding or antibonding displayed in this schematic diagram: electrons placed in a bonding orbital bring the nuclei closer together (that is, for σ_g, $\partial E/\partial R > 0$), while electrons put into an antibonding orbital push the nuclei apart (that is, for σ_u, $\partial E/\partial R < 0$). Returning to the ethylene correlation diagram (Figure 7), we find that the lowest SS level of two ethylenes is bonding in the region of approach of the two molecules to each other and thus will be stabilized by interaction. The SA level has a node, and consequently is antibonding in the region of approach. At large distances the interaction is inconsequential, but as the distance between the reacting molecules diminishes, this orbital is destabilized and moves to higher energy. Similarly, the antibonding π^* AS orbital becomes bonding in the region of approach. It will thus be stabilized as the reaction proceeds, while the π^* AA orbital will be destabilized.

On the cyclobutane side both the σ levels, SS and AS, are bonding in the region where the cyclobutane is being pulled apart. Thus, they resist the motion – that is, they are destabilized along the reaction coordinate. On the other hand, the σ^* levels SA and AA are antibonding along the reaction coordinate and thus move to lower energy as the cyclobutane is pulled apart.

That these qualitative conclusions are correct may be seen from a completed correlation diagram in which levels of like symmetry are connected (Figure 9). The most obvious and striking feature of this diagram is the correlation of a bonding reactant level with an antibonding product level, and *vice versa*.

We now approach a central tenet of our treatment of concerted reactions. Clearly, *if orbital symmetry is to be conserved*, two ground-state ethylene molecules cannot

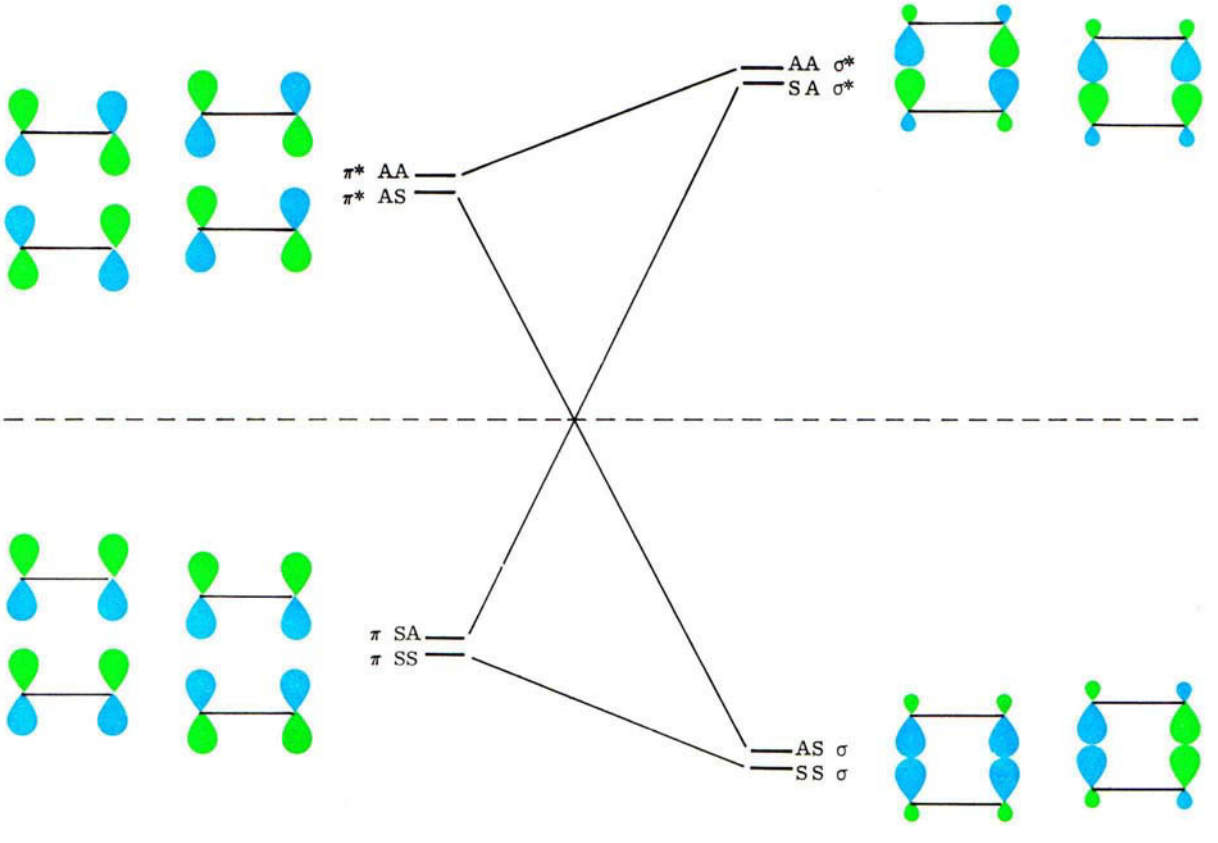


Figure 9. Complete correlation diagram for the formation of cyclobutane from two molecules of ethylene.

combine in a concerted reaction to give ground-state cyclobutane – nor can cyclobutane be decomposed in a concerted fashion to two ethylene molecules – through a transition state having the geometry assumed here. To put the matter in other words, there is a very large symmetry-imposed barrier to the reaction under discussion, in either direction. By the same token, there is no such symmetry-imposed barrier to the reaction of one molecule of ethylene with another, one of whose electrons has been promoted, say by photochemical excitation, to the lowest antibonding orbital. For these reasons we designate reactions of the first type *symmetry-forbidden*, and those of the second *symmetry-allowed.*

The matter may be further illuminated by inspection of the corresponding state diagram for the reaction (Figure 10). The ground state electron configuration of two ethylene molecules correlates with a very high-energy doubly excited state of cyclobutane; conversely the ground state of cyclobutane correlates with a doubly excited state of two ethylenes. Electron interaction

face combination of two ethylene molecules may be made by considering the energy required to raise two bonding electrons in the occupied bonding levels to the non-bonding level – perhaps 5 eV or about 115 kcal/mole.

The lowest excited state of two ethylenes, the configuration $(SS)^2(SA)^1(AS)^1$, correlates directly with the first excited state of cyclobutane. Consequently, there is no symmetry-imposed barrier to this transformation. This represents the course which is followed in many photochemical transformations. However, it should be emphasized that there are ambiguities in excited state reactions which do not exist in their simpler thermal counterparts. Thus, it may happen that the chemically reactive excited state is not that reached on initial excitation; in particular, singlet-triplet splittings for different excited states vary so widely that the symmetries of the lowest singlet and lowest triplet states may differ. Further, radiationless decay may be so efficient that the chemical changes subsequent to irradiation may be those of a vibrationally excited ground state. Finally,

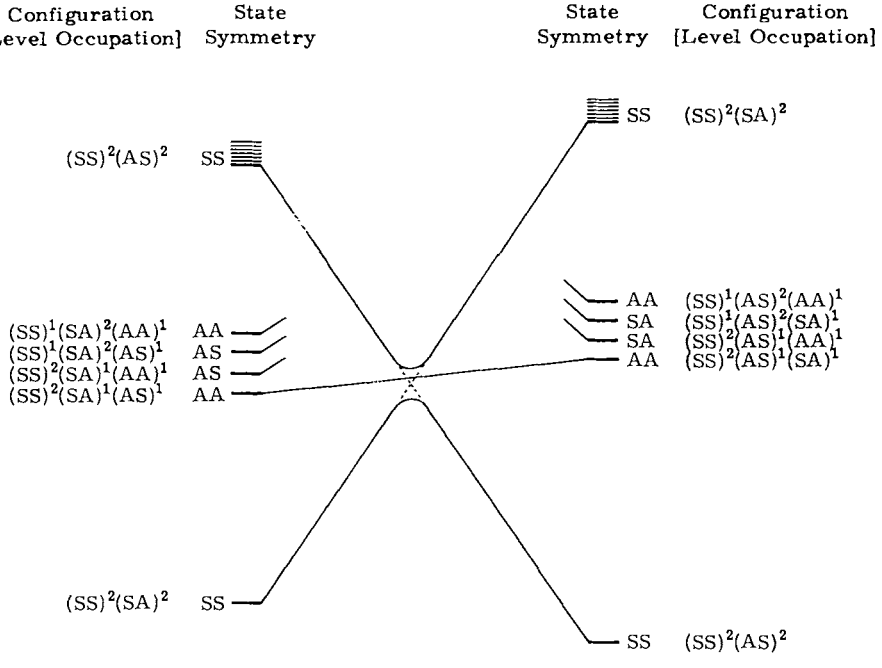


Figure 10. Electronic state diagram for the formation of cyclobutane from two molecules of ethylene. – Note that the symmetry of the states is obtained by multiplying the symmetry labels for each electron, following the rules [7]

$S \times S \longrightarrow S \longleftarrow A \times A$

$S \times A \longrightarrow A \longleftarrow A \times S$

Only singlet excited states are shown, and at this level of sophistication they should be regarded as degenerate in both reactants and products.

will prevent the resulting crossing, and force a correlation of ground state with ground state. But in the actual physical situation, the reaction still must pay the price in activation energy for the intended but avoided crossing. An order of magnitude estimate of the symmetry-imposed energy barrier to the concerted face-to-

the formation of a transition state for a given concerted reaction may be competitive with relaxation of the excited state component to an equilibrium geometry which renders the reaction geometrically impossible. It should be emphasized that none of these punctilios in any way vitiates the consequences of orbital symmetry

control. The principle of conservation of orbital symmetry remains applicable, *provided that the chemically reactive excited state is identified;* furthermore, the fact that the product state which correlates directly with the reactant state may lie higher in energy than the latter constitutes no special problem in orbital symmetry terms – though admittedly there is still much to be learned about the detailed physical nature of the processes accompanying the necessary energy cascade from electronically excited to ground states in such instances.

Many correlation diagrams differ sharply from that for the ethylene + ethylene reaction. Consider for example the prototype Diels-Alder reaction – the [4+2] cycloaddition of butadiene to ethylene. The most reasonable symmetric approach is characterized by a single plane of symmetry bisecting the two components (Figure 11).

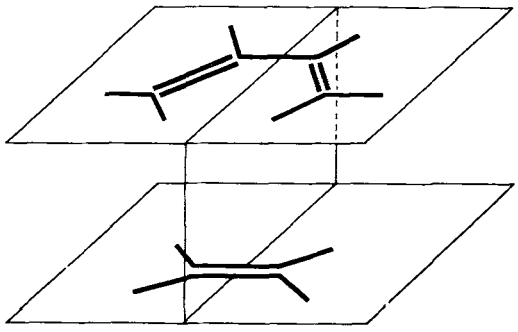


Figure 11. Symmetric approach of butadiene and ethylene in the Diels-Alder reaction.

The essential levels involved in the reaction are now six in number, and they are illustrated in the correlation diagram shown in Figure 12. The form of the four butadiene and two ethylene orbitals is self-evident. We have placed the ethylene π level between the two bonding diene orbitals, but the ordering is not consequential. On the product cyclohexene side note that one must construct delocalized σ bond combinations just as was done for cyclobutane.

The difference between this correlation diagram and that for the combination of two molecules of ethylene is striking. In this case every bonding level of reactants correlates with a bonding product level; there is no correlation which crosses the large energy gap between bonding and antibonding levels.

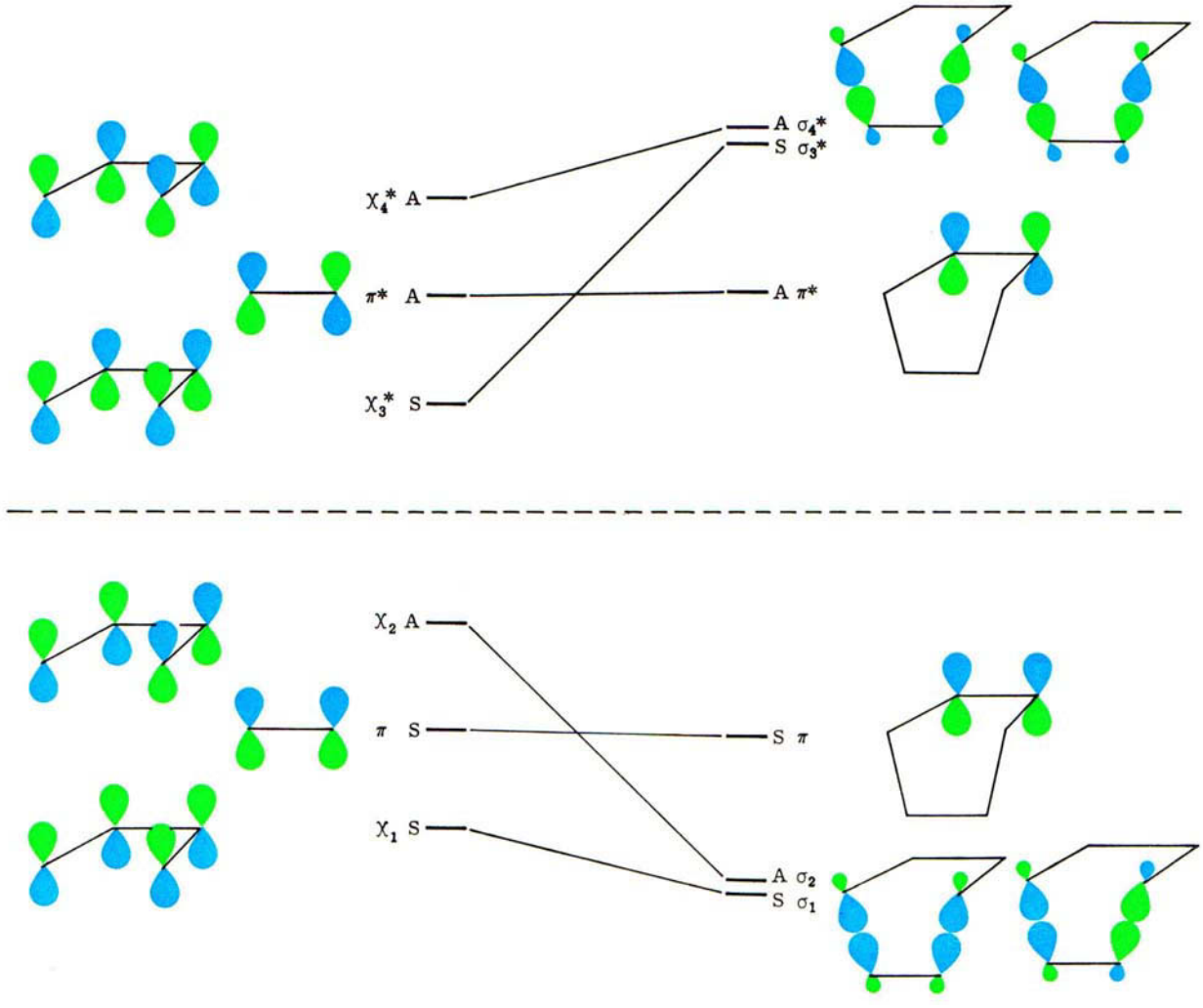


Figure 12. Correlation diagram for the Diels-Alder reaction of butadiene with ethylene.

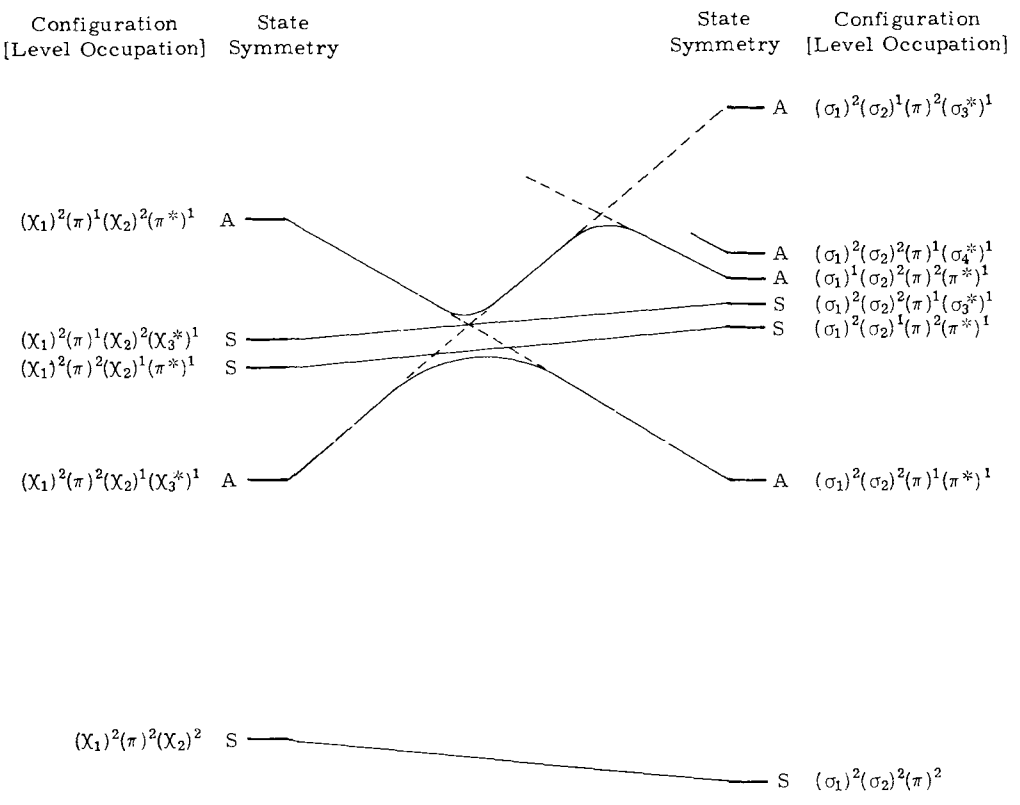
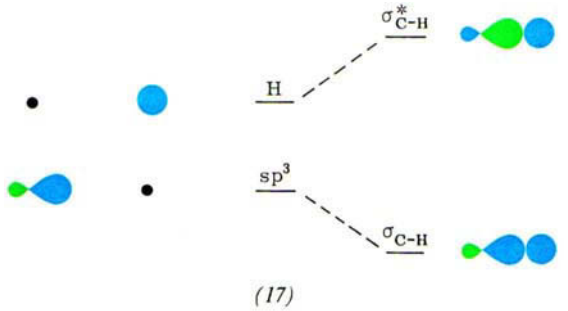


Figure 13. Electronic state diagram for the Diels-Alder reaction of butadiene with ethylene.

As before one may construct a state diagram (Figure 13). The ground state levels correlate directly, and the diagram implies that there is no activation energy at all for this thermal symmetry-allowed process. And indeed, *there is no symmetry-imposed barrier*, but of course there is an activation energy – experimentally found to approximate 20 kcal/mole – which arises from factors not simply related to orbital symmetry conservation; among them are energy changes accompanying rehybridization in the levels we have not included, and bond length extensions and contractions, as well as angle distortions.

The first excited state of the diene-ethylene complex does not correlate with the first excited state, $\pi \rightarrow \pi^*$, of cyclohexene. Consequently, in this case a symmetry-imposed barrier arises in the excited state process. These circumstances are perhaps most simply apprehended when it is realized that the first excited state is formed by promotion of an electron from an orbital decreasing in energy along the reaction coordinate to one increasing in energy.

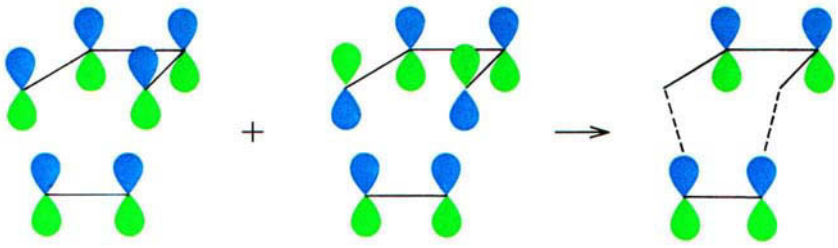
The physical correlations of some levels may seem non-intuitive, but in each case they are realistic, and can be understood if followed through carefully in detail. For instance, it may seem strange that an ethylene π level becomes a π level of the cyclohexene. To understand this relationship one must allow the ethylene π level to interact with the two other symmetric levels – the lowest occupied and lowest unoccupied diene levels. An important general rule of quantum mechanics is relevant here[10]: if two levels of unlike energy interact, that of the lower energy will mix into itself some of the higher-energy wave function in a bonding way, but the higher level will mix into itself some of the lower one in an antibonding way. If more than two levels interact, their mixing can be analyzed as a superposition of such pair-wise interactions. The application of this rule is illustrated here for the formation of a C–H σ bond from a carbon sp^3 hybrid and a hydrogen 1*s* orbital *(17)*. In the case of butadiene + ethylene we



(17)

find that the olefin π level mixes into itself χ_1 in an antibonding way and χ_3 in a bonding way *(18)*. The diene contributions cancel at C-1 and C-4 of the buta-

[10] The rule follows directly from perturbation theory and the correlation of higher energy with increasing number of nodes in a wave function.



(18)

diene, but reinforce at C-2 and C-3. Thus, in the transition state this orbital is essentially half in the one and half in the other of the reacting moieties.

If one considers further cases of the general cycloaddition reaction of an m π-electron system with an n π-electron system to form two new σ bonds, while maintaining a plane of symmetry, it becomes evident that there are only two types of correlation diagrams:

a) those similar to that of the Diels-Alder reaction, with no correlation of bonding and antibonding levels, and characterized as symmetry-allowed for ground states and symmetry-forbidden for excited states;

b) those similar to that for the ethylene + ethylene combination, which display bonding-antibonding correlations, and are consequently symmetry-forbidden for ground states and symmetry-allowed for excited states.

To derive a general rule, one may enumerate, say, bonding symmetric levels in reactants and products. If there are, for example, m π orbitals in a reactant, there will be $m/4$ symmetric bonding π orbitals if $m/2$ is even, or $(m+2)/4$ if $m/2$ is odd. That part of the product derived from this component will contain $(m-2)$ π orbitals, of which $m/4$ are symmetric bonding levels if $m/2$ is even, or $(m-2)/4$ if $m/2$ is odd. There are three possible cases (q_1 and q_2 are integers = 0, 1, 2 . . .):

Case	m	n	Total Symmetric Bonding π Levels	
			Before	After
1	$4q_1$	$4q_2$	q_1+q_2	q_1+q_2
2	$4q_1+2$	$4q_2$	q_1+q_2+1	q_1+q_2
3	$4q_1+2$	$4q_2+2$	q_1+q_2+2	q_1+q_2

Of the new bonding σ levels in the product, one is always symmetric; thus, for a thermal symmetry-allowed reaction, the total number of occupied symmetric π bonding levels in the reactants must exceed by one the number in the product; Case 2 satisfies this condition: for it,

$$m+n=4q_1+4q_2+2=4q+2.$$

Cases 1 and 3 necessarily lead to bonding-antibonding correlations; consequently, thermal reactions in which

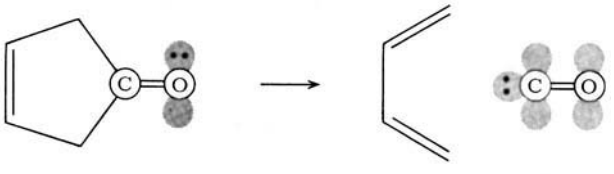
$$m+n=4q_1+4q_2 \text{ or } 4q_1+4q_2+4=4q$$

are symmetry-forbidden. In each case, of course, these rules are precisely reversed for reactions involving excited states. Further, it must be emphasized that these deductions apply only to cases in which the geometry of approach of the reacting molecules is that specified above; we shall demonstrate in the sequel that in some cases the same, and in others different, rules apply when the geometric relationships within the transition state are varied.

3.1. General Comments on the Construction of Correlation Diagrams

A crucial phase in the construction of a correlation diagram is the identification of pertinent σ and π levels and their delocalization to the full extent required by the transition state symmetry. The simplest procedure may be formulated as follows:

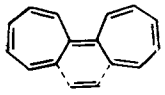
a) Identify all orbitals involved as σ, π, or n (nonbonded pair). Remember that for each σ and π level there will be corresponding σ* and π* levels; this is not the case for n orbitals. Thus, for the expulsion of carbon monoxide from cyclopentenone *(19)* the relevant orbitals are: in the cyclopentenone the C=C π and π* levels, two bonding C–C(O) σ levels and the corresponding σ* orbitals, and a lone pair on oxygen; in the products *(20)* and *(21)* the four diene π levels, two of which



(19) (20) (21)

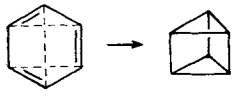
are bonding, a new CO bond and its π* counterpart, and a new nonbonding pair level on the carbon atom of the carbon monoxide. Left out of consideration as non-essential are another oxygen lone pair and the remaining C=O π bond. Note that there exists an auto-

matic check in that the number of levels of each symmetry type on the right-hand side of a correlation diagram must equal that on the left.



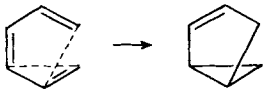
(22)

b) If a polyene system is present, the proper molecular orbitals of a polyene should be used. Thus, in the cycloaddition of a heptafulvalene *(22)*, one should consider the orbitals of a fourteen-membered polyene.



(23) (24)

For the cyclization of benzene *(23)* to prismane *(24)*, the proper orbitals on the left are those of benzene [*cf.* Section 6.4].



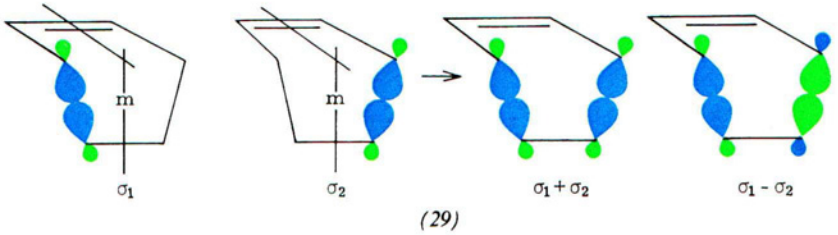
(25) (26)



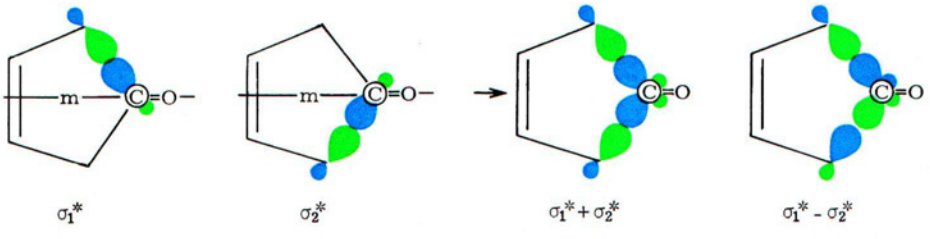
(27) (28)

bicyclo[2.2.0]hexene *(28)* must be treated as [4+2] and [2+2] cycloadditions respectively.

c) Mix all bonding σ orbitals which are not symmetric or antisymmetric with respect to every molecular symmetry element until they become so. For the vast majority of cases this process is one of identifying the symmetry-related orbitals, and forming their sums and differences. The procedure should then be repeated for σ* levels. As one example, consider the newly-formed σ bonds of a cyclohexene – the product of a [4+2] cycloaddition. The symmetry-related σ orbitals are



(29)

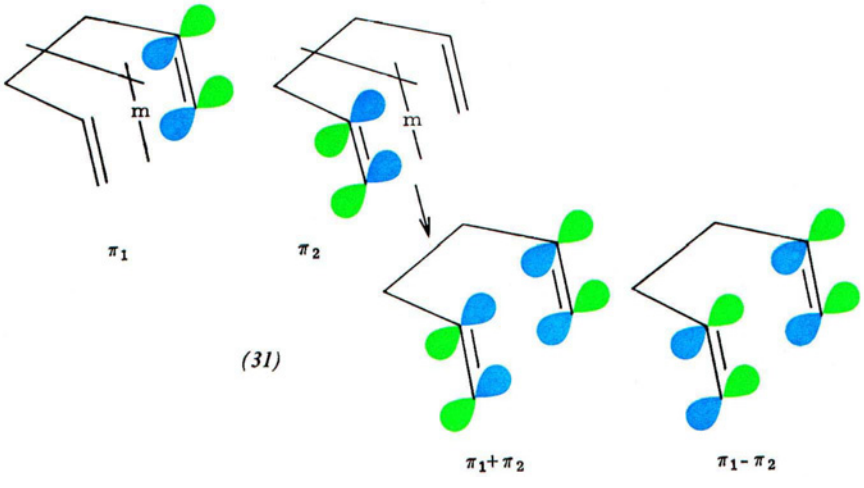


(30)

However, if only fragments of a polyene system participate in a reaction, the molecular orbitals of the component fragments must be used. Thus, the conversion of a hexatriene *(25)* to a bicyclo[3.1.0]hexene *(26)*, or to a

σ_1 and σ_2; they must be transformed as indicated in *(29)*, to $\sigma_1+\sigma_2$ and $\sigma_1-\sigma_2$.

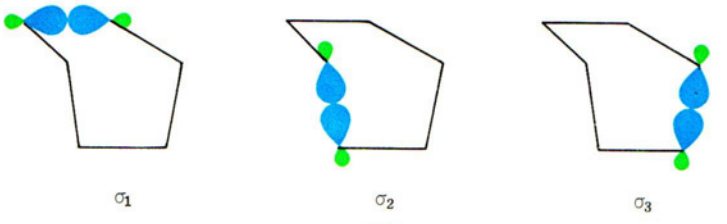
Again, consider the σ* orbitals of cyclopentenone *(30)*.



(31)

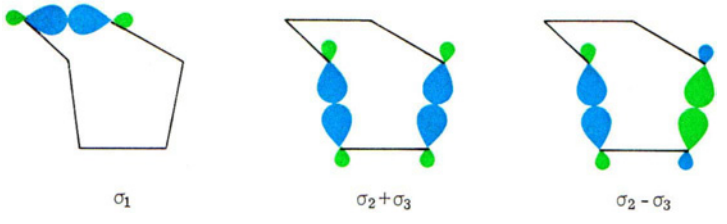
A similar mixing is required for nonconjugated π levels. Thus, in considering a [2+2] cycloaddition within a 1,5-hexadiene, leading to a bicyclohexane, the preparation of π orbitals is performed as shown in *(31)*.

d) A convenient, but not necessary, further step is to mix with each other all orbitals of a given symmetry. For example, consider the σ bonds of a [2+2+2] cycloreversion of a cyclohexane to three ethylenes. Assume a boat conformation of the cyclohexane. The three localized σ orbitals are σ_1, σ_2, and σ_3 *(32)*. The



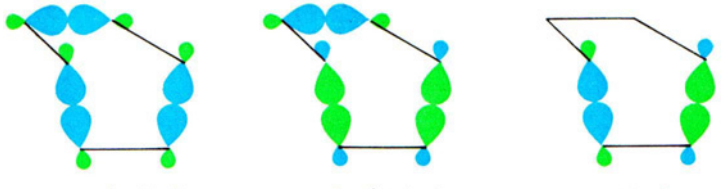
(32)

only symmetry element in the transition state is a plane bisecting σ_1. The orbital σ_1 is symmetric under reflection in that plane, but σ_2 and σ_3 are not. Thus, in accordance with rule c) above, we should form the delocalized combinations $\sigma_2+\sigma_3$ and $\sigma_2-\sigma_3$. This yields a new set of symmetry-adapted orbitals *(33)*.



(33)

Now σ_1 and $\sigma_2+\sigma_3$ are symmetric with respect to the symmetry plane, and it is convenient to delocalize further by taking their sum and difference *(34)*.



(34)

More extensive delocalization (a secondary effect – but one which can be of chemical significance) would follow from mixing of σ_1^* and $\sigma_2^*-\sigma_3^*$ into $\sigma_2-\sigma_3$, and $\sigma_2^*+\sigma_3^*$ into the symmetric combinations.

3.2. Precautions in the Construction of Correlation Diagrams

There are several pitfalls in the construction and application of correlation diagrams. To avoid these the following precautions must be observed:

a) Each basic process must be isolated and analyzed separately. Otherwise the superposition of two forbidden but independent processes may lead one to the erroneous conclusion that the combined process is symmetry-allowed. Two wrongs do not make a right.

b) The symmetry elements chosen for analysis must bisect bonds made or broken in the process. Here there are two corollaries:

(i) a symmetry element of no use in analyzing a reaction is one with respect to which the orbitals considered are either all symmetric or all antisymmetric – obviously an analysis based on such elements only (such as plane 3 in the approach of two ethylenes [*cf.* Figure 5]) would lead to the conclusion that every reaction is symmetry-allowed;

(ii) if the only symmetry element is one which does not bisect any bonds made or broken, then the correlation diagram constructed on the basis of this element can only lead to the conclusion – often false – that a reaction is symmetry-allowed.

c) Each case must be reduced to its highest inherent symmetry. Thus, if there are heteroatoms in a polyene component, they are to be replaced by their isoelectronic carbon groupings. If there are substituents with trivial electronic demands they should be replaced by hydrogens. Heteroatoms do offer the possibility of new reactions by the inclusion of nonbonding pairs or by the availability of low-lying unoccupied orbitals. These types of interaction should be carefully analyzed.

To consider an example of a), take the formation of cubane from cyclooctatetraene in one step (Figure 14).

Construction of a correlation diagram (Figure 15) without regard to precaution a) would lead to the con-

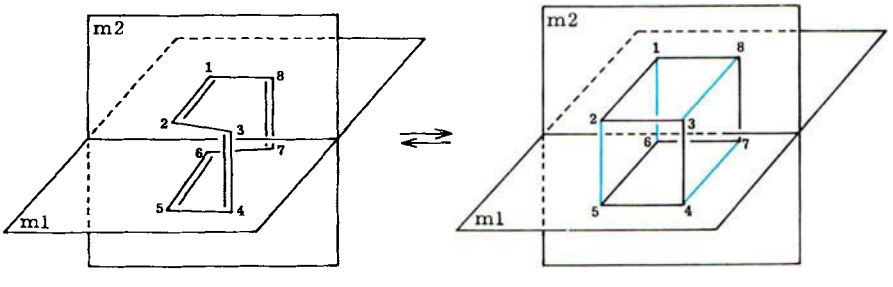


Figure 14. Formation of cubane from cyclooctatetraene in a concerted reaction.

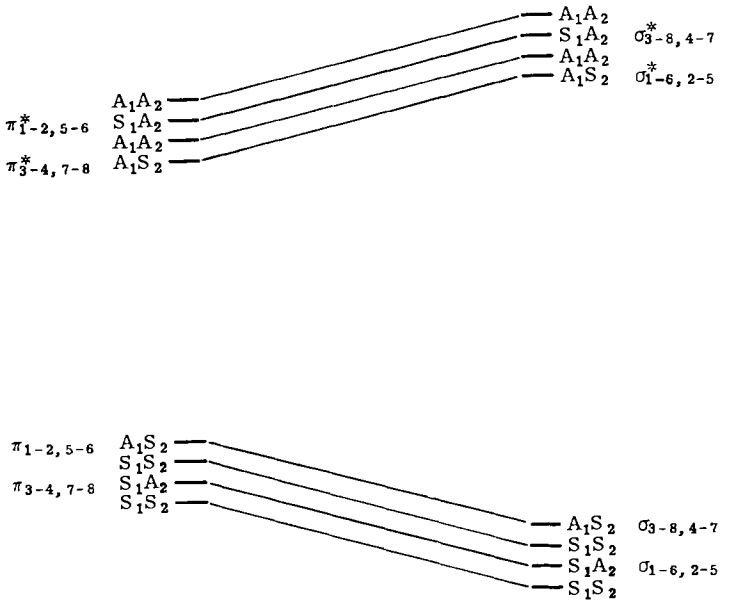


Figure 15. Incorrect correlation diagram for the formation of cubane from cyclooctatetraene.

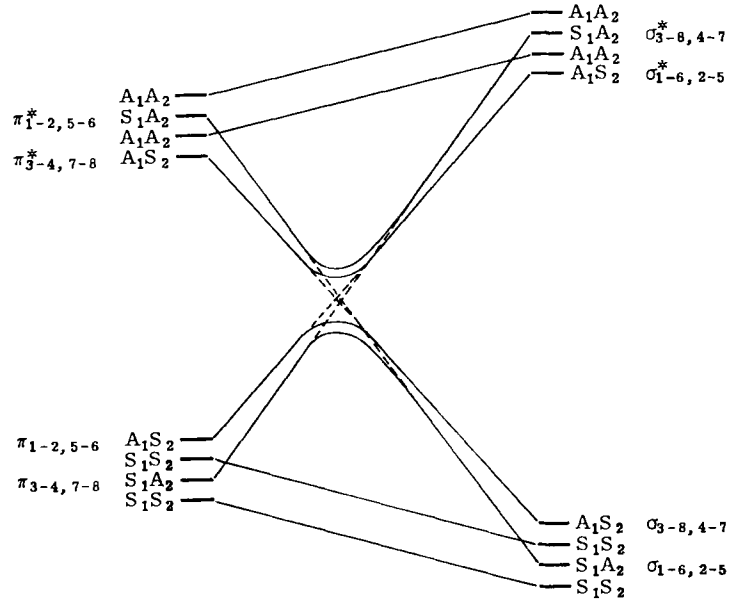


Figure 16. Correct correlation diagram for the formation of cubane from cyclooctatetraene. — Within any of the four groups of four closely spaced levels, those with both symmetric and antisymmetric labels, regardless of subscripts, are in fact degenerate, though shown here for clarity as differing slightly in energy.

clusion that this superposition of two [2+2] cycloadditions should be a symmetry-allowed thermal process.

In fact the diagram should really appear as in Figure 16. The intended correlation of the S_1A_2 orbital formed from $\pi_{3-4,7-8}$ is to an antibonding S_1A_2 $\sigma^*_{3-8,4-7}$ orbital. A small perturbation links the 3-4,7-8 cycloaddition with the 1-2,5-6 process. The latter by an accident of symmetry is forming an S_1A_2 orbital of the cubane. The result is that the intended bonding-antibonding correlation is accidentally avoided. But the reaction is none the less symmetry-forbidden. In fact, whether a reaction is symmetry-allowed or forbidden is determined by the height of the electronic hill that reactant or product orbitals must climb in reaching the transition state; and the presence or absence of a hill is a function of the *intended* correlation, or the initial

slope of the levels. From this point of view, we see that in the case at hand the 3-4,7-8 combination is in no wise facilitated by the concurrent 1-2,5-6 process, and *vice versa.*

An example of type b) is provided by consideration of the conversion of butadiene *(35)* to bicyclobutane *(36)*. Here the only molecular symmetry element is a



(39) *(40)*

The rationale for point c) will become apparent on comparison of the correlation diagram for the face-to-face addition of ethylene to ethylene with that for ethyl-

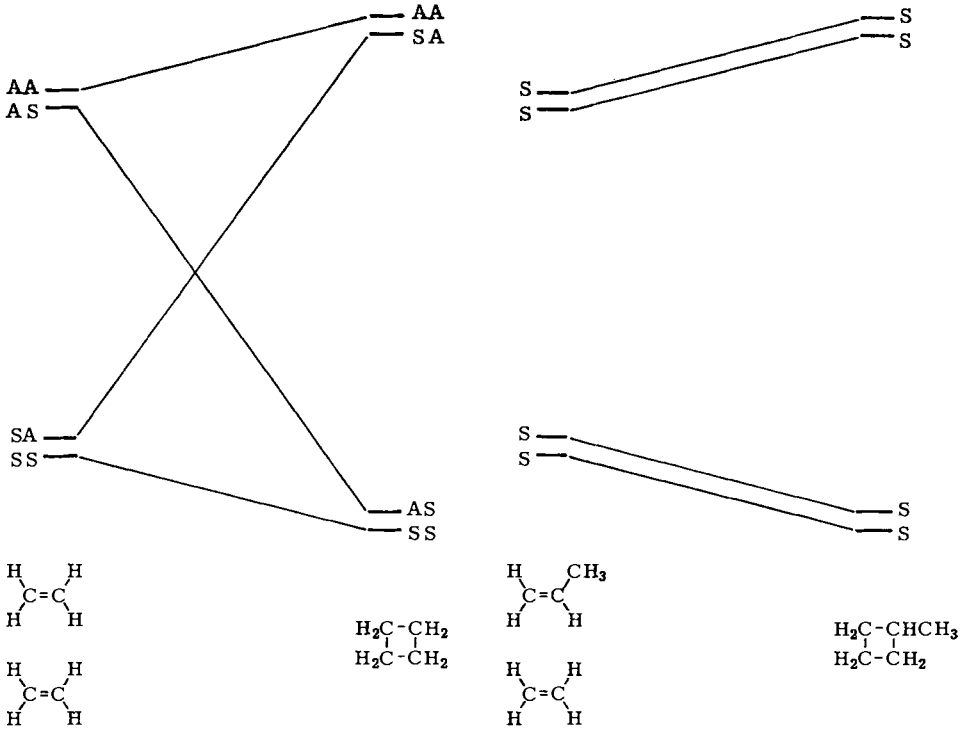
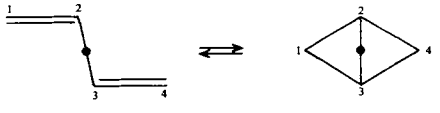


Figure 17. Left: Correlation diagram for the cycloaddition of two ethylene molecules. — Right: Incorrect correlation diagram for the cycloaddition of ethylene to propylene.

two-fold axis passing through a single bond which is not made or broken during the reaction. We will discuss this reaction in some detail in the sequel.



(35) *(36)*

Another instance is the case of two propylenes trading hydrogens [*(37)*→*(38)*], where only a center of symmetry (passing through no bonds) could be present.



(37) *(38)*

Still another example is the decomposition of pentalene to diacetylene and two acetylenes [*(39)*→*(40)*], where no element of symmetry bisects bonds broken or made.

ene to propylene. For the latter case there is, strictly speaking, no symmetry in the transition state. Thus, all levels are trivially symmetric and one might be tempted to draw the correlation diagram as shown at right in Figure 17.

The conclusion would be that methyl substitution had made the thermal [2+2] cycloaddition symmetry-allowed. This is incorrect. The proper level correlation diagram is shown in Figure 18.

Methyl substitution has in an absolute sense reduced all levels to the same symmetry. The level crossing has become impossible. But the perturbation is a very small one and so the crossing is barely avoided. A bonding level of reactants has still moved to high energy in the transition state. The corresponding state diagram differs trivially from that for ethylene + ethylene. The reaction remains symmetry-forbidden [11].

[11] A similar situation arises in other areas of chemistry. The n→π* transition in formaldehyde is electric-dipole forbidden. The source of the small intensity observed is still disputed. In the cases of acetaldehyde, or of unsymmetrically substituted ketones, the symmetry element which made the formaldehyde transition electric-dipole forbidden is removed. The transition becomes allowed. Does it therefore jump to a high intensity? Not at all; the intensity remains practically unchanged. This is because the *essential* symmetry, that of the local environment of the carbonyl group, is unchanged.

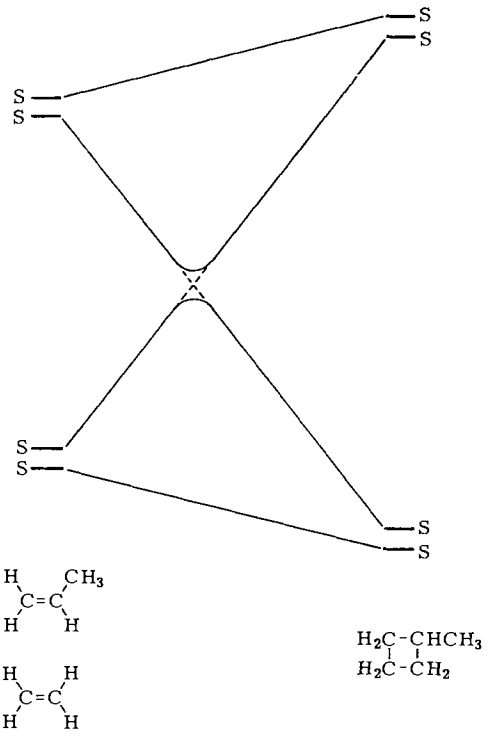


Figure 18. Correct correlation diagram for the cycloaddition of ethylene to propylene.

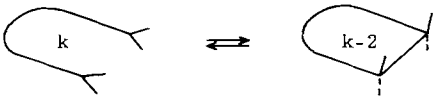
4. The Conservation of Orbital Symmetry

It is clear that the absence or presence of molecular symmetry in an absolute sense cannot be the ultimate source of the allowedness or forbiddenness of a reaction. Symmetry is discontinuous. It is either on or off, here or not here. Chemistry is obviously not like that. A slight perturbation, say substitution by a methyl group, may destroy total symmetry, but cannot be expected to change dramatically the mechanism of a reaction. The essential and decisive factor in making a reaction forbidden is that in the transition state there is at least one level that is no longer bonding, but at considerably higher energy. We have used symmetry as a crutch to aid us in denominating those high energy levels without doing the least bit of calculation. If symmetry is lacking, either as a result of trivial substitution, or more basically from the asymmetry of the components (*e.g.*, in the "ene" reaction), a reaction may still be analyzed by writing down the orbitals involved, allowing them to mix according to well-defined quantum mechanical principles and following the interacting orbitals through the reaction. High energy levels in the transition state may arise *pari passu* from real crossings or from intended but avoided ones. Such high energy levels will not be present if every bonding orbital of the product (reactants) is derivable from one bonding orbital of the reactants (product). For if a bonding orbital of the product is not derivable from any bonding orbital of reactants, it must be related to an antibonding reactant orbital. Whether or not it actually correlates to that antibonding orbital is dependent on the presence or absence of total symmetry; but even if the intended correlation is foiled, the level soars to high energy in the transition state.

In short, the most general, and at the same time physically most realistic view of orbital symmetry control of chemical reactions is obtained by specifying the relevant molecular orbitals of reactants, and observing their corresponding form in products, as reaction occurs *with conservation of orbital symmetry*. To illustrate our method at work we will first discuss some instances where correlation diagrams can be drawn, one of these in great detail, and then proceed to less symmetrical cases where no help may be expected from molecular symmetry.

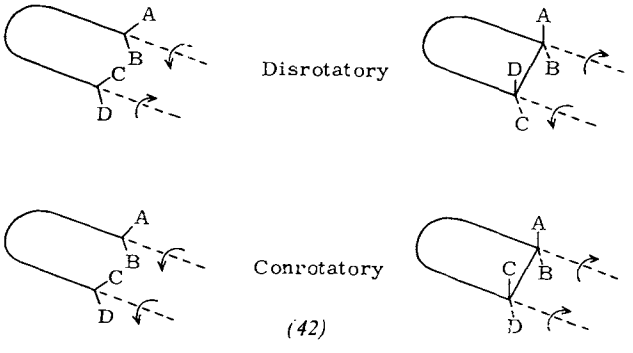
5. Theory of Electrocyclic Reactions

These intramolecular cycloadditions provided the stimulus for our study of molecular orbital symmetry and concerted reactions. We define as *electrocyclic* reactions the formation of a single bond between the termini of a linear system containing k π electrons, and the converse process *(41)*.



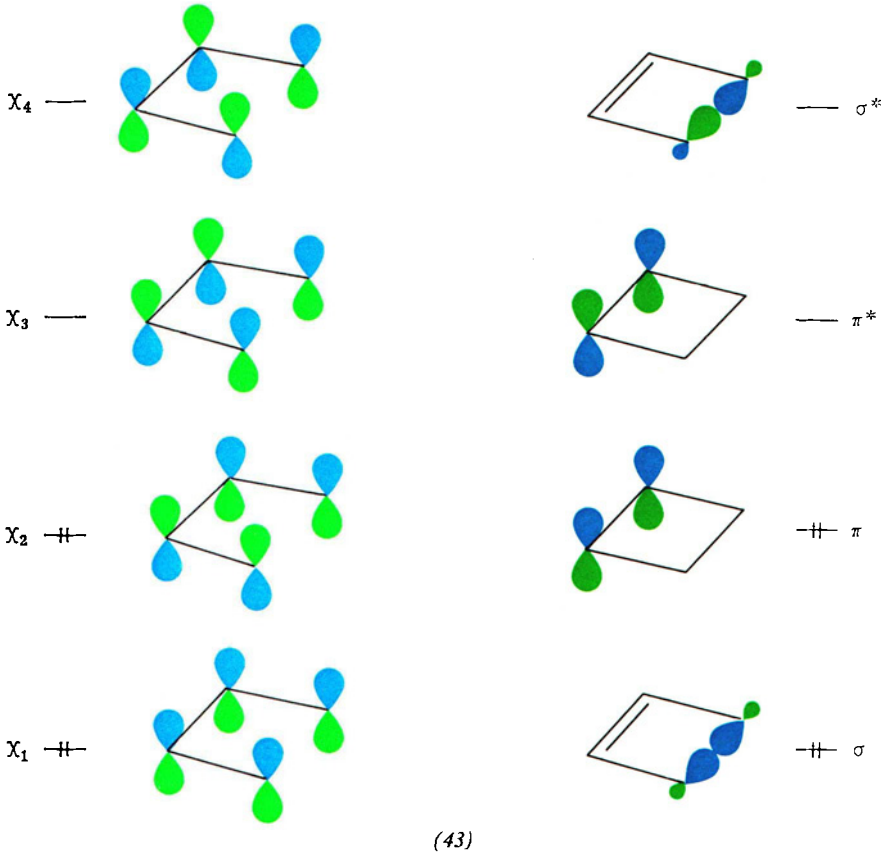
(41)

In such changes fixed geometrical isomerism imposed upon the open-chain system is related to rigid tetrahedral isomerism in the cyclic array. *A priori*, this relationship might be *disrotatory* or *conrotatory (42)*. In the former case the transition state is characterized by a plane of symmetry while in the latter a two-fold axis of symmetry is preserved.



(42)

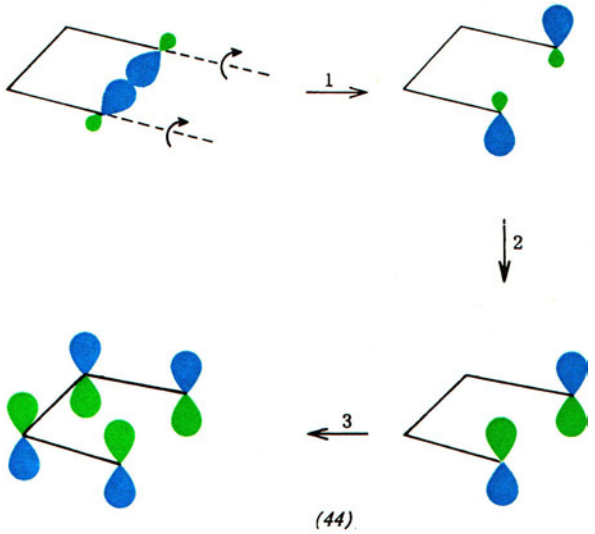
Consider the essential molecular orbitals in the conversion of cyclobutene to butadiene. These are the four π orbitals of the butadiene χ_1, χ_2, χ_3, χ_4, the π and π^* lev-



(43)

els of the cyclobutene double bond, and the σ and σ* orbitals of the single bond to be broken *(43)*.

Consider carrying out a conrotatory motion to completion on σ [step 1 in *(44)*] and follow through with a rehybridization (step 2). At this stage the orbital looks like a fragment of χ_2 (or χ_4) of butadiene and all that is needed is a growing-in (step 3) of orbitals at C-2 and C-3.



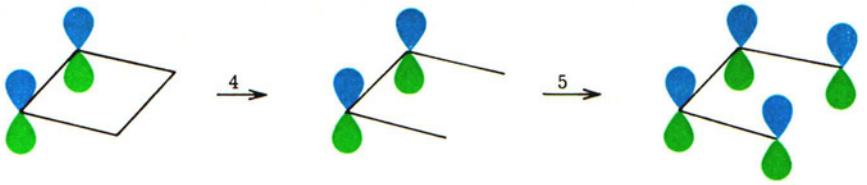
(44)

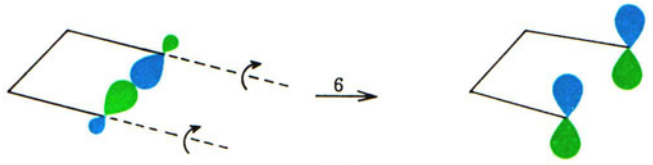
It should be kept in mind that in reality the steps 1, 2, and 3 will all be simultaneously proceeding along the reaction coordinate, and that the above factorization is only an aid to visualization. The growing-in of step 3 may seem like magic to those unfamiliar with molecular orbital manipulations. It is in fact a universal phenomenon, the detailed result in this case of mixing of π* with σ as the reaction proceeds. We have now followed σ through the reaction and correlated it with another bonding orbital, χ_2. Similarly we follow π through *(45)*. Note here that the growing-in step 5 is really a mixing of π with σ* (*cf.* step 6). π thus correlates with χ_1.

The correlations could of course have been obtained starting from butadiene. χ_1 by a conrotatory motion becomes π *(46)* and χ_2 is transformed into σ *(47)*.

In this analysis there appears a fading-away, in which extra nodes and contributions disappear. This is the precise reverse of the growing-in noted above and is again a result of mixing with higher orbitals of the proper symmetry. Very similar arguments lead to a correlation of σ* and χ_3, and of π* and $-\chi_4$ ($\equiv \chi_4$!). We have thus achieved a correlation of bonding levels of the reactant with bonding levels of the product, with conservation of orbital symmetry. The thermal reaction should be a facile one.

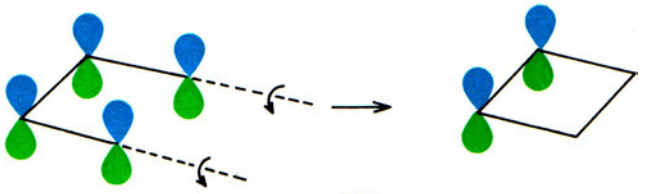
By contrast, consider now a disrotatory opening. The correlations are indicated in *(48)*. Both σ and π must correlate with χ_1 or χ_3 ($\equiv -\chi_3$!). But since only one can correlate with χ_1, the other must go up to χ_3, which is antibonding. Conservation of orbital symmetry requires in this case a high-lying transition state and the





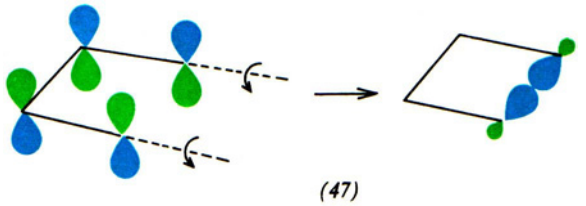
(45)

thermal reaction is symmetry-forbidden. Again the problem could have been approached from the other side *(49)*.



(46)

It is obvious that χ_2 is the troublesome orbital – it cannot transform into *any* bonding orbital of the cyclobutene, with conservation of orbital symmetry, in a disrotatory process.



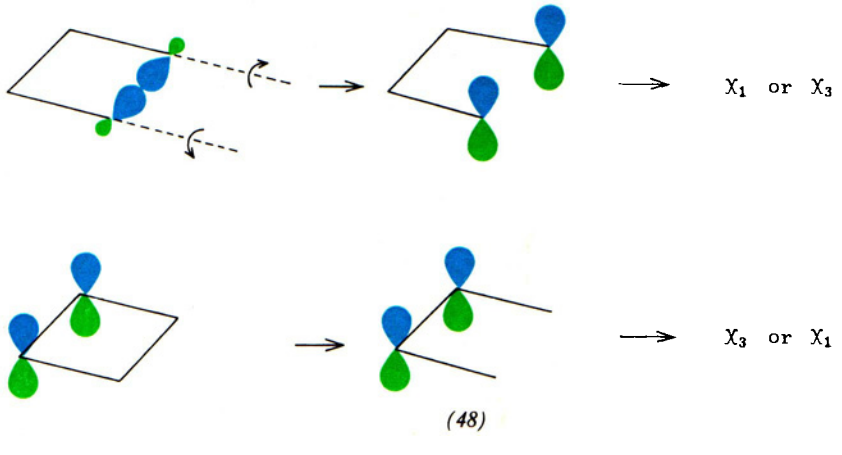
(47)

What we have somewhat laboriously described in words is equivalent to the construction of two level correlation diagrams (Figure 19). It is clear that in the conrotatory process a two-fold rotation axis is maintained at all times whereas in the disrotatory motion an invariant plane of symmetry is present. These diagrams are clearly analogous to those discussed in section 3 (above) for combination reactions of π electron systems. Obviously the diagram for the conrotatory process is characteristic of a symmetry-allowed reaction, while the pattern for the disrotatory process is that of a symmetry-forbidden reaction.

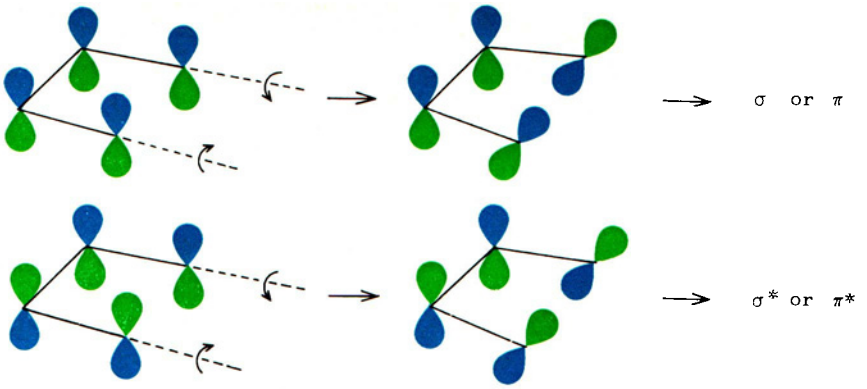
We should emphasize at this point that this detailed stepwise analysis has been presented primarily for pedagogic reasons. The high molecular symmetry present in these cases would have permitted very simple direct derivation of the relevant correlation diagrams. But soon we will encounter cases of such low symmetry that the stepwise analysis is the only possible one.

The highest occupied orbitals play a dominant role in these correlations. Their importance is easy to justify. First, we think of them as containing the valence electrons of the molecule, most easily perturbed during incipient reaction. In this sense their role has been stressed in the important work of *Fukui*[12]. Second, if there is little symmetry in a molecule and if there is a bonding level which is intending to cross the energy

[12] *K. Fukui, T. Yonezawa*, and *H. Shingu*, J. chem. Physics *20*, 722 (1952); *K. Fukui, T. Yonezawa, C. Nagata*, and *H. Shingu, ibid. 22*, 1433 (1954); *K. Fukui* in *O. Sinanoğlu*: Modern Quantum Chemistry. Academic Press, New York 1965, Vol. 1, p. 49, and references therein.



(48)



(49)

gap to correlate to an antibonding level, then that level will usually be the highest occupied level. Consequently, its motion determines the course of the cor-

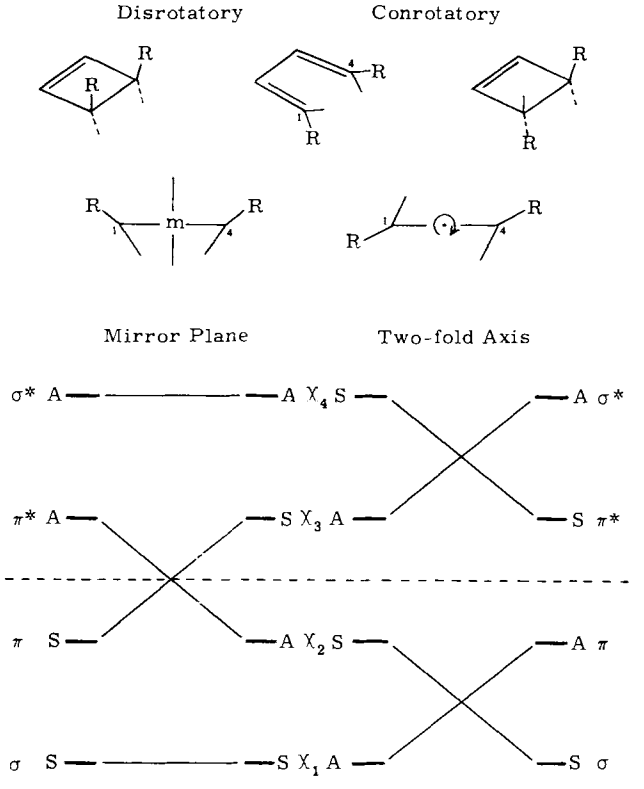


Figure 19. Correlation diagrams for the disrotatory and conrotatory conversion of cyclobutenes to butadienes.

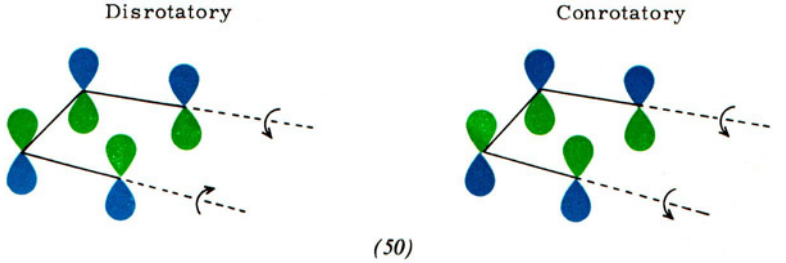
relation diagram and its initial slope is an important indication of whether the process is symmetry-allowed or forbidden. Consider the disrotatory and conrotatory motions as they affect χ_2 in butadiene *(50)*.

The disrotatory process pushes a plus lobe onto a minus lobe. Since one end of the molecule "feels" the phase of the wave function at the other end, this is an antibonding, destabilizing, repulsive interaction. The level moves up in energy along the reaction coordinate. Conrotatory motion brings a plus lobe onto a plus lobe (or minus on minus, which is equivalent). This is a bonding, stabilizing, attractive interaction terminating in the actual formation of the new σ bond.

A warning note should be sounded here. The sense of orbital symmetry control of any concerted reaction can always be determined through inspection of the behavior of the highest occupied molecular orbital in the reacting system, but the analysis is often less simple than it is in the case of the butadiene → cyclobutene transformation. A temptation especially to be avoided in making such analyses is that of inadvertently placing more than two electrons in a single molecular orbital.

The general rules for electrocyclic reactions are very easily derivable from the nodal properties of polyenes and polyenyl ions: the thermal electrocyclic reactions of a k π electron system will be disrotatory for $k = 4q+2$, conrotatory for $k = 4q$ ($q = 0, 1, 2\ldots$); in the first excited state these relationships are reversed. Some of the consequences of the rules are summarized in Figure 20.

We turn next to a consideration of secondary factors which influence the actual composition of the products of an electrocyclic reaction. The first is steric control. For every reaction there are two conrotatory and two disrotatory motions which may or may not be distinguishable. Thus, the two conrotatory modes of opening



(50)

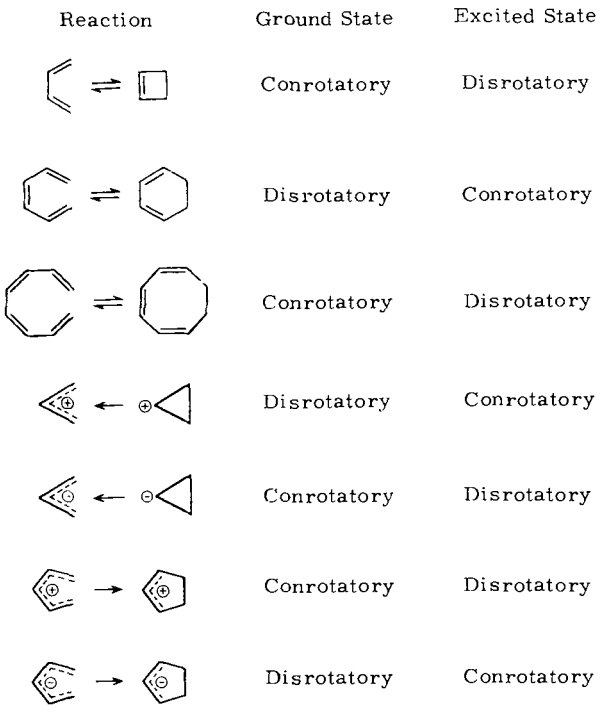
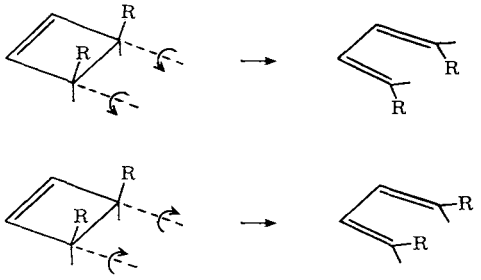


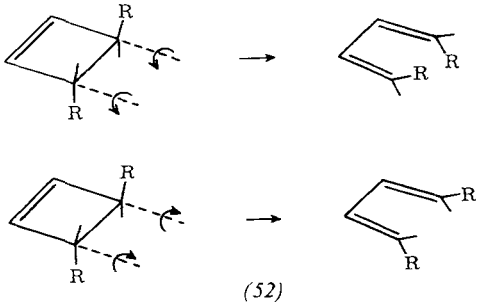
Figure 20. Conrotatory and disrotatory electrocyclic reactions.

of a *cis*-dimethylcyclobutene are enantiomeric and lead to the same product, *cis,trans*-1,4-dimethylbutadiene *(51)*.



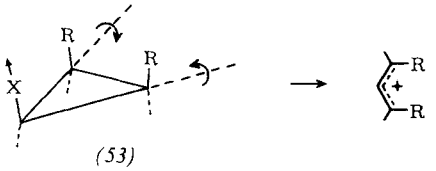
(51)

The two conrotatory motions for a *trans*-dimethylcyclobutene lead to two different isomers: *cis,cis*- and *trans,trans*-1,4-dimethylbutadiene *(52)*. In fact, the *trans,trans* product is found exclusively [13]; we attribute this to the unfavorable steric situation in the transition state leading to the *cis,cis* product.

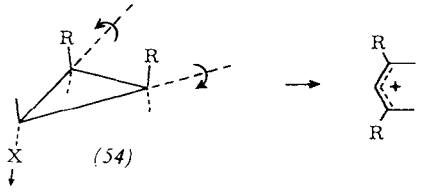


(52)

A most interesting subsidiary question in connection with the electrocyclic opening of a cyclopropyl cation to an allyl cation was first posed to us by *C. H. DePuy:* assuming that departure of a leaving group from a cyclopropane ring, and the bond-breaking electrocyclic reaction to give an allyl cation, are concerted, could there be a difference between the two *a priori* possible disrotatory modes, defined in relation to the position of the leaving group? Extended Hückel calculations provided the initial answer, which may be summarized by saying that the substituents on the same side of the three-membered ring as the leaving group rotate towards one another *(53)*, whereas those on the other side rotate apart *(54)*.

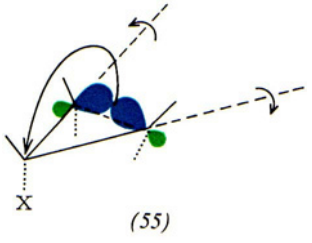


(53)



(54)

The result may be understood in qualitative terms when it is realized that as the 2,3 bond is broken by disrotatory outward rotation *(55)*, the electron density of that bond, which originally was more or less in the plane of the cyclopropane ring, shifts above the plane. It is then available for backside displacement of the leaving group – in other words, the reaction is a normal S_N2 displacement of the group X by the electrons of the backbone σ bond of the cyclopropane ring.

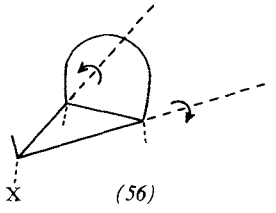


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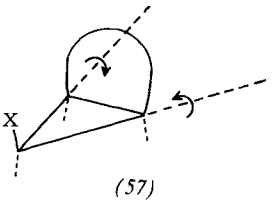
Several corollaries of these conclusions follow. If R in *(53)* or *(54)* is some bulky group then we should expect for steric reasons a faster solvolysis for compound *(54)*. On the other hand, when *cis* positions are linked by a short methylene chain, we should expect the opening of a compound such as *(56)* with leaving group *anti*

[13] *R. E. K. Winter*, Tetrahedron Letters *1965*, 1207.

to the ring to be severely disfavored, since the resulting rotation would lead to a *trans,trans*-allyl cation in a small ring. We should expect a facile opening only for a *syn* leaving group, as in *(57)*.



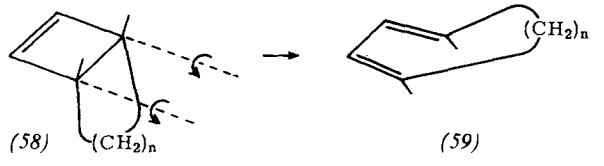
(56)



(57)

5.1. Electrocyclic Reactions Exemplified

The conrotatory electrocyclic change of a cyclobutene to a butadiene is a very well-known process. Its stereochemistry was established some ten years ago [14] and its scope and energetics have been very carefully studied [15]. Satisfactory rationalization of the striking stereospecificity of the reaction was lacking until the orbital symmetry control of electrocyclic changes was discovered. Given that in the thermal reaction conrotatory displacement is symmetry-allowed, it follows that



(58) *(59)*

a bicyclic cyclobutene containing a *cis*-fused methylene chain *(58)* leads to a cyclic *cis,trans*-diene *(59)*.

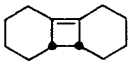
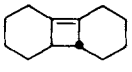
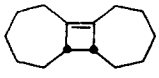
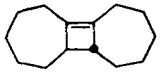
Such a *trans*-olefin becomes increasingly highly strained as the ring size diminishes. This trend is beautifully reflected in the temperatures at which the half-life of compound *(58)* is about 2 hours [16] as *n* is varied:

n	1	2	3	4	5	6
T(°C)	<100	195	>380	350	335	180

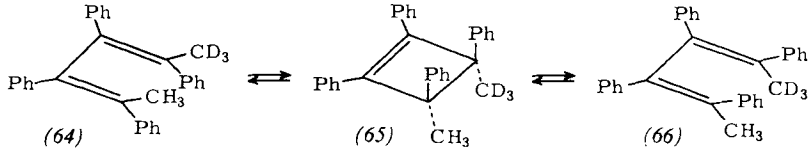
The half-life of *(58)* decreases for small *n* since, due to ring strain, the reaction itself becomes highly exothermic.

Molecules such as bicyclo[2.2.0]hexadiene and bicyclo[2.1.0]pentene clearly owe whatever stability they possess to the fact that the transformations, respectively to benzene and cyclopentadiene, are symmetry-forbidden.

Criegee and *Reinhardt* [17] have synthesized the laterally fused *cis*- and *trans*-cyclobutenes *(60)* – *(63)*. These exhibited dramatically different pyrolytic stabilities [18]. In the substances with *anti* backbones, the symmetry-imposed conrotatory motion leads to *cis* double bonds in the six- or seven-membered rings and the electrocyclic cleavage takes place readily. By contrast, the

		E_a (kcal/mole)	$k = 10^{-4}$ at °C
(60)		42	261
(61)		29	87
(62)		45	273
(63)		27	109

symmetry-allowed processes with the *syn* isomers would give substances containing a *trans* double bond in a six- or a seven-membered ring. Consequently, the



(64) *(65)* *(66)*

transformation occurs only at extreme temperatures; it might well proceed by a non-concerted mechanism.

The highly substituted butadienes *(64)* and *(66)* have been studied in a most ingenious and amusing experiment [19]. These substances are equilibrated through the intermediacy of the cyclobutene *(65)*. After fifty-one days at 124 °C, each cyclobutene molecule had faultlessly undergone 2.6×10^6 conrotatory openings, and a disrotatory mistake was yet to appear.

[14] *E. Vogel*, Liebigs Ann. Chem. *615*, 14 (1958); *R. Criegee* and *K. Noll*, *ibid. 627*, 1 (1959).

[15] *R. Criegee, D. Seebach, R. E. Winter, B. Börretzen*, and *H.-A. Brune*, Chem. Ber. *98*, 2339 (1965) and references therein; *G. R. Branton, H. M. Frey*, and *R. F. Skinner*, Trans. Faraday Soc. *62*, 1546 (1966) and references therein. *H. M. Frey* and *R. Walsh*, Chem. Rev. *69*, 103 (1969).

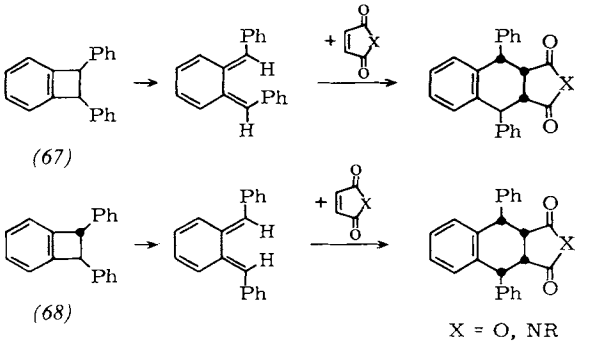
[16] *R. Criegee* and *G. Bolz*, unpublished work; *D. Seebach*, personal communication. The value for $n = 1$ is estimated from *J. I. Brauman, L. E. Ellis*, and *E. E. van Tamelen*, J. Amer. chem. Soc. *88*, 846 (1966). A more detailed study of the case *(58)*, $n = 4$, has been reported recently: *J. J. Bloomfield, J. S. McConaghy, jr.*, and *A. G. Hortmann*, Tetrahedron Letters, *1969*, 3723.

[17] *R. Criegee* and *H. G. Reinhardt*, Chem. Ber. *101*, 102 (1968).

[18] Indications of a similar preference in laterally fused nine-membered rings had been found earlier: *K. G. Untch* and *D. J. Martin*, J. Amer. chem. Soc. *87*, 4501 (1965).

[19] *G. A. Doorakian* and *H. H. Freedman*, J. Amer. chem. Soc. *90*, 5310, 6896 (1968).

Some fascinating transformations of the *cis*- and *trans*-benzocyclobutenes *(67)* and *(68)* are readily explicable as electrocyclic reactions followed by Diels-Alder additions [20].

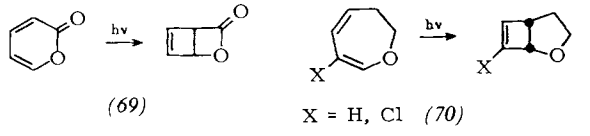


(67)

(68)

X = O, NR

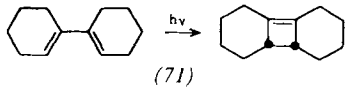
There are numerous examples of photochemical cyclobutene-butadiene interconversions. In the great majority of cases the diene is part of a cyclic system and is thus constrained to undergo the symmetry-allowed disrotatory process. Some typical examples are the reactions *(69)* and *(70)* [21,22].



(69)

X = H, Cl *(70)*

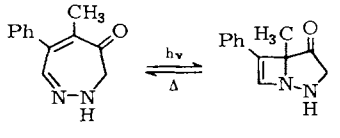
One case with greater stereochemical freedom *(71)* has been observed [23] and fits our expectations.



(71)

Recently it has been confirmed that *trans,trans*-2,4-hexadiene undergoes photochemical cyclization to *cis*-dimethylcyclobutene [24]; the case is of special interest in that geometric constraints are absent.

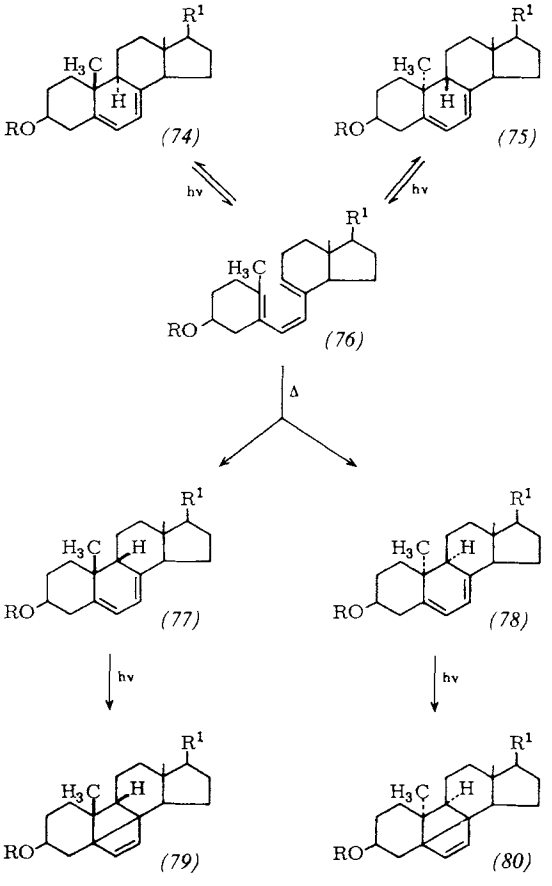
The diazepinone *(72)* yields on photolysis the bicyclic isomer *(73)*, which reverts readily thermally to the starting compound [25]. The reversibility is easily understood once it is realized that direct *cis*→*trans* interconversion, an impossible process in fused carbocyclic systems, is simply an inversion at the nitrogen atom in *(73)*.



(72) *(73)*

The symmetry-allowed photochemical conrotatory cyclization of *cis*-hexatrienes, and the reverse reaction, were first recognized in studies in the vitamin D field. The conversions *(74)* – *(80)* – all symmetry-allowed – were established in an extensive series of elegant investigations [26].

Of particular interest is the fact that the cyclohexadienes *(77)* and *(78)*, prevented by insurmountable geometrical restraints from undergoing symmetry-allowed electrocyclic cleavage, are photoisomerized to the cyclobutenes *(79)* and *(80)*, in an alternative symmetry-allowed process.



(74) *(75)* *(76)* *(77)* *(78)* *(79)* *(80)*

A further example of the photochemical cyclohexadiene→hexatriene reaction has recently been studied [27].

A related reaction presumably also takes place in the photocyclization of *cis*-stilbenes *(81)* and similar com-

[20] *R. Huisgen* and *H. Seidel*, Tetrahedron Letters *1964*, 3381; *G. Quinkert*, *K. Opitz*, *W. W. Wiersdorff*, and *M. Finke*, *ibid. 1965*, 3009.

[21] *E. J. Corey* and *J. Streith*, J. Amer. chem. Soc. *86*, 950 (1964).

[22] *L. A. Paquette*, *J. H. Barrett*, *R. P. Spitz*, and *R. Pitcher*, J. Amer. chem. Soc. *87*, 3417 (1965).

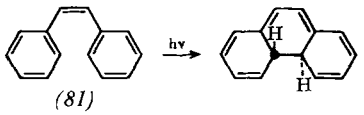
[23] *W. G. Dauben*, *R. G. Cargill*, *R. M. Coates*, and *J. Saltiel*, J. Amer. chem. Soc. *88*, 2742 (1966); *K. J. Crowley*, Tetrahedron *21*, 1001 (1965).

[24] *R. Srinivasan*, J. Amer. chem. Soc. *90*, 4498 (1968).

[25] *W. J. Theuer* and *J. A. Moore*, Chem. Commun. *1965*, 468.

[26] *E. Havinga*, *R. J. de Kock*, and *M. P. Rappold*, Tetrahedron *11*, 278 (1960); *E. Havinga* and *J. L. M. A. Schlattmann*, *ibid. 16*, 146 (1961); *G. M. Sanders* and *E. Havinga*, Rec. Trav. chim. *83*, 665 (1964); *H. H. Inhoffen* and *K. Irmscher*, Fortschr. Chem. org. Naturstoffe *17*, 70 (1959); *H. H. Inhoffen*, Angew. Chem. *72*, 875 (1960); *B. Lythgoe*, Proc. chem. Soc. *1959*, 141; *W. G. Dauben* and *G. J. Fonken*, J. Amer. chem. Soc. *81*, 4060 (1959).

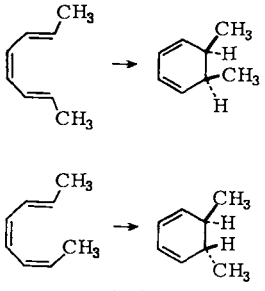
[27] *P. Courtot* and *R. Rumin*, Tetrahedron Letters *1968*, 1091.



(81)

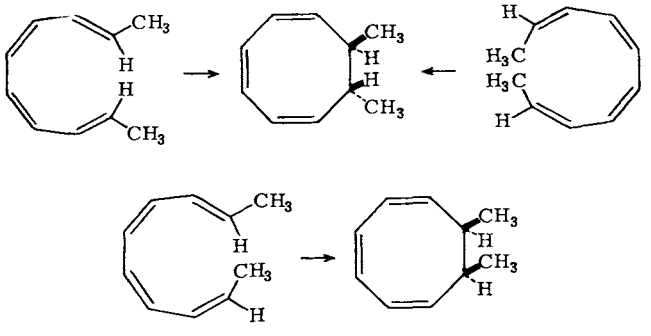
pounds [28], though the stereochemistry of the product has not been definitely established.

The earlier indications that the *thermal* cyclization of trienes was disrotatory [26] were confirmed by the study of simple model compounds *(82)* [29].



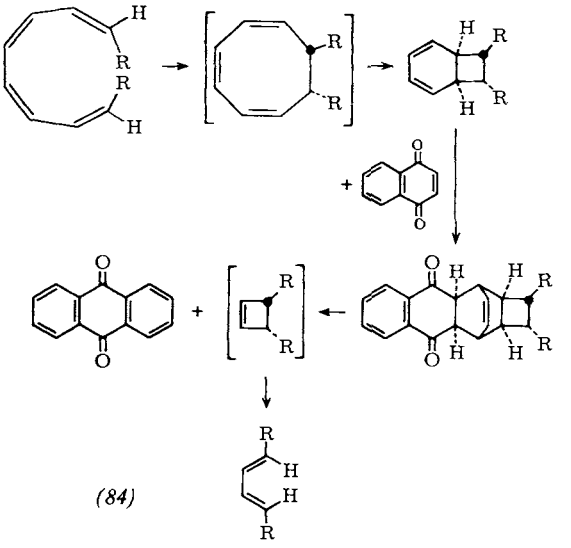
(82)

The electrocyclic closure *(83)* of a *cis,cis*-octatetraene should be thermally conrotatory, photochemically disrotatory. Though any conformation of a *cis,cis*-octatetraene is far from planarity, the nodal patterns in the orbitals are preserved. The predicted stereochemical course of the thermal reaction has been confirmed recently [30].



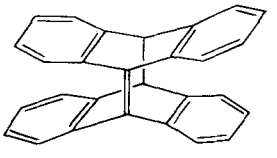
(83)

Some previous experiments can also be interpreted accordingly. Thus, in reactions *(84)* explored by *Meister* [31] the following sequence of symmetry-allowed changes can be adduced: an 8-electron conrotatory electrocyclic reaction, a 6-electron disrotatory reaction, a [4+2] cycloaddition, a reversion of the same, and a 4-electron conrotatory electrocyclic reaction.

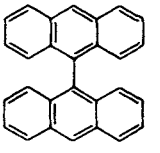


(84)

The preparation of the fantastic hydrocarbon *(85)* by *Greene* [32] presents a situation of great interest, related to the octatetraene→cyclooctatriene electrocyclic conversion. Undoubtedly, the substance would suffer instantaneous transformation to its isomer 9,9′-bianthryl *(86)* – in fact, $t_{1/2} \approx 30$ minutes at 80 °C – were it not for the circumstances that the symmetry-allowed conrotatory transformation is opposed by a necessary concomitant, and difficult, twisting motion about the 9,9′ double bond, while the geometrically simpler disrotatory cleavage is symmetry-forbidden.

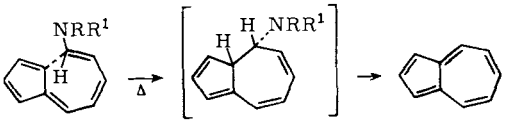


(85)



(86)

A ten-electron electrocyclic reaction may have been realized in the Ziegler-Hafner synthesis of azulene [33]. The crucial cyclization step is very probably a disrotatory electrocyclic reaction *(87)*.



(87)

There were some previous indications in the literature that the opening of cyclopropyl cations to allyl cations is a stereospecific process [34]. For instance, *Skell* and *Sandler* observed that the two epimers *(88)* and *(89)*

[28] *K. A. Muszkat* and *E. Fisher*, J. chem. Soc. *B, 1967*, 662; *F. B. Mallory, C. S. Wood*, and *J. T. Gordon*, J. Amer. chem. Soc. *86*, 3094 (1964). The subject has been recently reviewed by *M. Scholz, F. Dietz*, and *M. Möhlstadt*, Z. Chem. *7*, 329 (1967).

[29] *E. Vogel, W. Grimme*, and *E. Dinné*, Tetrahedron Letters *1965*, 391; *E. N. Marvell, G. Caple*, and *B. Schatz, ibid. 1965*, 385; *D. S. Glass, J. W. H. Watthey*, and *S. Winstein, ibid. 1965*, 377.

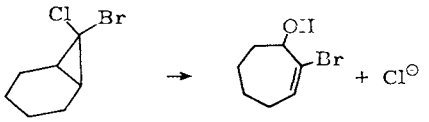
[30] *R. Huisgen, A. Dahmen*, and *H. Huber*, J. Amer. chem. Soc. *89*, 7130 (1967); *cf.* also *E. N. Marvell* and *J. Seubert, ibid. 89*, 3377 (1967).

[31] *H. Meister*, Chem. Ber. *96*, 1688 (1963).

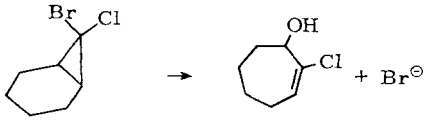
[32] *N. M. Weinshenker* and *F. D. Greene*, J. Amer. chem. Soc. *90*, 506 (1968).

[33] *K. Ziegler* and *K. Hafner*, Angew. Chem. *67*, 301 (1955); *K. Hafner, ibid. 67*, 301 (1955).

[34] (a) *P. S. Skell* and *S. R. Sandler*, J. Amer. chem. Soc. *80*, 2024 (1958); (b) *E. E. Schweizer* and *W. E. Parham, ibid. 82*, 4085 (1960); (c) *R. Pettit, ibid. 82*, 1972 (1960).



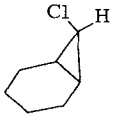
(88)



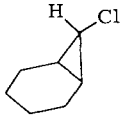
(89)

(structures not assigned) gave different solvolysis products. The hitherto mysterious phenomena are now readily explicable; the structures must be assigned as shown, since only loss of the *endo* halogen atoms can be concerted with the required disrotatory opening of the cyclopropane rings.

The first clear confirmations of our predictions for the electrocyclic opening were obtained in 1965. Whereas *(90)* undergoes solvolysis readily at 125 °C, its epimer *(91)* is recovered unchanged after prolonged treatment with acetic acid at 210 °C [35].

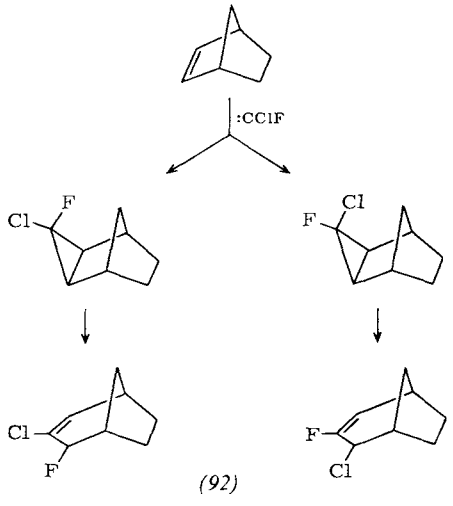


(90)



(91)

A detailed study of all methyl-substituted cyclopropyl tosylates clearly showed the steric effect of methyl groups forced against each other by the stereoelectronic factor [36].

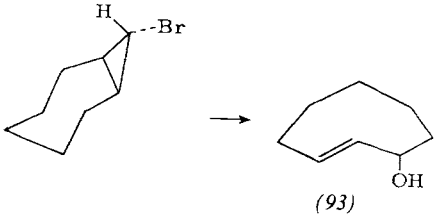


(92)

[35] *S. F. Cristol, R. M. Segueira,* and *C. H. DePuy,* J. Amer. chem. Soc. *87,* 4007 (1965). Similar results were communicated to us by *W. Kirmse. Cf.* also the behavior on pyrolysis of the closely related chlorobicyclo[3.1.0]hexanes: *M. S. Baird* and *C. B. Reese,* Tetrahedron Letters *1967,* 1379.

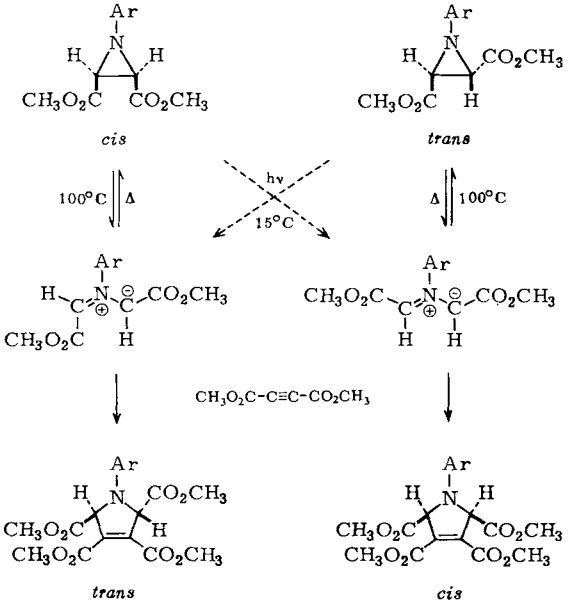
[36] *P. v. R. Schleyer, G. W. Van Dine, U. Schöllkopf,* and *J. Paust,* J. Amer. chem. Soc. *88,* 2868 (1966); *U. Schöllkopf,* Angew. Chem. *80,* 603 (1968); Angew. Chem. internat. Edit. *7,* 588 (1968).

Since then, numerous further confirmations have appeared. We mention here only two of these. *Ghosez* and co-workers [37] observed the reactions *(92),* and *Whitham* has shown that solvolysis of *exo*-8-bromobicyclo[5.1.0]octane gives the expected *trans*-cyclooctenol *(93)* [38].



(93)

The electrocyclic cleavage of the cyclopropyl anion has not been tested directly in the parent case, but an isoelectronic example, drawn from aziridine chemistry, provides a striking confirmation of the conservation of orbital symmetry. The beautiful observations of *Huisgen, Scheer,* and *Huber* [39] are summarized in the diagram *(94)*.



(94)

The 1,3-dipolar isomer of an aziridine is a 4 π electron molecule isoelectronic to allyl anion. The net inversion of stereochemistry observed in the thermal reaction would be extremely puzzling were it not the obvious consequence of a conrotatory opening, followed by a [4+2] cycloaddition.

The cyclization of pentadienyl cations to cyclopentenyl ions is a reaction extensively studied by *Deno* and by

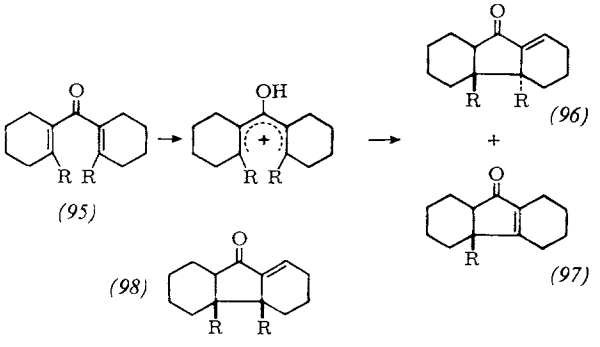
[37] *L. Ghosez, G. Slinckx, M. Glineur, P. Hoet,* and *P. Laroche,* Tetrahedron Letters *1967,* 2773. Related reactions with HCCl and HCBr are also observed: *C. W. Jefford, E. Huang Yen,* and *R. Medary, ibid. 1966,* 6317.

[38] *G. H. Whitham* and *M. Wright,* Chem. Commun. *1967,* 294.

[39] *R. Huisgen, W. Scheer,* and *H. Huber,* J. Amer. chem. Soc. *89,* 1753 (1967).

Sorensen [40]. However, the nature of the sulfuric acid medium predominantly used in these studies precludes elucidation of the stereochemistry of the reaction; hydrogen and methyl shifts intervene before product isolation. Further, it is now clear that the well-known Nazarov reaction [41] involves an electrocyclic reaction within a pentadienyl cation; again, no information about the stereochemistry of the change was forthcoming from the very extensive early work.

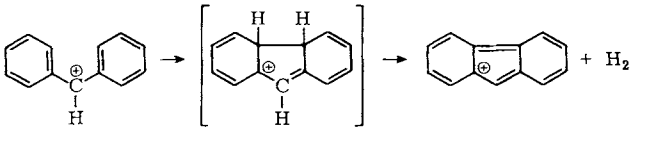
The stereochemistry of the reaction has now been established in recent studies at Harvard [42]. Treatment of dicyclohexenyl ketone *(95)*, R = H, with phosphoric



(95) *(96)* *(97)* *(98)*

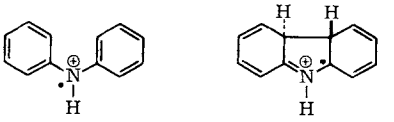
acid affords two ketones *(96)*, R = H, and *(97)*, R = H. Similarly, the substituted ketone *(95)*, R = Me, yields *(96)*, R = Me; in this case the process is not complicated by concomitant formation of a stereochemically uninformative product of type *(97)*. Thus, the predicted conrotatory course is cleanly followed in both cases. Moreover, the irradiation of *(95)*, R = H, yields a ketone *(98)* which is the product of disrotatory cyclization.

The opportunity for observing the excited state reactions of cations arises in mass-spectrometric studies. *Johnstone* and *Ward* [43] observed that the diphenylmethyl cation *(99)*, generated mass spectrometrically, cyclizes to a hydrofluorene species which loses *two* hydrogen atoms in a single step, and is therefore very



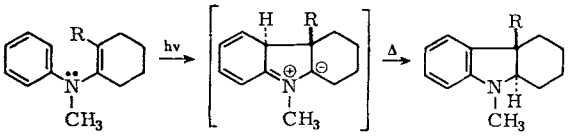
(99) *(100)*

probably the *cis* ion *(100)* – the expected product of the symmetry-allowed electrocyclization of the first excited state of the cation *(99)*. By contrast, the radical cation *(101)*, cyclizes to a hydrocarbazol species which loses hydrogen atoms one at a time, and is thus probably the *trans* ion *(102)* – again the result of the symmetry-allowed excited state process.



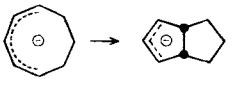
(101) *(102)*

Chapman [44] has observed photochemical cyclizations of the amines *(103)*. These are isoelectronic with pentadienyl anion, and their excited state closure should take a conrotatory course. The initially formed inter-



(103), R = H, CH_3 *(104)* *(105)*

mediate *(104)* apparently returns to the ground state and undergoes a hydrogen shift (a symmetry-allowed suprafacial [1,4] anionic shift – see Section 7) leading to the stable final product *(105)*.



(105a) *(105b)*

Very recently, the first example of the electrocyclic closure of a simple cyclopentadienyl anion has been observed [*(105a)*→*105b)*] [44a].

Winstein has studied an exceptionally interesting system in which nine- and ten-electron electrocyclic processes are operative [45]. When one electron is added to *cis*-bicyclo[6.1.0]nona-2,4,6-triene *(106)*, an ion-radical *(107)* is produced, clearly with symmetry-allowed



(106) *(107)*

disrotatory geometrical displacements. Moreover, yet another electron can be added, to give a ten-electron doubly charged anion. In spectacular contrast [46], addition of an electron to the isomeric *trans*-triene *(108)* is not accompanied by delocalization of the cyclopro-

[40] *N. C. Deno, C. V. Pittman, jr.*, and *J. O. Turner*, J. Amer. chem. Soc. *87*, 2153 (1965); *T. S. Sorensen*, Canad. J. Chem. *42*, 2768 (1964); *43*, 2744 (1965); J. Amer. chem. Soc. *89*, 3782, 3794 (1967).

[41] *I. N. Nazarov* and *I. I. Zaretskaya*, Zh. Obsh. Khim. *27*, 693 (1957) and references therein.

[42] *R. Lehr, D. Kurland*, and *R. B. Woodward*, unpublished observations. *Cf. Dorothy Kurland*, Dissertation, Harvard (1967); *Roland Lehr*, Dissertation, Harvard (1968).

[43] *R. A. W. Johnstone* and *S. D. Ward*, J. chem. Soc. *C, 1968*, 1805. However, *cf. M. J. Bishop* and *I. Fleming*, *ibid. 1969*, 1712.

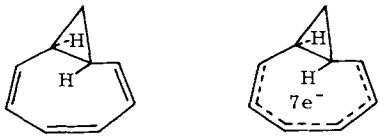
[44] *O. L. Chapman* and *G. L. Eian*, J. Amer. chem. Soc. *90*, 5329 (1968).

[44a] *R. B. Bates* and *D. A. McCombs*, Tetrahedron Letters *1969*, 977.

[45] *R. Rieke, M. Ogliaruso, R. McClung*, and *S. Winstein*, J. Amer. chem. Soc. *84*, 4729 (1966); *cf.* also *T. J. Katz* and *C. Talcott*, *ibid. 88*, 4732 (1966).

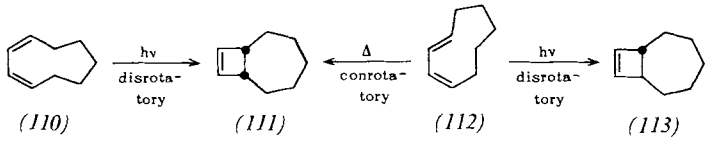
[46] *G. Moshuk, G. Petrowski*, and *S. Winstein*, J. Amer. chem. Soc. *90*, 2179 (1968).

pane electrons. In this case, the steric restraints present do not permit disrotatory displacements, and the seven-electron ion-radical *(109)* is produced.

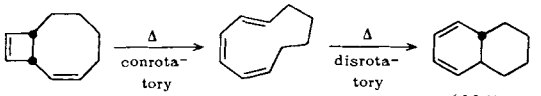


(108) *(109)*

The congeries of electrocyclic reactions *(110)–(116)* was studied by *Fonken* [47], who correctly assumed, but did not observe, the intermediacy of *(115)* in the transformation of *(114)* into *(116)*. In an independent investigation by *Radlick* [48] this course of events has been rigorously established.

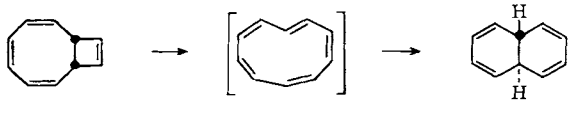


(110) *(111)* *(112)* *(113)*



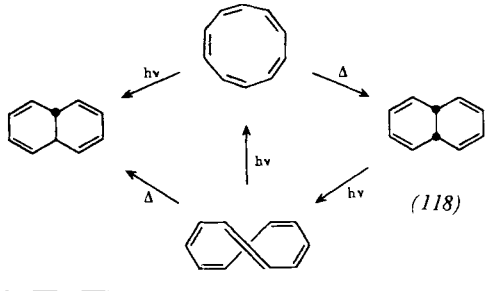
(114) *(115)* *(116)*

A similar sequence of electrocyclic reactions is provided by the pyrolysis of bicyclo[6.2.0]deca-2,4,6,9-tetraene to *trans*-9,10-dihydronaphthalene *(117)* [49].



(117)

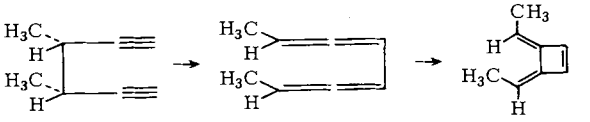
Trans-9,10-dihydronaphthalene is reported to be converted photochemically to a cyclodecapentaene (at –190 °C) which reverts thermally to the *cis*-9,10-dihydronaphthalene *(118)* [50]; in more recent studies the



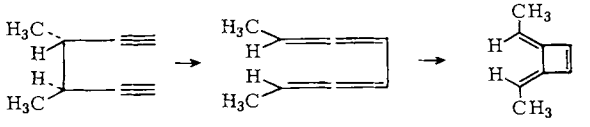
(118)

relationships shown in the diagram have been suggested [50a].

1,5-Alkadiynes undergo intramolecular rearrangement at elevated temperatures to give dimethylene cyclobutenes *(119)*, *(120)*. The observed stereospecificity [51] is

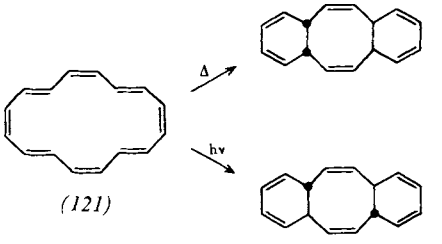


(119)



(120)

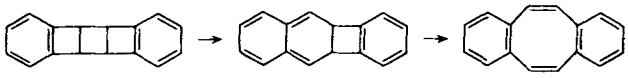
readily accounted for by the sequence of a symmetry-allowed [3,3] sigmatropic shift (see below, Section 7) and a four electron conrotatory electrocyclic reaction.



(121)

The recently synthesized [16]annulene isomerizes thermally and photochemically to two different isomers [52], the products of double disrotatory and double conrotatory closures, respectively.

Of very special interest is the recent discovery of metal catalysis of electrocyclic reactions. For example, the dibenzotricyclooctadiene *(122)* is reported to undergo



(122) *(123)* *(124)*

thermal isomerization to dibenzocyclooctatetraene *(124)* when heated at 180 °C for 4–5 hours [53]. But at room temperature, in the presence of silver ions, the isomerization is complete in 10 seconds [54]. A forbidden disrotatory opening [*(122)→(123)*] is here obviously made allowed by the extra orbitals and electrons available from the complexing metal ion. A similar dramatic reversal of the rules for cycloaddition and cyclore-

[47] *G. J. Fonken*, personal communication; *K. M. Schumate* and *G. J. Fonken*, J. Amer. chem. Soc. *87*, 3996 (1965); *88*, 1073 (1966).

[48] *P. Radlick* and *W. Fenical*, Tetrahedron Letters *1967*, 4901.

[49] *S. Masamune*, *C. G. Chin*, *K. Hojo*, and *R. T. Seidner*, J. Amer. chem. Soc. *89*, 4804 (1967).

[50] *E. E. van Tamelen* and *T. L. Burkoth*, J. Amer. chem. Soc. *89*, 151 (1967). Related cases were studied by *R. C. Cookson*, *J. Hudec*, and *J. Marsden*, Chem. Ind. *1961*, 21, and by *E. Vogel*, *W. Meckel*, and *W. Grimme*, Angew. Chem. *76*, 786 (1964); Angew. Chem. internat. Edit. *3*, 643 (1964).

[50a] *S. Masamune* and *R. T. Seidner*, Chem. Commun. *1969*, 542.

[51] *W. D. Huntsman* and *H. J. Wristers*, J. Amer. chem. Soc. *89*, 342 (1967).

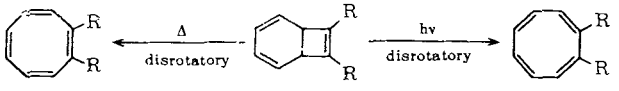
[52] *G. Schröder*, *W. Martin*, and *J. F. M. Oth*, Angew. Chem. *79*, 861 (1967); Angew. Chem. internat. Edit. *6*, 870 (1967).

[53] *M. Avram*, *D. Dinu*, *G. Mateescu*, and *C. D. Nenitzescu*, Chem. Ber. *93*, 1789 (1960).

[54] *W. Merk* and *R. Pettit*, J. Amer. chem. Soc. *89*, 4788 (1967).

version reactions has been observed, and analyzed in terms of orbital symmetry conservation [55].

We now conclude our exemplification of electrocyclic reactions by alluding to two interesting, but as yet unrealized, possibilities. The valence tautomerism of cyclooctatetraene and bicyclo[4.2.0]octatriene is familiar [56]. The requisite disrotatory process may be achieved thermally by an opening of the six-membered ring of *(126)* or photochemically by cleavage of the cyclobutene ring. Since these electrocyclic changes might



(125) *(126)* *(127)*

be faster than bond switching in cyclooctatetraenes [57], it is possible that the alternatives might be experimentally observable.

The as yet unsynthesized cyclodeca-1,2,4,6,7,9-hexaene *(128)* can exist in *meso* and *d,l* modifications. Both stereoisomers should be nearly strainless. The molecules are, of course, valence tautomers of naphthalene *(129)*, and closure to naphthalene is formally an electrocyclic conversion of a hexatriene to a cyclohexadiene. The *meso* form *(130)* is in fact sterically



(128) *(129)*

well-disposed for disrotatory closure to naphthalene; since that indeed is the symmetry-allowed electrocyclic mode, it would be expected that *(130)* would have a



(130) *(131)*

very fragile grasp on existence. By contrast, the molecules of the *d,l* form [*cf. (131)*] have two interesting features. First, a model shows that an interesting conformational flipping can take place, without change of chirality. Second, the geometric circumstances are such that isomerization to naphthalene can be completed only by a symmetry-forbidden conrotatory closure. Consequently, the racemic compound might have reasonable thermal (but not photochemical) stability with respect to transformation into its aromatic isomer. By the same token, *(131)* is the product of the conrotatory cleavage of the 9,10 bond of the naphthalene molecule, and might well be among the products of photochemical transformation of the latter.

6. Theory of Cycloadditions and Cycloreversions

In our discussion of correlation diagrams we have already derived the selection rules for one type of simple two-component cycloaddition, namely, that which is *suprafacial* on each component. A suprafacial process is one in which bonds made or broken lie on the same face of the system undergoing reaction. For example, in an ethylenic *(132)* or cisoid diene system *(133)*, formation of bonds in the senses indicated by the arrows takes place in a suprafacial manner.



(132) *(133)*

A priori however, there are alternative, *antarafacial* processes, in which the newly formed or broken bonds lie on opposite faces of the reacting systems [58] [*cf. (134)* and *(135)*].



(134) *(135)*

We shall use the terms *supra* and *antara* to designate these geometrical alternatives in making general allusions to reaction types, and the letters s and a as subscripts in defining particular reactions. Thus, the cycloadditions mentioned above are *supra,supra* reactions, and the Diels-Alder reaction is a $[4_s+2_s]$ process [59].

A priori, there are in fact four possible modes of combination of the termini of two unlike components in a cycloaddition reaction. Each mode has a characteristic stereochemical consequence, displayed in Figure 21.

In using the principle of orbital symmetry con. ervation to determine whether any cycloaddition is symme-

[55] *F. D. Mango* and *J. H. Schachtschneider*, J. Amer. chem. Soc. *89*, 2484 (1967); *H. Hogeveen* and *H. C. Volger*, *ibid. 89*, 2486 (1967).

[56] *E. Vogel*, *H. Kiefer*, and *W. R. Roth*, Angew. Chem. *76*, 432 (1964); Angew. Chem. internat. Edit. *3*, 442 (1964); *R. Huisgen* and *F. Mietzsch*, Angew. Chem. *76*, 36 (1964); Angew. Chem. internat. Edit. *3*, 83 (1964).

[57] *F. A. L. Anet*, *A. J. R. Bourn*, and *Y. S. Lin*, J. Amer. chem. Soc. *86*, 3576 (1964).

[58] The terms suprafacial and antarafacial were first used in our discussion of sigmatropic reactions; *cf.* ref. [3].

[59] We [Accounts of Chem. Res. *1*, 17 (1968)] and others have earlier used *cis* and *trans* to designate the geometrical relationships here denominated *supra* and *antara*. However, the use of *cis* and *trans* as nomenclatural qualifiers is firmly established, and their employment in different senses – often of necessity, simultaneously – can be cumbersome and confusing, especially in discussing multicomponent combinations.

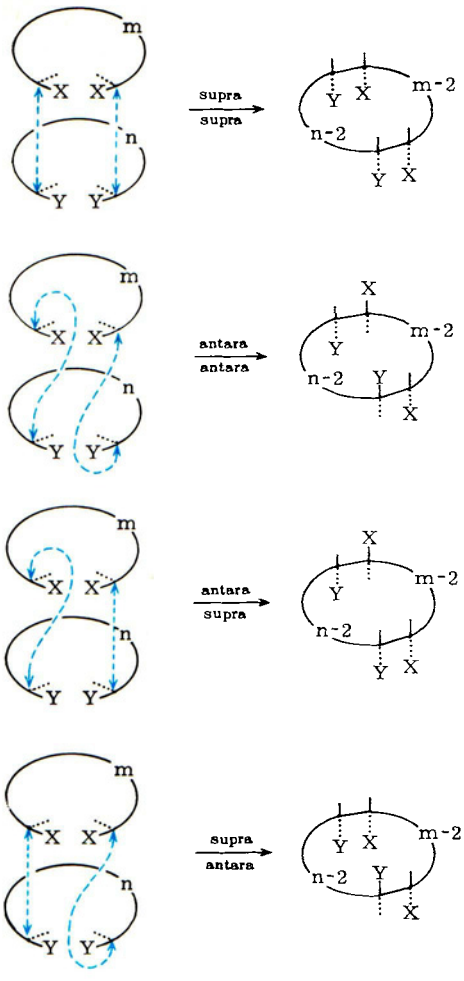


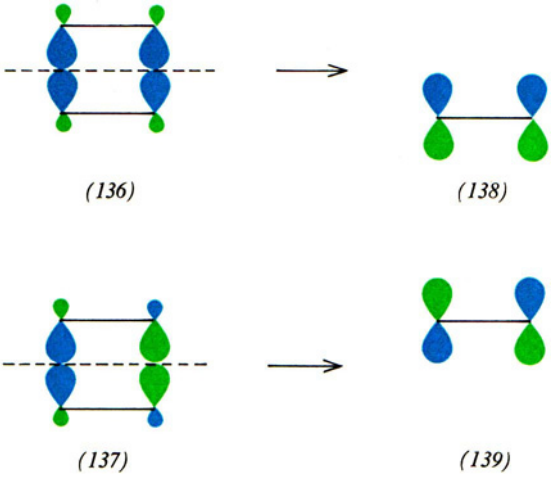
Figure 21. Stereochemical consequences of two-component cycloadditions. The diagrams are purely schematic, and do not reflect the actual geometry of the transition states, which of course differs markedly from case to case. Note that there are two possible *supra,supra* cases when *m* or *n*>2, differing in the mode of approach of the reactants [*exo* and *endo* additions]. Similar circumstances obtain in the other cases. When the two reactants are identical the *supra,antara* and the *antara,supra* processes are indistinguishable.

try-allowed or forbidden, a complete analysis requires that all orbitals – bonding and antibonding – be considered. But a simplified procedure is often useful. First, all relevant reactant electrons are placed in fully delocalized bonding σ molecular orbitals of the *product* of the cycloaddition under examination. Then, if the electrons occupying the σ orbitals can be moved into bonding orbitals of the products of the cycloreversion when the σ bonds are broken with symmetry conservation, the reaction is symmetry-allowed. When the system is one lacking any molecular symmetry, the signs of the orbital lobes are determined by point-to-point transference from an analogous symmetrical system involving the same numbers of orbitals of the same types.

We shall illustrate the procedure for all possible [2+2] reactions. In each case the four relevant electrons are first placed in pairs in the two generalized cyclobutane orbitals *(136)* and *(137)*.

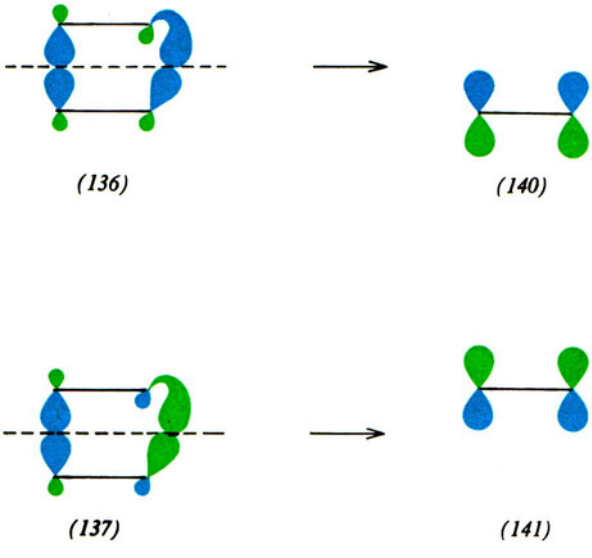


a) The $[2_s+2_s]$ process. When the σ bonds are cleaved, the two electrons in the orbital *(136)* can pass with symmetry conservation into a bonding orbital *(138)* of one ethylene molecule, but those in *(137)* can only enter an antibonding orbital *(139)* of the other ethylene.



The reaction is symmetry-forbidden.

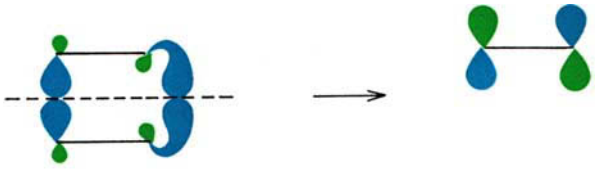
b) The $[2_s+2_a]$ process. When the σ bonds are cleaved, the two electrons in the orbital *(136)*, now shown distorted in a purely formal manner, can pass with symmetry conservation into a bonding orbital *(140)* of one ethylene molecule, while those in *(137)* likewise pass into a bonding orbital *(141)* of the other ethylene.



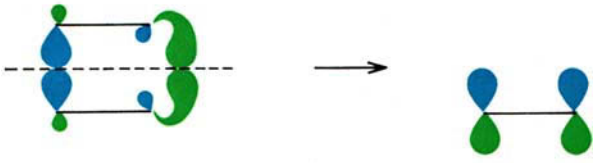
The reaction is symmetry-allowed.

c) The $[2_a+2_a]$ process. When the σ bonds are cleaved, two electrons in the orbital *(136)*, again, but different-

ly, distorted in a purely formal manner, can only enter an antibonding orbital *(142)* of one ethylene molecule, while those of *(137)* pass into a bonding orbital *(143)* of the other.



(136) *(142)*



(137) *(143)*

The reaction is symmetry-forbidden.

It will be noted that the analyses just completed reveal the existence of a concerted symmetry-allowed path for the combination of two ethylenic compounds to give a cyclobutane. What the simplified formal analysis does not render obvious is the actual geometry of approach for the allowed $[2_s+2_a]$ process, which clearly must differ from that of the symmetry-forbidden combinations. When one considers in detail the manner in which maximum overlap of the relevant orbital lobes may be achieved in the $[2_s+2_a]$ reaction, it is clear that the ethylenic components must approach one another orthogonally, as in *(144)*.

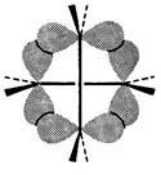


(144)

Bonding orbital of ethylene I + antibonding orbital of ethylene II

Bonding orbital of ethylene II + antibonding orbital of ethylene I

It is further worthy of comment that a complete correlation diagram may be constructed for the allowed $[2_s+2_a]$ reaction, using a two-fold axis of symmetry which passes through the midpoints of both of the ethylenic bonds. Similar circumstances obtain in the case of the $[2_a+2_a]$ reaction. In this case the geometry of approach is that shown in *(145)*, and the reaction is



(145)

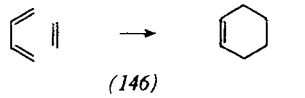
forbidden in the ground state, as deduced above, but allowed for the excited state (*cf.* Figure 22). A final point of much importance is that the principle of conservation of orbital symmetry is valid, *whether or not a formal correlation diagram can be constructed.* For example, no pertinent correlation diagrams can be drawn for the concerted $[4_s+2_a]$ and $[6_s+2_a]$ combinations, but orbital symmetry analysis readily reveals that the former is forbidden and the latter allowed.

The generalized cycloaddition rules are now easily derived. In the addition of an m to an n-electron system the rules shown in Figure 22 must be observed for concerted processes (q is an integer = 1, 2, 3 . . .).

$m+n$	Allowed in Ground State Forbidden in Excited State	Allowed in Excited State Forbidden in Ground State
$4q$	m_s+n_a m_a+n_s	m_s+n_s m_a+n_a
$4q+2$	m_s+n_s m_a+n_a	m_s+n_a m_a+n_s

Figure 22. Selection rules for $[m+n]$ cycloadditions.

An important generalization is that these rules depend not on the total number of orbitals but on the number of electrons. Thus, the [4+2] case may be achieved in each of the ways shown by formulae *(146)–(149)*.



(146)



(147)



(148)



(149)

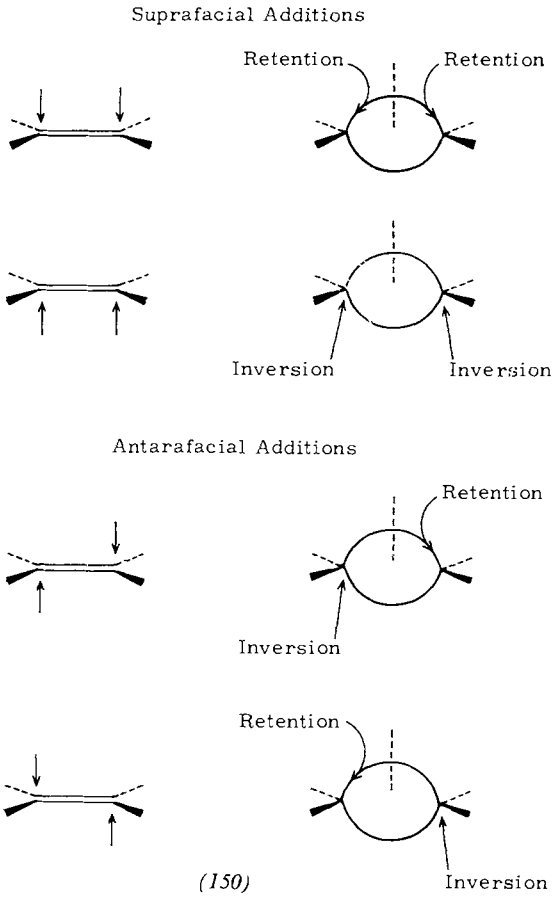
It should be noted also that *supra,antara* and *antara,antara* cycloadditions are not so unlikely as they might appear to be on simple steric grounds.

It remains to point out that σ *bonds can act as components in cycloaddition reactions.* In such cases, the following definitions are important:

a) A σ bond is considered to be involved in a cycloaddition reaction in a *supra* sense if configuration is retained, or inverted, at *both* of its termini in the course of reaction.

b) A σ bond is considered to be involved in a cycloaddition reaction in an *antara* sense if configuration is retained at one, and inverted at the other, terminus in the course of reaction.

The rationale underlying these important conventions will be apparent immediately upon consideration of additions to an ethylene molecule, regarded as containing two σ bonds *(150)*.



(150)

c) We adopt the simple and useful device of denominating the type of orbital involved in a concerted reaction by a subscript preceding the number of electrons in the relevant orbital. Thus

$\sigma 2_a$ $\pi 4_s$ *etc.*

In order to clarify and exemplify these matters, it may be pointed out that the electrocyclic transformation of cyclobutenes to butadienes may be regarded formally as a cycloaddition of a σ bond to a π bond, in either of two equivalent ways.

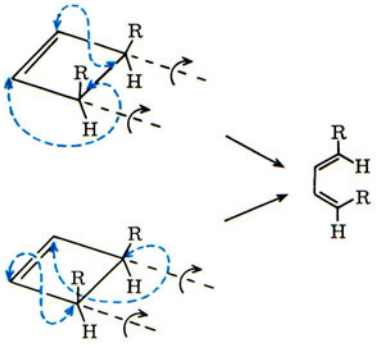


Figure 23. Electrocyclic conversion of cyclobutenes to butadienes as $[\sigma 2_s+\pi 2_a]$ cycloadditions.

a) As shown in Figure 23: *suprafacial* on the σ bond, *antarafacial* on the π bond, *i. e.* $[\sigma 2_s+\pi 2_a]$.

b) As shown in Figure 24: *antarafacial* on the σ bond, *suprafacial* on the π bond, *i. e.* $[\pi 2_s+\sigma 2_a]$.

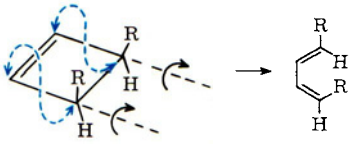
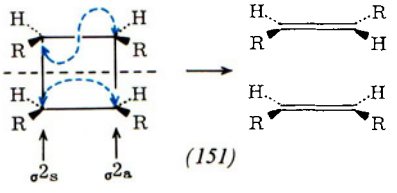


Figure 24. Electrocyclic conversion of cyclobutenes to butadienes as $[\pi 2_s+\sigma 2_a]$ cycloadditions.

It will be observed that whichever formal view is taken, the conrotatory processes represent symmetry-allowed cycloaddition reactions; by contrast, the disrotatory analogues must be regarded as $[\pi 2_s+\sigma 2_s]$ or $[\pi 2_a+\sigma 2_a]$ reactions, which are, of course, symmetry-forbidden in ground states.

As a final illustration we may now characterize the concerted scission of cyclobutane as a $[\sigma 2_s+\sigma 2_a]$ process *(151)*.



(151)

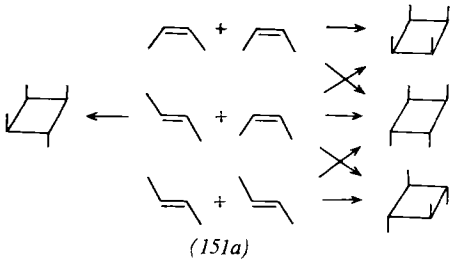
6.1. Cycloadditions and Cycloreversions Exemplified

The [2+2] cycloaddition is one of the most widely observed photochemical reactions, with more than one hundred examples quoted in a recent review [60]. It is likely that many of these reactions are not concerted, probably as a consequence of the fact that competitive relaxation of a participant excited state occurs, with transformation to an equilibrium geometry in which the ethylene moieties are 90 ° out of coplanarity. Thus, *trans* fusions are common in many of the cycloadducts [61]; of course, it should be noted that *trans* fused products would result from concerted symmetry-allowed $[\pi 2_s+\pi 2_a]$ combinations of vibrationally excited ground-state molecules. Nevertheless, two striking examples of concerted symmetry-allowed photo-induced $[2_s+2_s]$ processes have recently been observed. Thus, irradiation of the neat *cis*- and *trans*-2-butenes, separately and in admixture, gives the results shown in *(151a)* [61a].

[60] *R. N. Warrener* and *J. B. Bremner*, Rev. pure appl. Chem. *16*, 117 (1966). See also *W. L. Dilling*, Chem. Rev. *66*, 373 (1966).

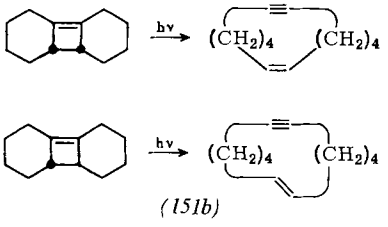
[61] *E. J. Corey*, *J. D. Bass*, *R. LeMahieu*, and *R. B. Mitra*, J. Amer. chem. Soc. *86*, 5570 (1964); *P. E. Eaton* and *K. Lin*, *ibid.* *86*, 2087 (1964); *A. Cox*, *P. de Mayo*, and *R. W. Yip*, *ibid.* *88*, 1043 (1966); *R. Robson*, *P. W. Grubb*, and *J. A. Barltrop*, J. chem. Soc. *1964*, 2153.

[61a] *H. Yamazaki* and *R. J. Cvetanović*, J. Amer. chem. Soc. *91*, 520 (1969).



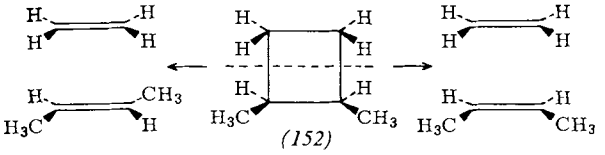
(151a)

Further, a pretty example *(151b)* of the photochemical $[\sigma 2_s+\sigma 2_s]$ reaction has been discovered [61b].



(151b)

It is quite possible that the reversal of the simplest [2+2] cycloaddition, the pyrolysis of cyclobutane, is not a concerted process. The pre-exponential factor of the Arrhenius equation has been regarded as consistent only with a stepwise decomposition through a tetramethylene radical [62]. Further, the fact that pyrolysis of *cis*- or *trans*-dimethylcyclobutane *(152)* yields a mixture of *cis*- and *trans*-butenes, among other products [63], has been adduced in support of the diradical mechanism. Nevertheless, if the cycloreversion is concerted, it must be of the type $[\sigma 2_s+\sigma 2_a]$, and the same stereochemical result would be observed.

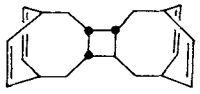


(152)

A beautiful example of the symmetry-allowed $[\pi 2_s+\pi 2_a]$ combination has been discovered by *Kraft* and *Koltzenburg* [64]. The olefin *(153)* dimerizes spontaneously to *(154)*.



(153)

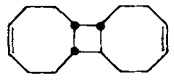


(154)

Earlier observations [65] that *cis*, *trans*-cycloocta-1,5-diene *(155)* dimerizes spontaneously at room temperature to a cyclobutane are less illuminating, since the stereochemistry of the product – now predictable as *(156)* – has not been established.



(155)



(156)

It is worthy of note that when a double bond is twisted about its axis – as it must be in *(153)* and *(155)* – the concomitant orbital twisting is such as distinctly to favor the $[\pi 2_s+\pi 2_a]$ process.

A further very interesting point which emerges from a detailed consideration of the general case (Figure 25) is that the reaction-facilitating twisting motions generate systems of opposite chirality in the two ethylene components. Consequently, *we may predict that the optically active forms of the olefins (153) and (155) will dimerize less readily than the racemic substances.*

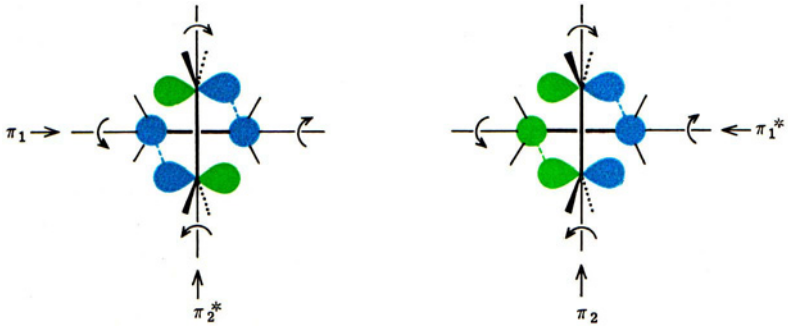


Figure 25. Combination of systems of opposite chirality in the $[\pi 2_s+\pi 2_a]$ cycloaddition of two ethylene molecules.

Bicyclobutanes are produced on irradiation of some substituted butadienes [66] as well as butadiene itself [67]. The bicyclobutanes are remarkably stable, considering their strain energy (*ca.* 69 kcal/mole). The activation energy for isomerization to butadiene is 41 kcal/mole [68,69]. The temptation arises then to consider the rearrangement of bicyclobutane to butadiene

[61b] *J. Saltiel* and *L.-S. Ng Lim*, J. Amer. chem. Soc. *91*, 5404 (1969).

[62] *S. W. Benson* and *P. S. Nangia*, J. chem. Physics *38*, 18 (1963); see also the review by *H. M. Frey* in *V. Gold:* Advances in Physical Organic Chemistry. Academic Press, New York 1966, Vol. 4, p. 170.

[63] *H. R. Gerberich* and *W. D. Walters*, J. Amer. chem. Soc. *83*, 3935, 4884 (1961).

[64] *K. Kraft* and *G. Koltzenburg*, Tetrahedron Letters, *1967*, 4357, 4723.

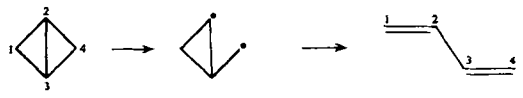
[65] *K. Ziegler*, *H. Sauer*, *L. Bruns*, *H. Froitzheim-Kühlhorn*, and *J. Schneider*, Liebigs Ann. Chem. *589*, 122 (1954); *K. Ziegler* and *H. Wilms*, *ibid. 567*, 1 (1950); *A. C. Cope*, *C. F. Howell*, and *A. Knowles*, J. Amer. chem. Soc. *84*, 3190 (1962).

[66] *W. G. Dauben* and *W. T. Wipke*, Pure appl. Chem. *9*, 539 (1964), and references therein.

[67] *R. Srinivasan*, J. Amer. chem. Soc. *85*, 4045 (1963).

[68] *H. M. Frey* and *I. D. R. Stevens*, Trans. Faraday Soc. *61*, 90 (1965).

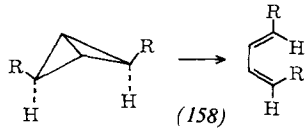
[69] *R. Srinivasan*, *A. A. Levi*, and *I. Haller*, J. phys. Chem. *69*, 1775 (1965).



(157)

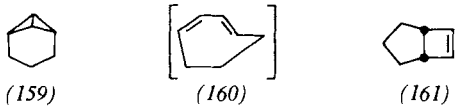
as a non-concerted process proceeding through a diradical intermediate *(157)*.

If, however, the reaction is a concerted one, it is clear that it must be a $[\sigma 2_s+\sigma 2_a]$ process, with the stereochemical consequences shown in *(158)* [70].



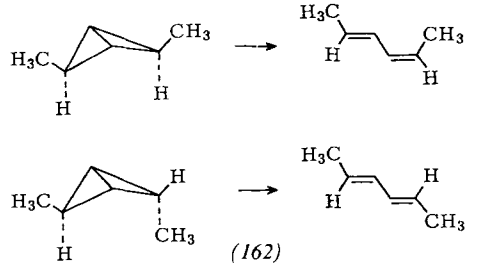
(158)

The evidence is now compelling that the reaction is in fact a concerted $[\sigma 2_s+\sigma 2_a]$ process. A first, indirect indication that such is the case, was provided by the observation that *(159)* is converted to *(161)* on pyrolysis [71]. The result is best accommodated by assuming the



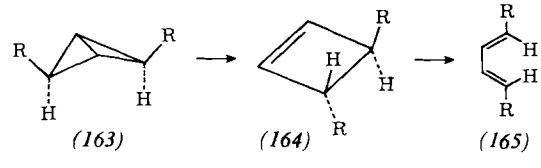
(159) (160) (161)

intermediacy of *(160)*, which closes in a conrotatory fashion to the observed product. The decisive experiment was recently reported by *Closs* and *Pfeffer* [72]. Their results are summarized in *(162)*.



(162)

Remarkably, there exists in principle an alternative pathway relating bicyclobutane and butadiene, with precisely opposite stereochemical consequences. This route *[(163)→(164)→(165)]* entails the intermediacy of a cyclobutene, which then undergoes conrotatory cleavage to the product butadiene. Thermodynamically, the sequence is feasible [73]. In formal terms, the change may be described as involving successive symmetry-allowed $[\sigma 2_s+\sigma 2_a]$ and $[\sigma 2_s+\pi 2_a]$ reactions. The possibility that special substitution patterns – perhaps operating through attendant simple steric effects – may bring this path to light should not be dismissed.



(163) (164) (165)

The reader may find it illuminating to verify for himself the relationships displayed in Figure 26, which presents the stereochemical pattern for all possible symmetry-allowed processes relating bicyclobutanes, cyclobutenes, and butadienes.

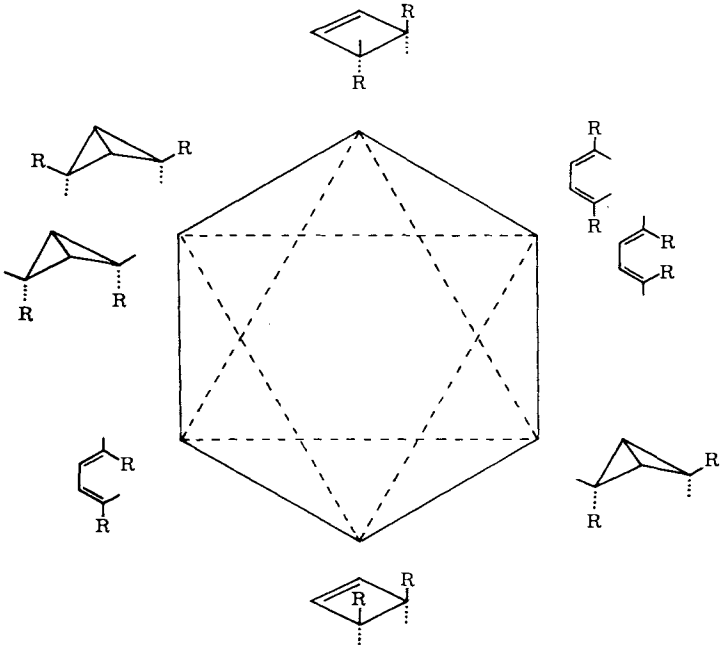


Figure 26. Symmetry-allowed processes relating bicyclobutanes, cyclobutenes, and butadienes. — Allowed ground state paths. --- Allowed excited state paths.

The number of known Diels-Alder reactions – the $[\pi 4_s+\pi 2_s]$ cycloadditions – is legion [74, 75]. Though a diradical mechanism has been advanced on numerous occasions [76], the overwhelming body of experimental facts is consistent only with a concerted mechanism [77].

There is a growing body of photochemical Diels-Alder reactions [78], but in most instances there is no evidence which provides information as to whether the reactions are concerted or not. However, it is very probable that concerted symmetry-allowed excited-state $[\pi 4+\pi 2]$ processes are involved in the ubiquitous conversion of

[70] Similar conclusions have been reached by *Wiberg* on the basis of semi-empirical MO calculations [*K. B. Wiberg*, Tetrahedron *24*, 1083 (1968)].

[71] *K. B. Wiberg* and *G. Szeimies*, Tetrahedron Letters, *1968*, 1235.

[72] *G. L. Closs* and *P. E. Pfeffer*, J. Amer. chem. Soc. *90*, 2452 (1968).

[73] *R. B. Turner, P. Goebel, W. von E. Doering*, and *J. F. Coburn, jr.*, Tetrahedron Letters *1965*, 997.

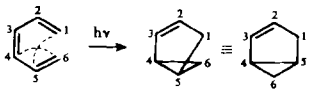
[74] *R. Huisgen, R. Grashey*, and *J. Sauer* in *S. Patai:* The Chemistry of Alkenes. Interscience, New York 1964, p. 739.

[75] *A. Wassermann:* The Diels-Alder Reaction. Elsevier, Amsterdam 1965.

[76] Most recently by *S. W. Benson*, J. chem. Physics *46*, 4920 (1967).

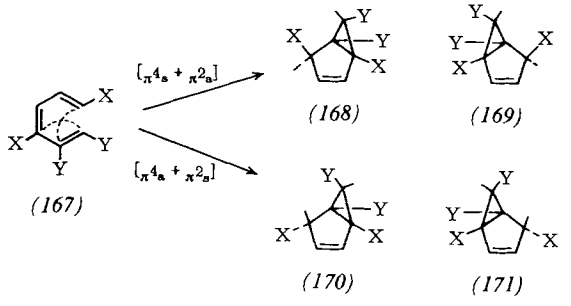
[77] *R. B. Woodward* and *T. J. Katz*, Tetrahedron *5*, 70 (1959).

[78] For example, *G. S. Hammond, N. J. Turro*, and *R. S. H. Liu*, J. org. Chem. *28*, 3297 (1963); *G. S. Hammond* and *R. S. H. Liu*, J. Amer. chem. Soc. *85*, 477 (1963); *D. Valentine, N. J. Turro*, and *G. S. Hammond, ibid. 86*, 5202 (1964); *R. S. H. Liu, N. J. Turro*, and *G. S. Hammond, ibid. 87*, 3406 (1965); *G. O. Schenck, S.-P. Mannsfeld, G. Schomburg*, and *C. H. Krauch*, Z. Naturforsch. *19b*, 18 (1964).



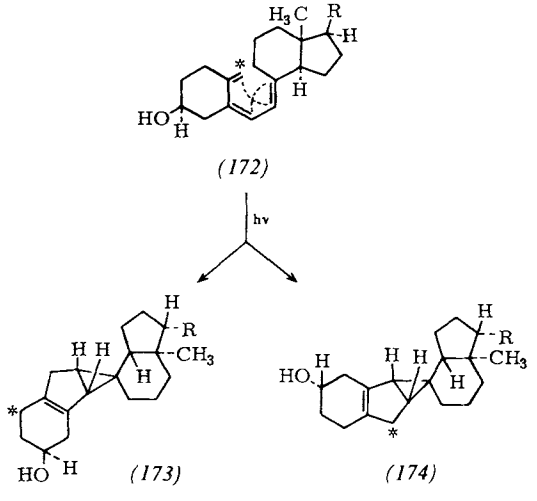
(166)

cis-hexatrienes *(166)* to bicyclo[3.1.0]hexenes [79]. If concerted, these reactions must be either $[\pi 4_s+\pi 2_a]$ or $[\pi 4_a+\pi 2_s]$ processes. Excluding the formation of a *trans* fused bicyclohexene, the stereochemical consequences of the allowed processes are seen from formulae *(167)–(171)*.



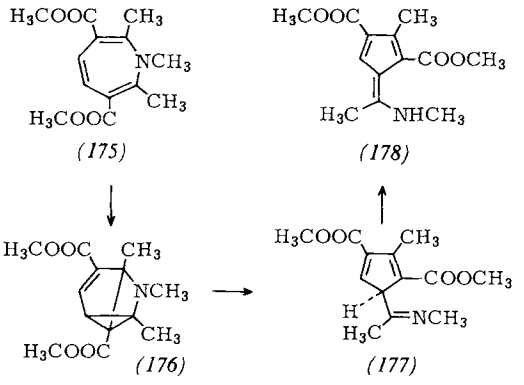
(167) *(168)* *(169)* *(170)* *(171)*

No reaction involving a substance sufficiently extensively labeled as to provide a test of these conclusions has been studied. In vitamin D_2 *(172)*, the top and bottom faces of the triene system are no longer equivalent, and the processes which lead in the general cases to enantiomers must in this instance afford different structures. In fact, irradiation of vitamin D_2 leads to two bicyclohexenes – suprasterol I *(173)* [80] and suprasterol II *(174)* [81]. These structures are precisely those which must result from concerted symmetry-allowed excited-state $[\pi 4_s+\pi 2_a]$ processes, but in the absence of further labeling at the starred atoms it is not possible to discern whether the $\pi 4$ system participates in the reactions in a suprafacial manner.



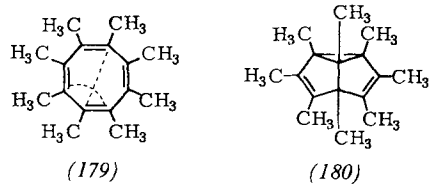
(172) *(173)* *(174)*

A proposed mechanism for the observed transformation of the azepine *(175)* into the fulvene *(178)* invokes the symmetry-allowed ground-state $[\pi 4_a+\pi 2_a]$ reaction *(175)→(176)* [82].

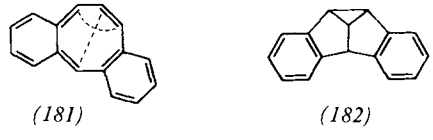


(175) *(178)* *(176)* *(177)*

At elevated temperatures, in the presence of base, octamethylcyclooctatetrasne *(179)* is smoothly converted to octamethylsemibullvalene *(180)* [83]. It seems possible that the base serves merely to protect the reactant from alternative acid-catalyzed changes, and that the reaction is a simple symmetry-allowed $[\pi 4_a+\pi 2_a]$ intramolecular cycloaddition. Further, *Pettit* [84] has made observations which are best interpreted by assuming that dibenzo[*a*,*c*]cyclooctatetraene *(181)* undergoes spontaneous transformation to *(182)*; the special points worthy of note in this case are that the $[\pi 4_a+\pi 2_a]$ reaction is favored both by concomitant loss of *o*-quinoid character as reaction proceeds, and by deviation in *(181)* from normal cyclooctatetraene geometry, induced by the fused six-membered rings. The difficulty of the $-[\pi 4_a+\pi 2_a]$ process [84a] in the absence of favorable steric constraints is shown by the fact that the ketone *(183)* fails to undergo cycloreversion to butadiene and



(179) *(180)*



(181) *(182)*

[79] *J. Meinwald* and *P. H. Mazzocchi*, J. Amer. chem. Soc. *88*, 2850 (1966); *J. Meinwald, A. Eckell*, and *K. L. Erickson, ibid. 87*, 3532 (1965); *H. Prinzbach* and *H. Hagemann*, Angew. Chem. *76*, 600 (1964); Angew. Chem. internat. Edit. *3*, 653 (1964); *H. Prinzbach* and *E. Druckrey*, Tetrahedron Letters *1965*, 2959; *K. J. Crowley*, *ibid. 1965*, 2863.

[80] *W. G. Dauben*, personal communication; *W. G. Dauben, I. Bell, T. W. Hutton, G. F. Laws, A. Rheiner*, and *H. Urscheler*, J. Amer. chem. Soc. *80*, 4116 (1958).

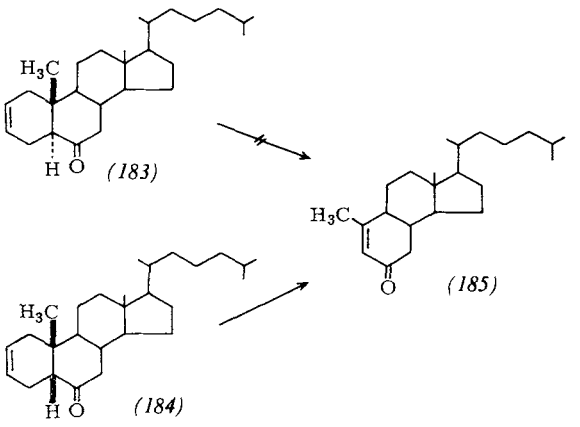
[81] *W. G. Dauben* and *P. Baumann*, Tetrahedron Letters *1961*, 565; *C. P. Saunderson* and *D. C. Hodgkin, ibid. 1961*, 573.

[82] *R. F. Childs, R. Grigg*, and *A. W. Johnson*, J. chem. Soc. *C*, *1967*, 201.

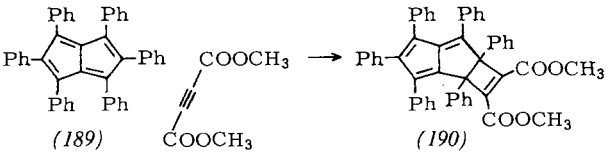
[83] *R. Criegee* and *R. Askani*, Angew. Chem. *80*, 531 (1968); Angew. Chem. internat. Edit. *7*, 537 (1968).

[84] *G. F. Emerson, L. Watts*, and *R. Pettit*, J. Amer. chem. Soc. *87*, 131 (1965); *W. Merk* and *R. Pettit, ibid. 89*, 4787 (1967).

[84a] Here and in the sequel we use the device of placing a negative sign before the bracket whenever a reaction is characterized in terms of its products.



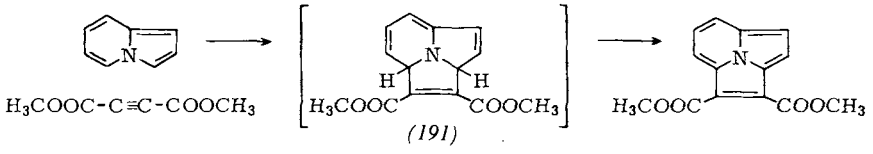
(185) even at 400 °C; the corresponding $-[\pi 4_s+\pi 2_s]$ reaction *(184)*→*(185)* takes place readily [85].

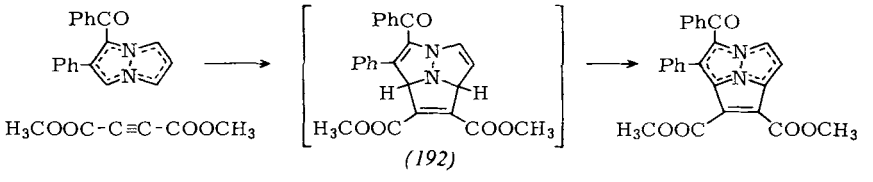


with the acetylenic ester, producing an azulene by way of an adduct *(190)*, as yet not isolated, which is the product of an [8+2] reaction [89].

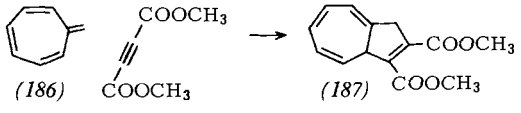
Two unusual [8+2] cycloadditions, discovered by *Boekelheide* [90], are portrayed in *(191)* and *(192)*.

[6+4] Cycloadditions were unknown until our enunciation of the principle of orbital symmetry conservation stimulated the search for them. The cases *(193)*–*(198)* are now known.

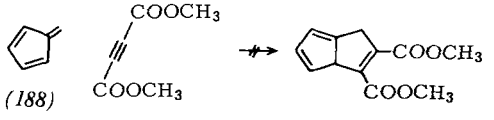




[4+4] Cycloadditions are well known [86]. As yet, they have been encountered only in photochemical reactions, and no detailed stereochemical information is available.



[8+2] Cycloadditions have been relatively rarely observed. Heptafulvene *(186)* readily combines with dimethyl acetylenedicarboxylate [87] to give *(187)*, whereas fulvene *(188)* does not react in a similar sense (note that the $[\pi 6_s+\pi 2_s]$ combination is symmetry-forbidden). Similar reactions of calicenes have been observed [88]. Hexaphenylpentalene *(189)* also combines



[6+6] Cycloadditions of presumed *p*-xylylene intermediates are known [96], but no information is available about the detailed mechanism of the reactions. Irradiation of tropone in acidic solution gives a symmetrical dimer *(199)* [97], which is the product to be expected from a concerted symmetry-allowed excited-state $[\pi 6_s+\pi 6_s]$ combination; the unusual experimental conditions, and the fact that other photoinduced dimerizations of tropone may proceed in a non-concerted fashion [98] suggest caution in adopting the conclusion that the concerted process is in fact involved in the formation of *(199)*.

[85] *H. R. Nace*, personal communication.

[86] *L. A. Paquette* and *G. Slomp*, J. Amer. chem. Soc. *85*, 765 (1963); *P. de Mayo* and *R. W. Yip*, Proc. chem. Soc. *1964*, 84; *D. E. Applequist* and *R. Searle*, J. Amer. chem. Soc. *86*, 1389 (1964); *J. S. Bradshaw* and *G. S. Hammond*, *ibid. 85*, 3953 (1963); *K. Kraft* and *G. Koltzenburg*, Tetrahedron Letters *1967*, 4357.

[87] *W. von E. Doering* and *D. W. Wiley*, Tetrahedron *11*, 183 (1960).

[88] *H. Prinzbach*, *D. Seip*, and *G. Englert*, Liebigs Ann. Chem. *698*, 57 (1966); *H. Prinzbach*, *D. Seip*, *L. Knothe*, and *W. Faisst*, *ibid. 698*, 34 (1966).

[89] *E. Le Goff*, J. Amer. chem. Soc. *84*, 3975 (1962).

[90] *A. Galbraith*, *T. Small*, *R. A. Barnes*, and *V. Boekelheide*, J. Amer. chem. Soc. *83*, 453 (1961); *V. Boekelheide* and *N. A. Fedoruk*, Proc. nat. Acad. Sci. *55*, 1385 (1966).

[91] *K. Houk*, Dissertation, Harvard (1968).

[92] *R. C. Cookson*, *B. V. Drake*, *J. Hudec*, and *A. Morrison*, Chem. Commun. *1966*, 15; *S. Itô*, *Y. Fujise*, *T. Okuda*, and *Y. Inoue*, Bull. chem. Soc. Japan *39*, 135 (1966).

[93] *T. Nozoe*, *T. Mukai*, *K. Takase*, and *T. Takase*, Proc. Japan Acad. *28*, 477 (1952).

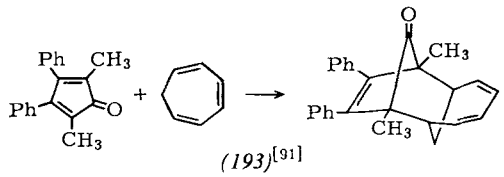
[94] *S. Itô*, *Y. Fujise*, and *M. C. Woods*, Tetrahedron Letters *1967*, 1059.

[95] *L. A. Paquette* and *J. H. Barrett*, J. Amer. chem. Soc. *88*, 2590 (1966).

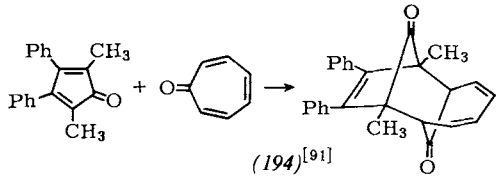
[96] *H. E. Winberg*, *F. S. Fawcett*, *W. E. Mochel*, and *C. W. Theobald*, J. Amer. chem. Soc. *82*, 1428 (1960); *D. J. Cram*, *C. S. Montgomery*, and *G. R. Knox*, *ibid. 88*, 515 (1966); *D. J. Cram*, *C. K. Dalton*, and *G. R. Knox*, *ibid. 85*, 1088 (1963); *D. T. Longone* and *F.-P. Boettcher*, *ibid. 85*, 3436 (1963).

[97] *T. Mukai*, *T. Tezuka*, and *Y. Akasaki*, J. Amer. chem. Soc. *88*, 5025 (1966).

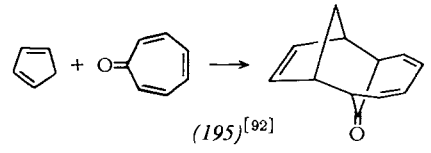
[98] *A. S. Kende* and *J. E. Lancaster*, J. Amer. chem. Soc. *89*, 5283 (1967).



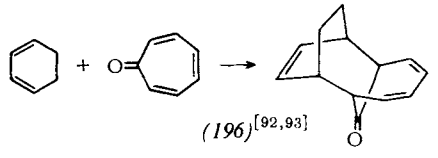
(193)[91]



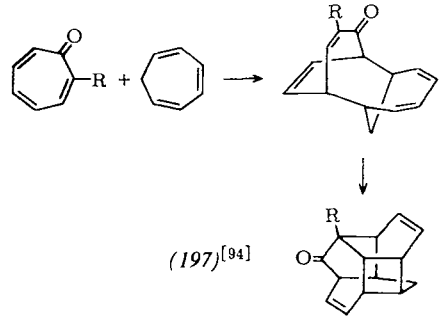
(194)[91]



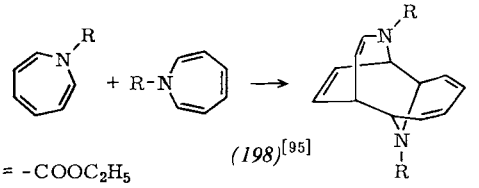
(195)[92]



(196)[92,93]

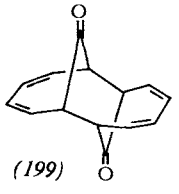


(197)[94]



R = $-COOC_2H_5$ *(198)*[95]

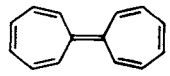
Heptafulvalene *(200)* combines with tetracyanoethylene to give the adduct *(201)*, whose structure has been firmly established by X-ray crystallographic



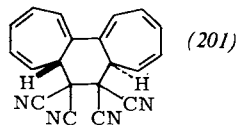
(199)

methods[99]. The adduct is the expected product of the symmetry-allowed ground-state $[\pi 14_a+\pi 2_s]$ process; it may be noted that the twisted shape of the heptafulvalene molecule sets the stage ideally for *antara* addition to the 14-electron system.

[99] *W. von E. Doering*, personal communication.

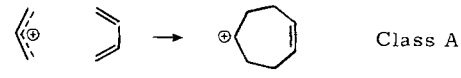


(200)

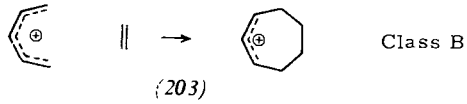


(201)

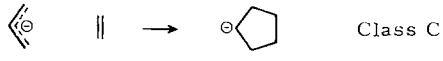
Cycloadditions involving ionic components are as yet not common. Ionic [4+2] cycloadditions may be realized in a number of different ways *[(202)–(204)]*.



(202) Class A



(203) Class B



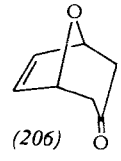
(204) Class C

We may assign to class A the cycloaddition reactions of cyclopropanones *(205)*. It is not unlikely that cyclopropanones are in equilibrium with an isomeric dipolar species. The latter can act as a 2 π-electron system, and,



(205)

predictably, combines with dienes in $[\pi 4_s+\pi 2_s]$ processes – for example, with furans to give adducts of the type *(206)*[100].



(206)

Most recently, the direct combination of the 2-methylallyl cation *(207)* with cyclopentadiene and with cyclohexadiene, to give the bicyclic cations *(208)*, Z = $-CH_2-$ or $-CH_2-CH_2-$, has been demonstrated[101].



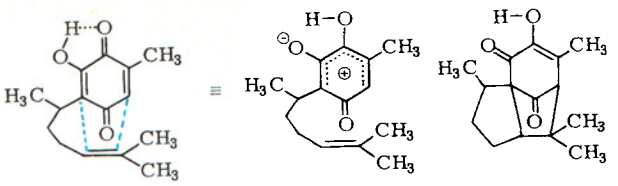
(207) *(208)*

A remarkable cycloaddition of class B is that which occurs in the formation of the pipitzols *(210)* from perezone *(209)*[102].

[100] *R. C. Cookson, M. J. Nye*, and *G. Subrahmanyam*, J. chem. Soc. *C*, *1967*, 473; *1965*, 2009; *A. W. Fort*, J. Amer. chem. Soc. *84*, 2620, 2625, 4979 (1964); *N. J. Turro* and *W. B. Hammond*, *ibid.* *87*, 3258 (1965); *88*, 3672 (1966); *W. B. Hammond* and *N. J. Turro*, *ibid.* *88*, 7880 (1966).

[101] *H. M. R. Hoffmann, D. R. Joy*, and *A. K. Suter*, J. chem. Soc. *B*, *1968*, 57.

[102] *F. Walls, J. Padilla, P. Joseph-Nathan, F. Giral*, and *J. Romo*, Tetrahedron Letters *1965*, 1577.



(209) (210)

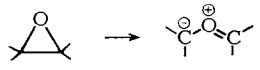
As yet, no simple instances of class C ionic [4+2] cycloadditions have been discovered. However, a very important and numerous group of reactions – the 1,3-dipolar additions [103] – may be placed in this class, since the 1,3-dipolar substances which participate in cycloaddition reactions, although formally neutral molecules, generally function as three-orbital 4π-electron species. *Huisgen*, whose own magnificent researches have transformed 1,3-dipolar addition from an obscure phenomenon, exemplified only by a few curiosities, into a major reaction-type, has presented excellent surveys of the field [103], and has analyzed the process in terms of orbital symmetry conservation [104]. Consequently, it is only necessary here to summarize briefly the major fundamental factors, and to allude to



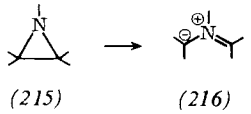
(211) (212)

a few special points. The great majority of known participants in 1,3-dipolar addition reactions are isoelectronic either with ozone *(211)* or with nitrous oxide *(212)*, and unambiguously contain a three-orbital system occupied by four π electrons.

Another class of reactants is represented by labile molecules which undergo ready transformation into species containing the requisite 4-electron system, *e.g.* the carbonyl ylides *(214)* and the azomethine ylides *(216)* are produced by electrocyclic transformation of ethylene oxides *(213)* and ethylene imines *(215)*, substituted in such wise as to facilitate ring cleavage; the



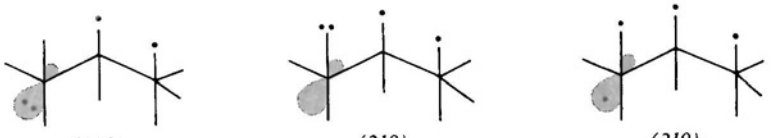
(213) (214)



(215) (216)

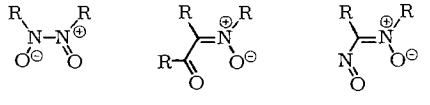
symmetry-determined conrotatory course of these antecedent processes has already been discussed above (*cf.* Section 5).

The situation in respect to the possibility of the participation, in concerted cycloaddition reactions, of fugitive species such as vinylcarbene and its isoelectronic analogues, presents interesting ambiguities. Such molecules may exist in three forms, differing in the number of π electrons occupying the allyl orbital. The first, *(217)*, containing two electrons in the allyl system, may be expected to combine with dienes in a [2+4] process, but independent reaction as a simple substituted carbene could supervene. The second, *(218)*, with four electrons in the allyl system, should undergo normal concerted combination with 2 π-electron molecules, while the third, *(219)*, is an analogue of triplet carbene. These systems have not been extensively studied; it may be expected that their electronic structures, and consequently the courses of their reactions will vary as the backbone atoms, and attached substituents, are varied.



(217) (218) (219)

Brief mention may be made of the possibility of analogues of 1,3-dipolar additions, in which larger numbers of electrons are incorporated in the π system of the dipolar component. As speculative examples, the *cis* form *(220)* of a dimeric nitroso compound, the α-ketonitrones *(221)*, and the α-nitrosonitrones *(222)*, all contain 6 π-electron systems, and concerted combination with dienes is symmetry-allowed.



(220) (221) (222)

A special word of caution should be added in relation to 1,3-dipolar additions. There may well be instances of such reactions in which the complementary polar character of the reactants is sufficiently extreme as to favor two-step combination, proceeding through a relatively stable dipolar intermediate.

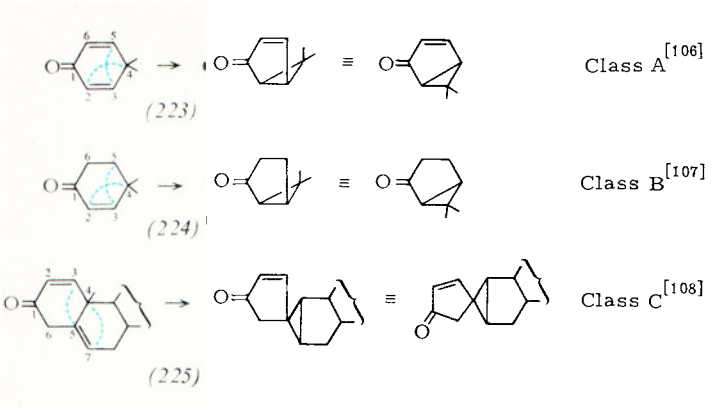
6.2. [2+2] Cycloadditions in the Photochemistry of the Cyclohexadienones and Cyclohexenones

Following the pioneering work of *Barton*, *Jeger*, and their co-workers, the beautiful complexity of the photochemistry of cyclohexadienones and cyclohexenones has been most ably explored by *Chapman*, *Schaffner*, *Schuster*, *Zimmerman*, and their collaborators [105].

[103] *R. Huisgen*, Angew. Chem. *75*, 604 (1963); Angew. Chem. internat. Edit. *2*, 565 (1963); *R. Huisgen*, *R. Grashey*, and *J. Sauer*, in *S. Patai:* The Chemistry of Alkenes. Interscience, New York 1964, p. 739; *R. Huisgen*, Helv. chim. Acta *50*, 2421 (1967).

[104] *A. Eckell*, *R. Huisgen*, *R. Sustmann*, *G. Wallbillich*, *D. Grashey*, and *E. Spindler*, Chem. Ber. *100*, 2192 (1967).

[105] Two recent reviews serve as excellent guides to the elegant structural work accomplished. (a) *K. Schaffner*, Advances in Photochemistry *4*, 81 (1966); (b) *P. J. Kropp*, Organic Photochemistry *1*, 1 (1967).



The primary isomerization processes which have been noted are of three types *(223)–(225)*.

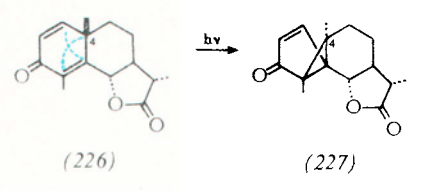
It seems probable that all, and has been established that some, of these cases involve reactions proceeding through n,π* triplet states. It has also been clearly established that the quantum efficiency of the processes varies over a very wide range[109]. Detailed mechanisms have been proposed for these reactions[110]; the most elaborate and ingenious of these mechanisms is that suggested by *Zimmerman*[111].

We would like to examine the stereochemical constraints imposed by conservation of orbital symmetry on these transformations. These constraints are operative only if the reactions are concerted. We are aware of the elegant physical measurements which have been interpreted as supporting the proposed non-concerted mechanisms. But we regard it as worth while to stipulate the stereochemical imperatives associated with concerted paths from the starting materials to the observed products.

Formally, all of the reactions are $[\sigma 2+\pi 2]$ cycloadditions. If they are concerted changes within excited states, such cycloadditions must be $[\sigma 2_s+\pi 2_s]$ or $[\sigma 2_a+\pi 2_a]$ reactions.

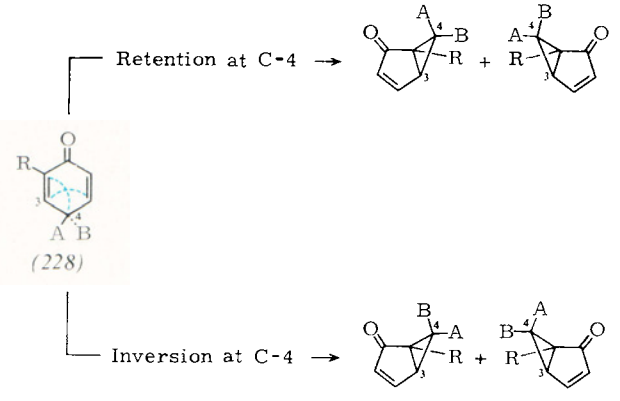
In classes A and B suprafacial participation of double bond 2,3 is a stereochemical impossibility, since it leads to *trans* fused three- and five-membered rings. Consequently, these reactions must follow the $[\sigma 2_a+\pi 2_a]$ course, which requires antarafacial addition at double bond 2,3, and inversion at C-4. In class C the special constraint present in classes A and B is absent. Both $[\sigma 2_a+\pi 2_a]$ and $[\sigma 2_s+\pi 2_s]$ processes are feasible.

Antara addition at the double bond and inversion at the migrating saturated carbon atom is of course precisely what occurs in the classic conversion of santonin



(226) into lumisantonin *(227)*[112]. Unfortunately, in this case the alternative symmetry-forbidden change, taking place with retention at C-4, would lead to a sterically unlikely *trans* ring fusion; consequently, it might be argued that the observed path, though symmetry-allowed, would in any event be imposed by the geometry of the system.

The simplest labeling of the parent cyclohexadienone which would endow it with a center of chirality would also allow in principle a resolution of this question. Consider the consequences of retention or inversion at C-4 on such a chiral cyclohexadienone *(228)*[113]. Inversion or retention at C-4 can each be performed in



two distinct ways, depending on whether the addition at C-3 is on top or bottom. If A and B are different substituents these pathways become distinct, each with its own steric factors. It is thus likely that even a stereospecific process will yield two products in differing proportions. The products of inversion are diastereomeric, and enantiomeric to the products of retention. The actual course followed in the rearrangement of a simple chiral cyclohexadienone has not yet been determined,

[106] *D. H. R. Barton, J. McGhie,* and *R. Rosenberger*, J. chem. Soc. *1961*, 1215; *D. H. R. Barton, P. de Mayo,* and *M. Shafiq, ibid. 1958*, 140, 3314; *D. Arigoni, H. Bosshard, H. Bruderer, G. Büchi, O. Jeger,* and *L. J. Krebaum*, Helv. chim. Acta *40*, 1732 (1957) and other papers referred to in ref. [105].

[107] *W. W. Kwie, B. A. Shoulders,* and *P. D. Gardner*, J. Amer. chem. Soc. *84*, 2268 (1962); *O. L. Chapman, T. A. Rettig, A. A. Griswold, A. I. Dutton,* and *P. Fitton*, Tetrahedron Letters *1963*, 2049; *B. Nann, D. Gravel, R. Schorta, H. Wehrli, K. Schaffner,* and *O. Jeger*, Helv. chim. Acta *46*, 2473 (1963) and other papers referred to in ref. [105].

[108] *B. Nann, D. Gravel, R. Schorta, H. Wehrli, K. Schaffner,* and *O. Jeger*, Helv. chim. Acta *46*, 2473 (1963); *B. Nann, H. Wehrli, K. Schaffner,* and *O. Jeger, ibid. 48*, 1680 (1965).

[109] *H. E. Zimmerman, R. G. Lewis, J. J. McCullough, A. Padwa, S. Staley,* and *M. Semmelhack*, J. Amer. chem. Soc. *88*, 159 (1966); *O. L. Chapman, J. B. Sieja,* and *W. J. Welstead, jr., ibid. 88*, 161 (1966).

[110] *H. E. Zimmerman*, Advances in Photochemistry *1*, 183 (1963); *O. L. Chapman, ibid. 1*, 323 (1963).

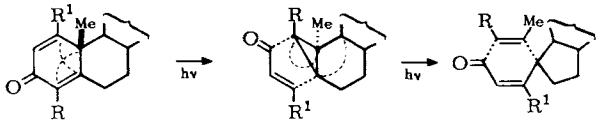
[111] *H. E. Zimmerman*, 17th National Organic Symposium of the American Chemical Society, Bloomington, Indiana, 1960, Abstracts, p. 31; *H. E. Zimmerman* and *D. I. Schuster*, J. Amer. chem. Soc. *83*, 4486 (1961); *84*, 4527 (1962); *H. E. Zimmerman*, Tetrahedron *19*, Supplement 2, 393 (1963).

[112] *D. H. R. Barton, P. de Mayo,* and *M. Shafiq*, J. chem. Soc. *1958*, 140; *D. Arigoni, M. Bosshard, H. Bruderer, G. Büchi, O. Jeger,* and *L. J. Krebaum*, Helv. chim. Acta *40*, 1732 (1957); *W. Cocker, K. Crowley, J. T. Edward, T. B. H. McMurry,* and *E. R. Stuart*, J. chem. Soc. *1957*, 3416; *D. H. R. Barton* and *P. T. Gilham*, J. chem. Soc. *1960*, 4596.

[113] Only the consequences of an addition on the double bond next to R are sketched. Of course the addition on the opposite side is feasible, and will double the number of possible products.

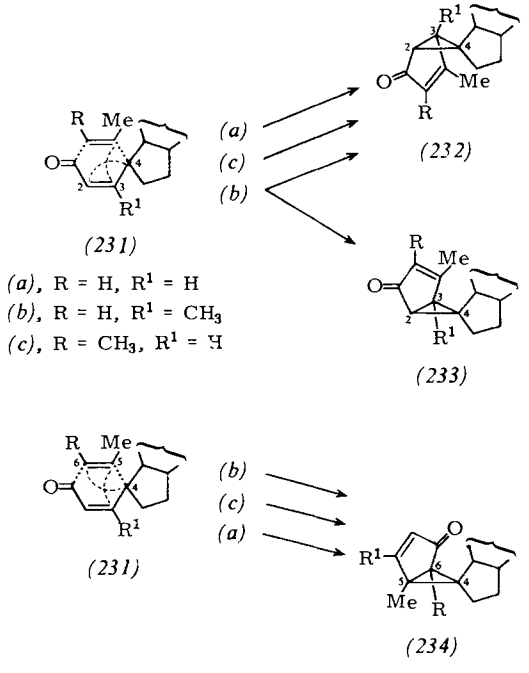
but is being studied by *Schuster*[114] who has independently recognized that the matter is one of great interest.

The versatile field of steroid derivatives appears already to have provided verifications of our predictions. The remarkably rich photochemistry of 1-dehydrotestosterone acetate and its methyl derivatives[115] begins with the now familiar conversion of a 2,5-cyclohexadienone *(229)* into a bicyclo[3.1.0]hexenone *(230)*, and thence to a new cyclohexadienone *(231)* of assigned



(229) *(230)* *(231)*

stereochemistry. On further photolysis *(231)* furnishes two or three isomers, depending on the pattern of substitution. The ingeniously assigned[115] structures of the products are shown in formulae *(232)–(234)*.



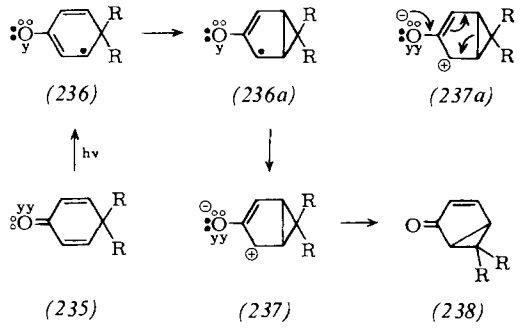
(231)

(a), R = H, R^1 = H
(b), R = H, R^1 = CH_3
(c), R = CH_3, R^1 = H

(232) *(233)* *(234)*

The molecules *(232)*, *(233)*, and *(234)* are all products of $[\pi 2_a + \sigma 2_a]$ processes, precisely as predicted from orbital symmetry considerations for concerted changes; it is especially to be noted that inversion must occur at C-4 during each of the photoisomerizations. For the substitution patterns *(a)* and *(c)* only one product *(232)* of the two which might result from symmetry-allowed changes involving the 2,3 double bond is observed. Similarly, only *(234)* is produced from *(a)* and *(c)* when the 5,6 double bond is implicated. In the case of *(b)*, three of the four possible products of symmetry-allowed processes have been isolated. Not one of the four products which might result from symmetry-forbidden or non-stereospecific processes has been found.

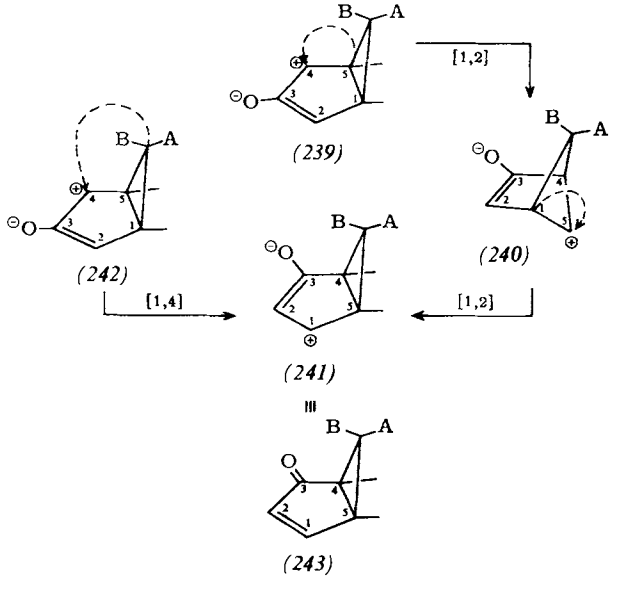
Unfortunately, the Zimmerman mechanism[111] for reactions of class A, illuminated with the insight afforded by orbital symmetry considerations, leads to precisely the same products which must be obtained in a concerted reaction. Formulae *(235)–(238)* show the basic mechanism suggested by *Zimmerman*[111].



(236) *(236a)* *(237a)*

(235) *(237)* *(238)*

The final step, following bond reorganization [*(236)→(236a)*] (symmetry-allowed!) and demotion [*(236a)→(237)*] is formally a ground-state cyclopropylcarbinyl rearrangement; note that reversion of *(237)* to the original cyclohexadienone *(235)* [*cf.* arrows in *(237a)*] is symmetry-forbidden! There are actually two possibilities for the last step of this sequence. They are best described as [1,2n] sigmatropic shifts (*cf.* Section 7, below). The first process consists of two sequential [1,2] shifts [*(239)→(240)→(241)* ≡ *(243)*], while the second is a [1,4] rearrangement [*(242)→(241)* ≡ *(243)*]. Since [1,2] sigmatropic shifts must



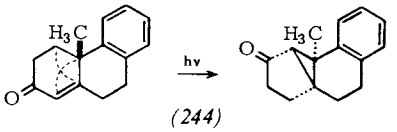
(239) *(240)* *(242)* *(241)* *(243)*

proceed with *retention*, but [1,4] shifts, if forced to be suprafacial, must proceed with *inversion* at the migrating carbon, it follows that the consequences of the two alternatives are stereochemically indistin-

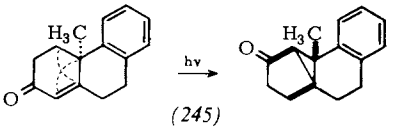
[114] *D. I. Schuster*, personal communication.

[115] *H. Dutler, M. Bosshard*, and *O. Jeger*, Helv. chim. Acta *40*, 494 (1957); *K. Weinberg, E. C. Utzinger, D. Arigoni*, and *O. Jeger*, *ibid. 43*, 236 (1960); *H. Dutler, C. Ganter, H. Ryf, E. C. Utzinger, K. Weinberg, K. Schaffner, D. Arigoni*, and *O. Jeger*, *ibid. 45*, 2346 (1962); *C. Ganter, F. Grzuter, D. Kägi, K. Schaffner*, and *O. Jeger*, *ibid. 47*, 627 (1964); *F. Frei, C. Ganter, D. Kägi, K. Kocsis, M. Miljković, A. Siewinski, R. Wenger, K. Schaffner*, and *O. Jeger*, *ibid. 49*, 1049 (1966).

guishable. Thus, for reactions of class A, either a totally concerted mechanism or a stepwise one involving concerted elements leads to the same stereochemical results. While the physical evidence adduced for the chronology proposed by *Zimmerman* is very impressive, we do not regard it as conclusive: either mechanism remains a possibility.

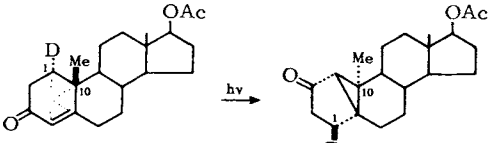


(244)



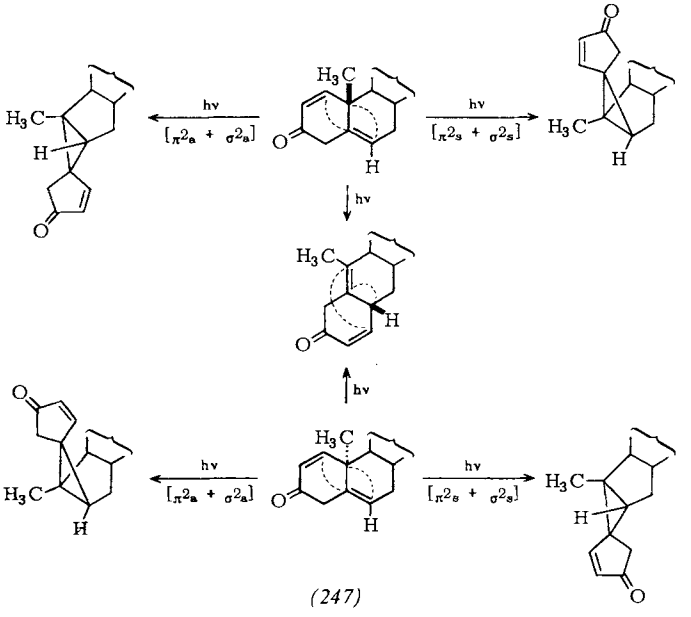
(245)

The photochemical rearrangement of cyclohexenones (the class B reactions) is a highly stereospecific process, and very probably follows a concerted course. Thus, *Chapman* found [116] retention of chirality in the reactions *(244)* and *(245)*.



(246)

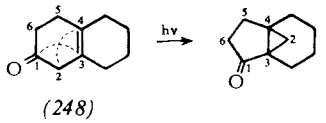
Belluš and *Schaffner* [117] studied the reaction with a very subtle probe; the isomerization of *(246)* proceeds with retention at C-1 and inversion at C-10. The inversion at C-10 is forced by the steric situation, but the retention at C-1 is not, and is clearly inconsistent with a radical fragmentation of the C(1)-C(10) bond.



(247)

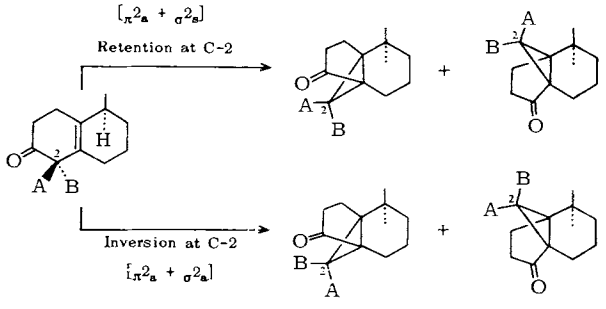
We turn now to reactions of class C. In this case there are no steric restraints operative against either the $[\pi 2_s+\sigma 2_s]$ or the $[\pi 2_a+\sigma 2_a]$ concerted processes. In the beautiful case *(247)* that has been studied [108] just the products predicted for the two allowed cycloadditions are found. But once again avoidance of *trans* fused rings would lead to the very same stereochemical consequences for stepwise processes.

There are two further photochemical transformations of enones which fall into the category of [2+2] cycloadditions. The first of these is an isomerization of a nonconjugated cyclohexenone *(248)* [118].



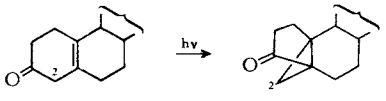
(248)

Formulae *(249)* show the consequences of the stereochemically feasible reactions *antara* on the double bond with options of retention or inversion at C-2.



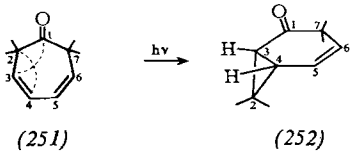
(249)

A steroidal derivative of this class has been photolyzed [118]. Of the two distinct possible products, only that one is produced whose cyclopropane ring is α-oriented *(250)*. Since labels are lacking at C-2, the primary question of retention or inversion is as yet unanswered. We predict that the reaction will be found to proceed with inversion at C-2. Similar circumstances obtain in the case of a further example *[(251)→(252)]* [119].



(250)

There appear to be a number of examples of photochemically induced $[\pi 2_a+\sigma 2_a]$ cycloadditions involving



(251) *(252)*

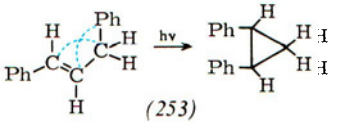
[116] *O. L. Chapman, J. B. Sieja,* and *W. J. Welstead, jr.*, J. Amer. chem. Soc. *88*, 161 (1966).

[117] *D. Belluš, D. R. Kearns,* and *K. Schaffner*, Helv. chim. Acta *52*, 971 (1969).

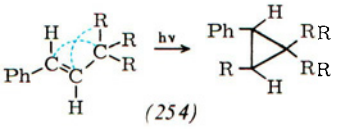
[118] *J. R. Williams* and *H. Ziffer*, Chem. Commun. *1967*, 194, 469; Tetrahedron *24*, 6725 (1968).

[119] *L. A. Paquette, R. F. Eizember,* and *O. Cox*, J. Amer. chem. Soc. *90*, 5153 (1968).

simple olefins and dienes. Thus, *Griffin* [120] observed unusual propylene→cyclopropane cyclizations accompanied by group migrations [*(253)*, *(254)*]. These could well be concerted transformations, but definitive stereochemical information is lacking.

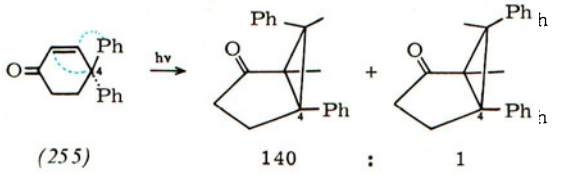


(253)



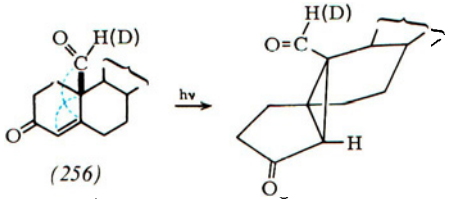
(254)

An instance of this type of reaction in which the stereochemical course has been established is available in the photolysis of 4,4-diphenylcyclohexenone *(255)* [121]. The predominant product is the result of an antarafacial addition on the double bond and inversion at C-4.



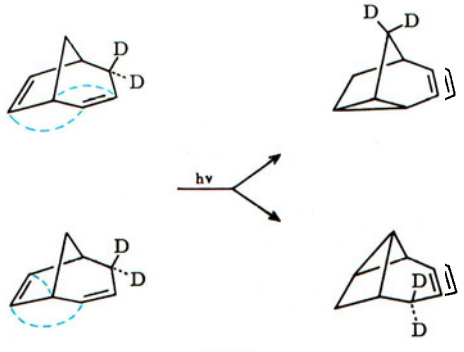
(255) 140 : 1

A probable further example of a $[\sigma 2_a + \pi 2_a]$ reaction has emerged in a recent study of the photolysis of 3,19-dioxo-4-androsten-17β-yl acetate *(256)* [122].



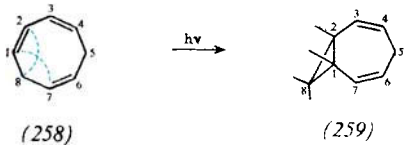
(256)

Still other possible $[\sigma 2_a + \pi 2_a]$ changes, constrained to proceed as such, are available in the case *(257)* studied by *Sauers* [123].

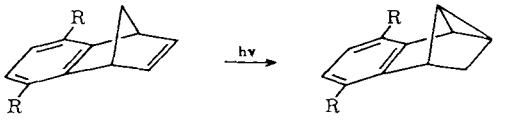


(257)

The formation of *(259)* on photolysis of cyclooctatriene *(258)* is also constrained to follow the $[\pi 2_a + \sigma 2_a]$ course, if concerted; it has been shown that the process occurs without a hydrogen shift [124].

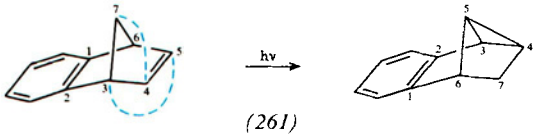


(258) *(259)*

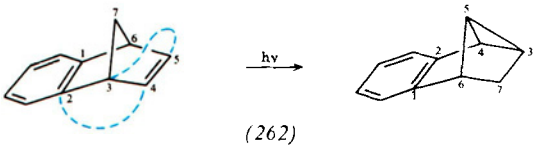


(260)

A related case *(260)* has been observed by *Edman* [125]. A concerted cycloaddition may involve either the σ bond at 3,7 *(261)* or that at 2,3 *(262)*. The concerted



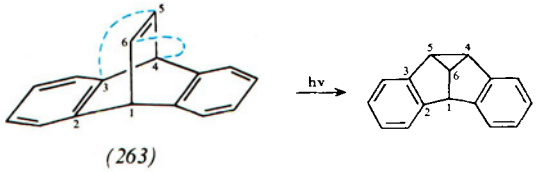
(261)



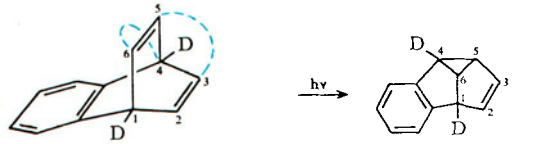
(262)

nature of the reaction could be ascertained using a chiral reactant.

Still other reactions of this type are found in the conversion of a dibenzobicyclo[2.2.2]octatriene *(263)* to a dibenzosemibullvalene [126] and of a labeled benzobicyclo[2.2.2]octatriene *(264)* to a benzosemibullvalene [127]



(263)



(264)

[120] *G. W. Griffin, J. Covell, R. C. Petterson, R. M. Dodson*, and *G. Klose*, J. Amer. chem. Soc. *87*, 1410 (1965); *H. Kristinsson* and *G. W. Griffin, ibid. 88*, 378 (1966).

[121] *H. E. Zimmerman* and *K. G. Hancock*, J. Amer. chem. Soc. *90*, 3749 (1968). See also *H. E. Zimmerman* and *R. L. Morse, ibid. 90*, 954 (1968).

[122] *E. Pfenninger, D. E. Poel, C. Berse, H. Wehrli, K. Schaffner*, and *O. Jeger*, Helv. chim. Acta *51*, 772 (1968).

[123] *R. R. Sauers* and *A. Shurpik*, J. org. Chem. *33*, 799 (1968).

[124] *W. R. Roth* and *B. Peltzer*, Liebigs Ann. Chem. *685*, 56 (1965).

[125] *J. R. Edman*, J. Amer. chem. Soc. *88*, 3454 (1966).

[126] *E. Ciganek*, J. Amer. chem. Soc. *88*, 2882 (1966).

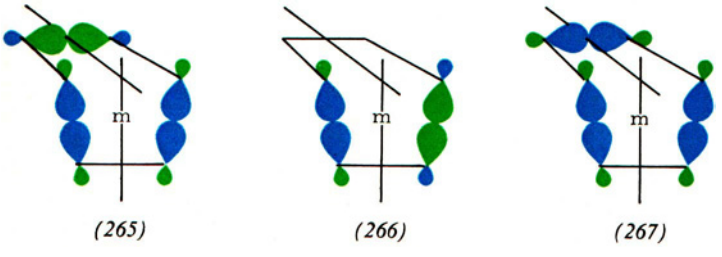
[127] *H. E. Zimmerman, R. S. Givens*, and *R. M. Pagni*, J. Amer. chem. Soc. *90*, 4192 (1968). See also *J. P. N. Brewer* and *H. Heaney*, Chem. Commun. *1967*, 811; *P. W. Rabideau, J. B. Hamilton*, and *L. Friedman*, J. Amer. chem. Soc. *90*, 4465 (1968).

We emphasize that neither of these cases need be concerted; indeed, there is evidence for a stepwise process in the corresponding reaction of the parent barrelene [128].

We must now examine the question of how a process shown to proceed through an excited triplet state of a molecule could possibly be concerted. We believe that orbital symmetry relationships dictate to a molecule in an excited state a certain set of motions, leading to reaction, which are facile, and another set of motions which are difficult. There is no necessity to reach the excited state of products. The symmetry-allowed motions are initiated in the excited state of the reactant. In their course they are accompanied by a radiationless transition to the ground-state of the product. While the physical rationale of such a transition is still lacking, the occurrence of such a process presents no more difficulty than does any other radiationless transition.

6.3. The [2+2+2] Cycloaddition Reaction

Further useful practice in the application of the principle of orbital symmetry conservation may be gained from a detailed consideration of the [2+2+2] concerted cycloaddition (or cycloreversion) reaction; the exercise is made the more valuable through the emergence from it of some new factors, and through the fact that it sets the stage for comparisons, in the sequel, which deepen our understanding of orbital symmetry conservation as a fundamental extension of our knowledge of the phenomenon of chemical bonding.



(265) (266) (267)

Let us consider the decomposition of cyclohexane, through a boat-shaped transition state, into three molecules of ethylene. First, we assign six electrons – those involved in the bonds to be broken – in pairs, to the generalized σ orbitals *(265)*, *(266)*, and *(267)* [*cf.* Section 3.1]. Note that the only symmetry element imposed by the geometry of the system is the mirror plane *m*, and that the orbitals shown are, as required, either symmetric or antisymmetric with respect to that element. *It is of especial importance in this case to observe the fundamental principle that unsymmetrical molecular orbitals are not permissible:* thus, the orbital *(268)* is not real, and must be expunged by addition to its equally unreal conjugate *(269)*. It is also worthy of



(268) (269)

note that the orbitals *(267)* and *(265)* may be replaced by their sum *(270)* and difference *(271)*, with no change in any conclusion which may be discovered from their use; but in general the most obviously informative practice is to make use of those designations

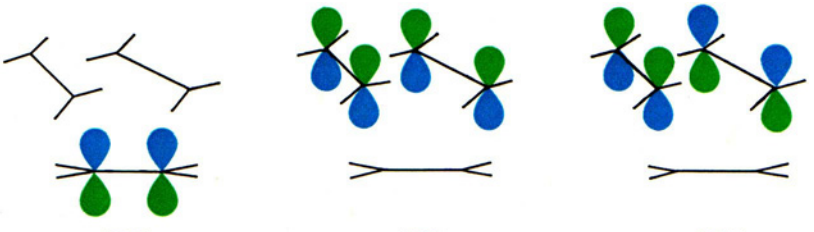


(270) (271)

which most explicitly reveal the largest extent of delocalization in the generalized molecular orbitals – in this case *(265)* and *(267)*, rather than *(270)* and *(271)*. In any event, no other acceptable orbitals are available for the case at hand, and it is important to realize that in consequence there is no element either of arbitrariness or of ambiguity in the conclusions we shall reach.

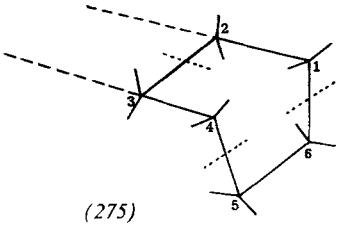
We next note that the six electrons in the π orbitals of the product ethylene molecules must be assigned to the generalized molecular orbitals *(272)*–*(274)*.

One further, and very important, factor must now be recognized. The geometrical relationships among starting material and products, as revealed by inspection of *(275)*, require that in the course of reaction, rotations about the axes 1,2 and 3,4 must take place, in such wise as to bring the substituent groups at C-1 and C-2 on the one hand, and those at C-3 and C-4 on the other, into the common planes in which they lie in the respective product ethylene molecules. *A priori*, on purely geometrical grounds, these displacements might be *conrotatory (276)* or *disrotatory (277)*, and there are, of



(272) (273) (274)

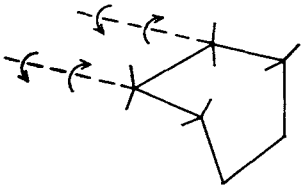
[128] *H. E. Zimmerman, R. W. Binkley, R. S. Givens,* and *M. A. Sherwin,* J. Amer. chem. Soc. *89*, 3932 (1967).



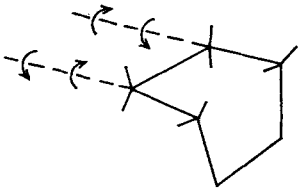
(275)

course, in each case two possibilities [arrows in *(276)* and *(277)*].

Now we are properly prepared to annihilate our cyclohexane molecule. We shall see that there are *two*,



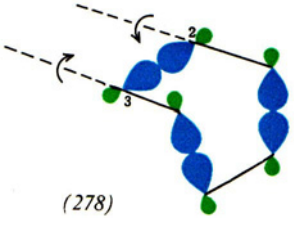
(276)



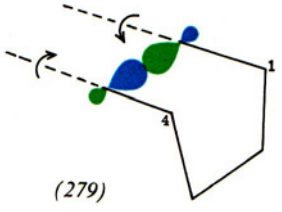
(277)

and only two, symmetry-allowed ways in which this decomposition may occur – given the transition state geometry we have chosen.

1. Let us first permit the two electrons in orbital *(265)* to enter orbital *(272)*, as of course they may do with conservation of orbital symmetry. It is then at once clear that the two electrons in orbital *(267)* must occupy orbital *(278)* of the product array – *and that of the rotational displacements adumbrated above, the inward disrotatory one (278)* must obtain. It remains only to place the remaining σ pair – those in the orbital *(266)*



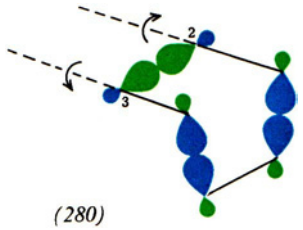
(278)



(279)

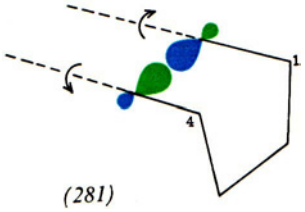
at the outset of reaction – into orbital *(274)* of the product assemblage; a special point here is that mixing of the occupied orbital *(266)* with the unoccupied antibonding backbone σ* orbital *(279)* is consistent with the same inward disrotatory motion about axes 1,2 and 3,4. The symmetry-allowed process which we have now depicted in full detail may be designated a $-[\pi 2_s+\pi 2_s+\pi 2_s]$ cycloreversion reaction. Naturally, a precisely analogous analysis applies to the reverse process – the symmetry-allowed $[\pi 2_s+\pi 2_s+\pi 2_s]$ cycloaddition reaction.

2. Alternatively, let us first permit the two electrons in orbital *(267)* to take up new positions in orbital *(272)* as cycloreversion proceeds Now those in orbital *(265)* have no choice but to enter orbital *(273)* of the product array. And, in sharp contrast to the case discussed above, the cleavage of the backbone bond (2,3) must be accompanied by *outward* disrotatory displacements *(280)*. As before, the remaining pair, occupying orbital



(280)

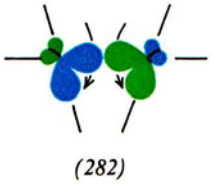
(266), takes up new positions in orbital *(274)*, and, as before, mixing of *(266)* with the unoccupied antibonding backbone σ* orbital *(281)* is consistent with the outward disrotatory motion required by the symmetry relationships between orbitals *(280)* and *(274)*. The process here delineated may be designated a symme-



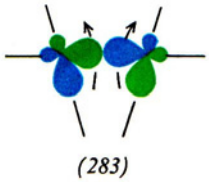
(281)

try-allowed $-[\pi 2_s+\pi 2_a+\pi 2_a]$ cycloreversion reaction; it is the reverse of the allowed $[\pi 2_s+\pi 2_a+\pi 2_a]$ cycloaddition reaction.

Thus, we have found that there are two possible symmetry-allowed [2+2+2] cyclic processes which proceed through a transition state possessing a single plane of symmetry. Structural, steric, and entropy factors may favor one or the other of these paths in various special circumstances. Is one or the other favored by inherent stereoelectronic factors not so far delineated? Indeed, when one considers in greater detail the mixing of the antisymmetric bonding orbital *(266)* with the antisymmetric antibonding orbital *(279)* [or *(281)*], it is found that the *s*, *s*, *s* process is favored over the alternative *s*, *a*, *a* path. Thus, the dihedral angle between the relevant orbitals at the outset of reaction is represented in plan in *(282)* and *(283)*. The geometry of the alternatives indicates clearly that favorable, energy-lowering overlap will develop more readily from the motions depicted in *(282)*, and that the ascent to the transition state



(282)



(283)

will be considerably steeper for the *s*, *a*, *a* process of *(283)* [128a].

Several facets of the [2+2+2] reactions deserve further, if now briefer, consideration. The reader may wish to sharpen his apprehension of symmetry considerations through verifying for himself the propositions which follow:

a) There is a continuum of topologically equivalent symmetry-allowed thermal $[\pi 2_s+\pi 2_s+\pi 2_s]$ processes, whose transition states vary from that depicted above to one whose geometry resembles that of a chair cyclohexane ring.

b) There are two further symmetry-allowed thermal $[\pi 2_s+\pi 2_a+\pi 2_a]$ processes, topologically different from the one described above, which proceed through enantiomeric transition states possessing a two-fold axis of symmetry.

c) There are *no* symmetry-allowed thermal $[\pi 2_s+\pi 2_s+\pi 2_a]$ processes.

d) There are *no* symmetry-allowed thermal $[\pi 2_a+\pi 2_a+\pi 2_a]$ processes.

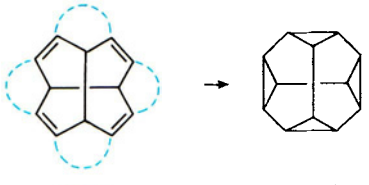
e) For reactions involving occupied antibonding levels – for example, reactions of molecules in photochemically excited states – there are no *s*, *s*, *s* or *s*, *a*, *a* symmetry-allowed [2+2+2] processes, but there are two allowed enantiomeric *s*, *s*, *a*, as well as two permitted, and also enantiomeric, *a*, *a*, *a* paths.

f) Every all-*antara* [2+2+2+. . .] combination is symmetry-forbidden in ground states, and symmetry-allowed for excited states in which the antibonding orbital of one participating ethylene unit is occupied.

Lest any might cavil at the discussion of processes which on casual consideration could appear to be so improbable of realization as only to merit summary dismissal, we may allude to the essentially strain-free, as yet unknown, molecules *(284)* and *(286)*, whose double bonds are so constrained by the frameworks in which they are embedded as to favor photochemical conversion to *(285)* and *(287)*, by the all-*antara* paths mentioned above.



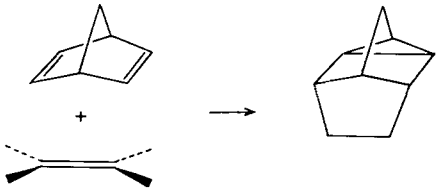
(284) *(285)*



(286) *(287)*

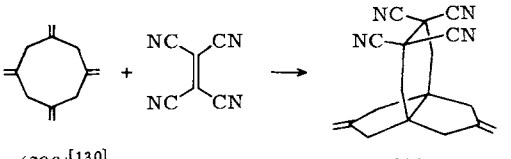
[128a] Since the above was written, this prediction has received elegant experimental confirmation: *J. A. Berson* and *S. S. Olin*, J. Amer. chem. Soc. *91*, 777 (1969).

It remains to exemplify some of the above processes through presentation of selected known cases. Most of those so far discovered fall in the symmetry-allowed thermal *s*, *s*, *s* class. Perhaps best known is the addition of olefins to bicycloheptadiene [129] [*(288)*→*(289)*].

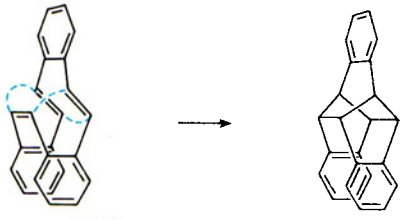


(288) *(289)*

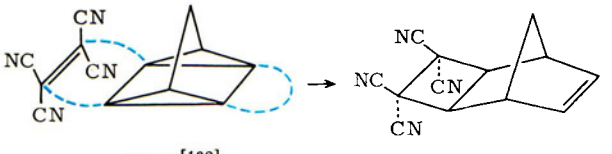
Further examples in this group are the reactions *(290)*→*(291)*, *(292)*→*(293)*, and *(294)*→*(295)*.



(290) [130] *(291)*



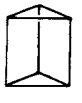
(292) [131] *(293)*



(294) [132] *(295)*

6.4. Prismane

To what does this fantastic molecule *(296)* owe its capacity to survive? In it there is stored at least ninety kilocalories of energy more than is contained in its iso-



(296)

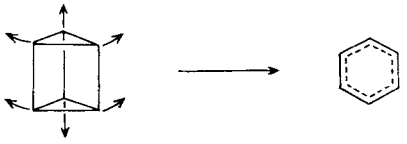
[129] *Inter alia*: *A. T. Blomquist* and *Y. C. Meinwald*, J. Amer. chem. Soc. *81*, 667 (1959); *R. C. Cookson*, *S. S. H. Gilani*, and *I. D. R. Stevens*, Tetrahedron Letters *1962*, 615; *H. K. Hall*, J. org. Chem. *25*, 42 (1960).

[130] *J. K. Williams* and *R. E. Benson*, J. Amer. chem. Soc. *84*, 1257 (1962).

[131] *H. A. Staab*, *F. Graf*, and *B. Junge*, Tetrahedron Letters, *1966*, 743.

[132] *C. D. Smith*, J. Amer. chem. Soc. *88*, 4273 (1966). *Cf.* also *H. Prinzbach*, Pure appl. Chem. *16*, 24 (1968); *H. Prinzbach* and *J. Rivier*, Angew. Chem. *79*, 1102, (1967); Angew. Chem. internat. Edit. *6*, 1069 (1967).

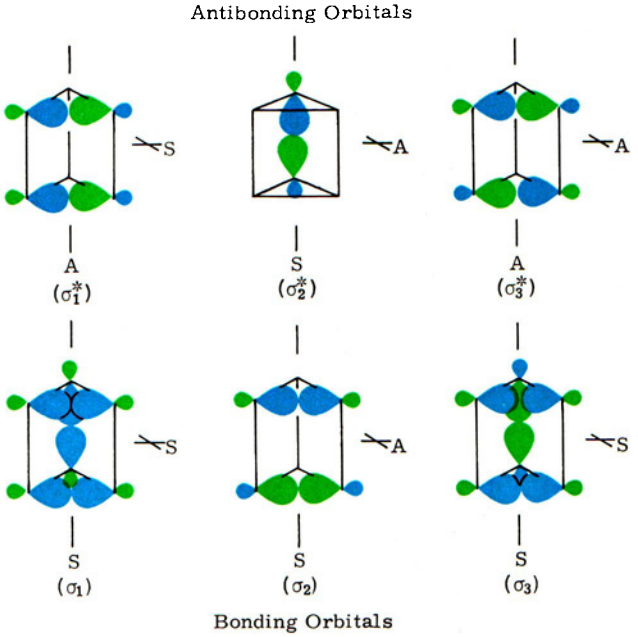
mer benzene[133]; a graceful process of atomic displacements may readily be envisaged for the conversion of the one molecule into the other [*cf. (297)→(298)*]. Yet, no less than a further thirty-three



(297) *(298)*

kilocalories must be added to the already exorbitantly strained hexamethylprismane molecule in order to bring about its conversion to hexamethylbenzene[133]. To the mind uninformed by an appreciation of the limitations placed upon bond-breaking and bond-making processes by orbital symmetry relationships, the excess energy of the prismane molecule must have the aspect of an angry tiger unable to break out of a paper cage.

When we examine this situation in detail from the vantage point of the principle of orbital symmetry conservation, we shall see that there is no paper cage, but rather one quite properly barred to contain its tiger. First, we must construct the generalized molecular orbitals *(299)* into which must be placed the six electrons



(299)

of the three σ bonds which must be broken if prismane is to be converted to benzene.

Now, let us break the three σ bonds, *while conserving the symmetry imposed upon the orbitals of the prismane molecule by its geometry*; note that σ_2 and σ_2^*, of like symmetry, interact to produce a new pair, represented by the sum and the difference of the originals. The specified changes are shown in Figure 27.

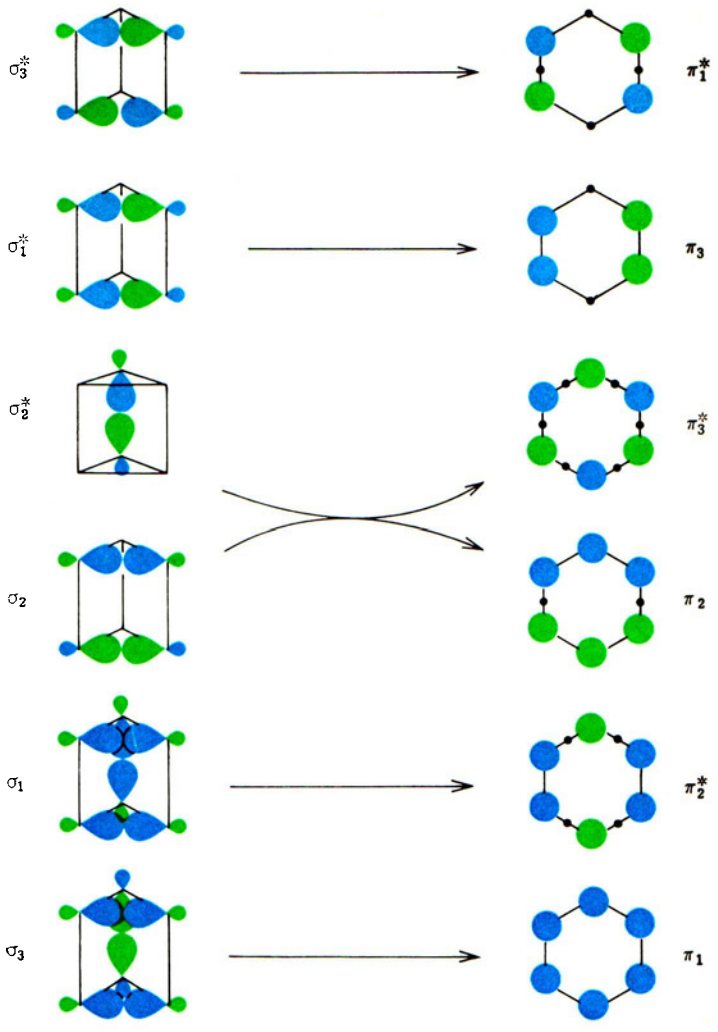


Figure 27. Formation of the π orbitals of benzene from σ orbitals of prismane.

What are the new orbitals thus generated? They are precisely the molecular orbitals of the benzene molecule. But while two of the bonding σ orbitals of prismane (σ_2 and σ_3) have transformed into two bonding orbitals of benzene (π_2 and π_1), *the third becomes an antibonding orbital of the product* ($\sigma_1 \rightarrow \pi_2^*$). Physically, this correlation introduces an antibonding, energy-raising component into the transition state for the transformation. It is that component which makes the transformation of prismane into benzene symmetry-forbidden, and permits the former to exist.

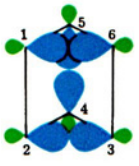
Further insight into the basic nature of symmetry-determined bonding relationships can be gained by amplifying our discussion of prismane in a number of ways. First, let us note that, in a formal sense, the transformation of prismane into benzene might be regarded as a $-[\pi 2_s + \pi 2_a + \pi 2_a]$ cycloreversion reaction [*(300)→(301)*]. We have seen in the preceding section that thermal reactions of that class are symmetry-allowed. What then excludes the prismane→benzene



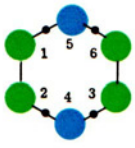
(300) *(301)*

[133] *J. F. M. Oth*, Angew. Chem. *80*, 633 (1968); Angew. Chem. internat. Edit. *7*, 646 (1968); Rec. Trav. chim. Pays-Bas *87*, 1185 (1968).

transformation from the symmetry-allowed class to which it might formally be assigned on casual inspection? When we scrutinize the offending bonding-antibonding correlation of the orbitals σ_1 *(302)* and π_2^* *(303)*, we see at once that it is the development of nodal, antibonding, energy-raising relationships at the 1,5, 5,6 , 2,4 , and 3,4 bonds, necessitated by the presence of the invariant framework σ bonds in the prismane molecule, which differentiates the prismane→benzene



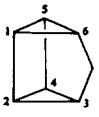
(302)



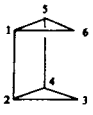
(303)

transformation from the general [2+2+2] cycloreversion reaction. When, as in the latter, those σ bonds are absent, these antibonding, energy-raising components are also absent.

The point may be illustrated further by considering certain molecules closely related to prismane. Consider first quadricyclene *(304)* and the tricyclohexane *(305)*.

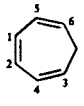


(304)

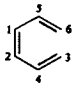


(305)

These molecules might at first sight be expected to be susceptible of symmetry-allowed transformation to cycloheptatriene *(306)* and hexatriene *(307)*, but analysis along the lines set down above shows that, as in the case of prismane, the presence of the framework σ bonds places the changes in the symmetry-forbidden category. It is worthy of note that, in fact, quadricyclene is not converted to cycloheptatriene, even at very high

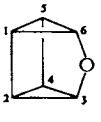


(306)

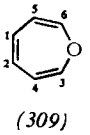


(307)

temperatures [134]. In that light, the oxygen analogue *(308)* is of special interest. In this case, the product of a $-[\pi 2_s+\pi 2_a+\pi 2_a]$ cycloreversion is oxepine *(309)*, and the orbital correlation analogous to that which leads in the other cases to an antibonding level, gives now the highest occupied ground-state level, which is probably weakly bonding. It is gratifying to note that derivatives of the oxa analogue are smoothly transformed to oxepines when heated [135,136].

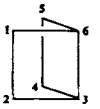


(308)



(309)

Another relative of the prismane molecule is the bicyclo[2.2.0]hexane *(310)*. In this case, lacking as it does σ



(310)



(311)

bonds joining C-1 to C-5, and C-2 to C-4, no offensive nodes develop as the transition state for $-[\pi 2_s+\pi 2_a+\pi 2_a]$ cycloreversion is approached; consequently, the thermal transformation of *(310)* to ethylene and butadiene *(311)* is symmetry-allowed. In fact, it has not as yet been observed. When the unsubstituted bicyclohexane



(312)



(313)

itself is heated, it is converted to 1,5-hexadiene *(312)* [137] – either by a two-step mechanism involving an intermediate *(313)*, or by a symmetry-allowed $[\sigma 2_s+\sigma 2_a]$ path.

6.5. [2+2+2+2] Cycloadditions

The $[\pi 2+\pi 2+\pi 2+\pi 2]$ cycloaddition reaction is symmetry-allowed:

a) For ground state reactants, when an *odd* number of components is involved in a suprafacial manner.

b) For reactions in which one component is in an excited state, when an *even* number of components is involved in a suprafacial manner.

Obviously, entropy factors render polymolecular reactions of this type very highly improbable. Just as obviously, this difficulty can be surmounted by the manoeuvre of building all the components into a single molecule, geometrically prepared for their eventual dispersal. Such examples have already been mentioned above [*(284)* and *(286)*].

Symmetry-allowed many-component fragmentations are also opposed by a special factor; for each σ bond which is transformed into a π bond an endothermicity of some twenty kilocalories must be expected.

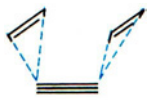
There are instances of $[\pi 2+\pi 2+\pi 2+\pi 2]$ cycloadditions masquerading as other processes. Consider for exam-

[134] *H. Prinzbach* and *J. Rivier*, Tetrahedron Letters *1967*, 3713.

[135] *H. Prinzbach, M. Argüelles*, and *E. Druckrey*, Angew. Chem. *78*, 1057 (1966); Angew. Chem. internat. Edit. *5*, 1039 (1966).

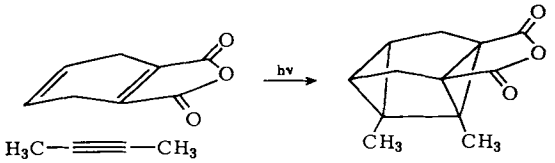
[136] *H. Prinzbach, P. Vogel*, and *W. Auge*, Chimia *21*, 469 (1967).

[137] *C. Steel, R. Zand, P. Hurwitz*, and *S. G. Cohen*, J. Amer. chem. Soc. *86*, 679 (1964).

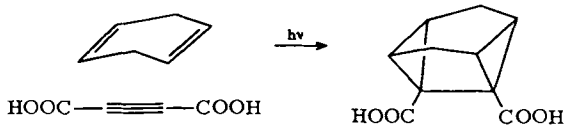


(314)

ple the double cycloaddition of an acetylene to two ethylenes *(314)*. Examination of the orbitals reveals that the two acetylene π bonds are acting independently. At least two such reactions [*(315)→(316)* and *(317)→(318)*] have been observed [138,139].

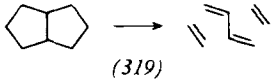


(315) (316)



(317) (318)

An amusing fragmentation would be the reaction *(319)*; the analogous decomposition of pentalene to di-



(319)

acetylene and two acetylenes has been suggested in the literature as a theoretical possibility [140]; we now recognize this to be a symmetry-forbidden thermal process.

We defined as a sigmatropic change of order [i,j] the migration of a σ bond, flanked by one or more π electron systems, to a new position whose termini are $i-1$ and $j-1$ atoms removed from the original bonded loci, in an uncatalyzed intramolecular process. Thus, the well-known Claisen and Cope rearrangements are sigmatropic changes of order [3,3].

A priori, there are two topologically distinct ways of effecting a sigmatropic migration. These are illustrated in Figure 28 for the [1,5] shifts of a hydrogen atom. In the first, *suprafacial* process, the transferred hydrogen atom is associated at all times with the same face of the π system. In the second, *antarafacial* process, the migrating atom is passed from the top face of one carbon terminus to the bottom face of the other.

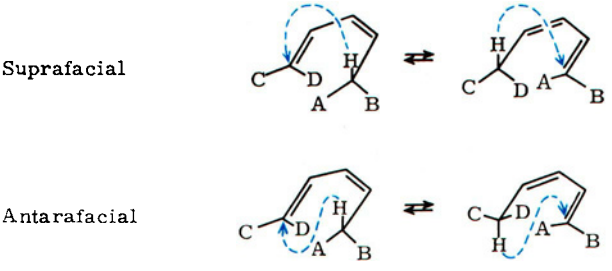


Figure 28. Suprafacial and antarafacial [1,5] shifts of a hydrogen atom.

For the analysis of these reactions correlation diagrams are not relevant since it is only the transition state and not the reactants or products which may possess molecular symmetry elements. We shall present several equivalent methods for analyzing these reactions.

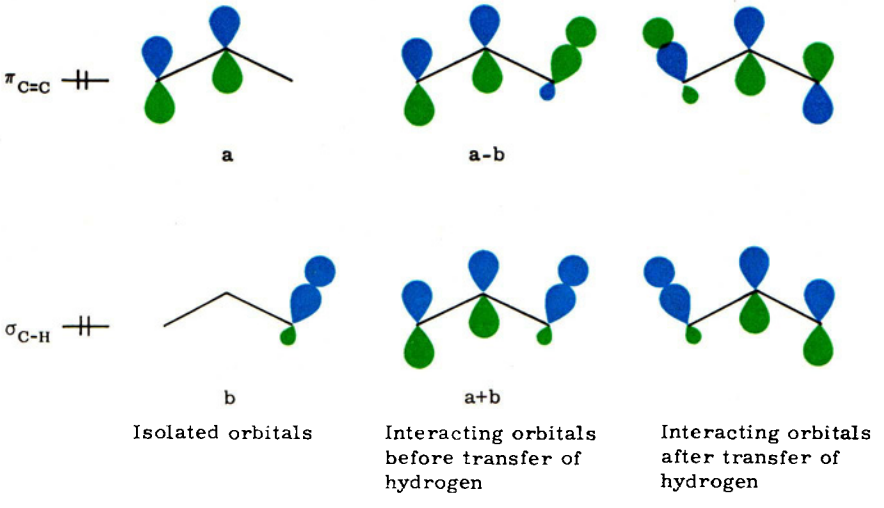


Figure 29. Conservation of orbital symmetry in a suprafacial [1,3] hydrogen shift.

1. The use of the principle of *conservation of orbital symmetry* is here illustrated for the case of a supra-

[138] *R. Askani*, Chem. Ber. *98*, 3618 (1965).

[139] *M. Takahashi, Y. Kitahara, I. Murata, T. Nitta*, and *M. C. Woods*, Tetrahedron Letters *1968*, 3387.

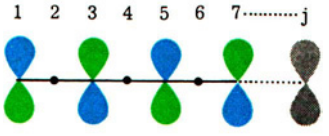
[140] *H. C. Longuet-Higgins* in: Theoretical Organic Chemistry. The Kekulé Symposium. Butterworths, London 1959, p. 17.

facial [1,3] hydrogen shift. The relevant correlations are shown in Figure 29. Clearly, two electrons can enter a bonding orbital, either σ or π, of the product, but the other two must be placed either in a σ^* or a π^* orbital, if orbital symmetry is to be conserved. *The reaction is symmetry-forbidden.*

2. In the [1,j] sigmatropic migration of hydrogen within an all-*cis*-polyene framework [*(320)*→*(321)*], one may envisage the transition state as made up by the combination of the orbital of a hydrogen atom with those of a radical containing $2k+3$ π electrons. The highest oc-

$$\underset{(320)}{R_2\overset{1}{C}=\overset{2}{C}H\text{-}(CH=CH)_k\text{-}\overset{j}{C}HR_2} \rightarrow \underset{(321)}{R_2\overset{1}{C}H\text{-}(CH=CH)_k\text{-}CH=CR_2}$$

cupied orbital of the framework system is the nonbonding allylic orbital which possesses the symmetry shown in *(322)*. Consider a hydrogen atom bonding to



(322)

the termini of such systems. In order to avoid a high energy orbital in the transition state, it is required that positive overlap between the framework orbital and the migrating hydrogen orbital be maintained. The result is symmetry-allowed suprafacial migration for odd k, while the antarafacial path must be followed for even k.

3. Let us now examine the transition state from a different, but equivalent, viewpoint. First, we write down an explicit three-center bond involving the termini of the carbon chain and the migrating hydrogen atom. The three-center bond has the typical level pattern indicated in Figure 30. There remains a $2k+1$ π orbital system in the carbon chain. The molecular orbitals of

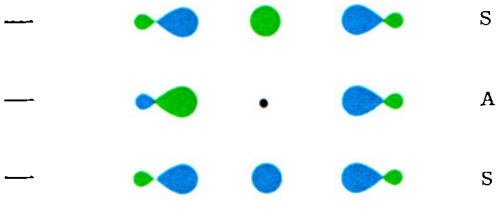


Figure 30. Orbital relationship in a three-center bond. Note that the symmetry labels are invariant whether a mirror plane or a two-fold axis of rotation is used as the basis for classification.

this remnant are next classified with respect to the symmetry element (two-fold axis or mirror plane) present in the transition state. There now arise two cases, differing in the symmetry of the nonbonding orbital of the remnant. In the first case (Figure 31) this orbital is antisymmetric and interacts strongly with the central orbital of the three-center bond. In the second case (Figure 32) the remnant orbital is symmetric and cannot interact in a similar way. The presence of the interaction

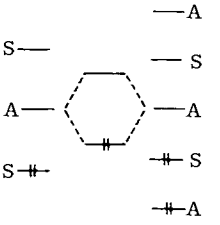


Figure 31. Interaction of nonbonding antisymmetric levels of three-center bond and remnant, for the antarafacial [1,7] shift of a hydrogen atom ($k = 2$).

typically stabilizes one level, and destabilizes the other. Now, since there are in all $2k+4$ electrons to be accommodated $-2k$ electrons in bonding polyenyl levels, and

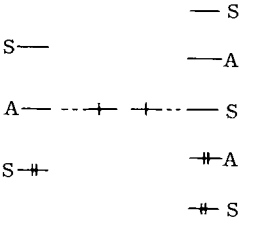


Figure 32. Noninteraction of nonbonding levels of three-center bond and remnant, for the suprafacial [1,7] shift of a hydrogen atom ($k = 2$).

2 in the lowest orbital of the three-center bond – there remain 2 electrons to be placed in the lower component of this interacting pair. It follows that for the ground-state reaction, the first case is symmetry-allowed. Thus, in general, in order that the nonbonding orbital of the $(2k+1)$-orbital remnant π system shall be antisymmetric under the appropriate symmetry operation, these reactions must proceed through a transition state having a mirror plane when k is odd, or one having a two-fold axis when k is even.

For excited-state reactions, as in the cases of electrocyclic reactions and cycloadditions, the selection rules are precisely reversed, as compared with those for ground states.

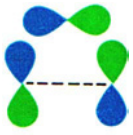
For sigmatropic changes of order [i,j] in which both i and j are greater than 1, the migrating group of the above analyses consists of more than one atom, and appropriate topological distinctions must be made in

$i+j$	Ground State	Excited State
$4q$	antara-supra supra-antara	supra-supra antara-antara
$4q+2$	supra-supra antara-antara	antara-supra supra-antara

Figure 33. Selection rules for sigmatropic reactions of order [i,j] with i and $j > 1$.

relation to *both* π systems through which the σ bond is moving. The selection rules are summarized in Figure 33.

In the above treatment of [1,j] sigmatropic changes, we have considered only those cases in which a σ orbital of the migrating group interacts with a π system in the transition state, and migration occurs *with retention of configuration at the shifting site*. When the migrating group possesses an accessible π orbital and is not so substituted as to create an impossible steric situation in the transition state, alternative processes using that π orbital must be considered. Clearly, such changes *must proceed with inversion at the migrating center* [*cf. (323)*], and the selection rules are precisely reversed from those given in Figure 33.



(323)

A number of special points pertinent to sigmatropic changes should be noted.

a) Antarafacial processes are obviously impossible for transformations which occur within small or medium-sized rings.

b) Distortion of the carbon framework, with concomitant impairment of coupling within the π system, may render a symmetry-allowed process difficult or impossible of realization; for example, this factor makes the antarafacial process difficult or perhaps impossible in the [1,3] case, but is not an impediment for the [1,7] reaction.

c) A cyclopropane ring may replace a π bond in the framework system for a sigmatropic change.

d) Orbital symmetry arguments are applicable to sigmatropic changes within ionic species. Thus, the suprafacial [1,2] shift within a carbonium ion is symmetry-allowed and is very well known. The predicted [1,4] shift with inversion of the migrating group, within a but-2-en-1-yl cation has recently been observed. We may expect that the [1,6] shift within a hexa-2,4-dien-1-yl cation will take place through a readily accessible suprafacial transition state.

It remains to point out that the insights afforded by the discussions presented in the preceding sections allow us to view sigmatropic changes as cycloaddition reactions. Thus, the [1,3] sigmatropic process *(324)*→*(325)*



(324) *(325)*

is a $[\sigma 2+\pi 2]$ reaction, and the [3,3] sigmatropic rearrangement *(326)*→*(327)* is a $[\pi 2+\sigma 2+\pi 2]$ concerted cycloaddition.



(326) *(327)*

From this standpoint, let us now examine in detail the stereochemical aspects of the [1,3] sigmatropic change. We know that the symmetry-allowed processes must fall in either the $[\sigma 2_s+\pi 2_a]$ or the $[\sigma 2_a+\pi 2_s]$ class. All of the possibilities are shown in Figure 34. It is at once apparent that the first two alternatives depicted in Figure 34 are simply different ways of regarding one and the same physical process. Consequently, the analysis yields, as it must, precisely the conclusions reached in our prior discussions of sigmatropic reactions.

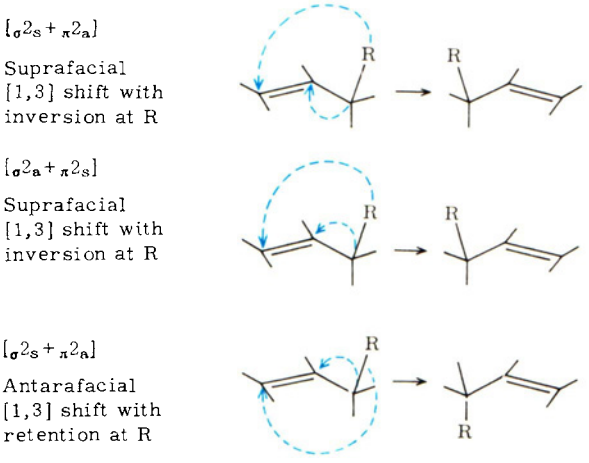


Figure 34. Stereochemical possibilities in sigmatropic [1,3] shifts.

7.1. Sigmatropic Reactions Exemplified

Few thermal uncatalyzed [1,3] shifts are known [141]. Those which formally might be considered in this category, such as the vinylcyclopropane→cyclopentene rearrangement, proceed with such high activation energies (*ca.* 50 kcal/mole) that the energy surface for concerted reaction cannot be far removed from that for alternative stepwise processes. None the less, *Berson* and *Nelson* [142] recently made the dramatic observation that *(328)* undergoes a concerted symmetry-allowed suprafacial [1,3] shift, *with inversion at the migrating center* [starred in *(328)*], to give *(329)*, at 307 °C.

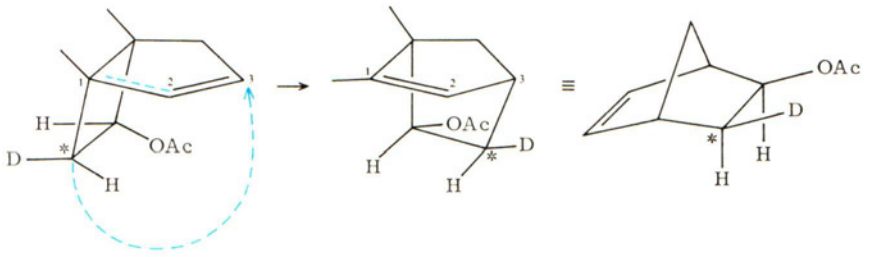
The triene *(330)* owes its relative stability [143] to the requirement of a symmetry-forbidden [1,3] shift for an uncatalyzed rearrangement to toluene.

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[141] For example, [1-^{14}C]-propylene does not rearrange to [3-^{14}C]-propylene: *B. Sublett* and *N. S. Bowman*, J. org. Chem. *26*, 2594 (1961).

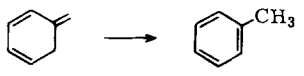
[142] *J. A. Berson* and *G. L. Nelson*, J. Amer. chem. Soc. *89*, 5303 (1967); *J. A. Berson*, Accounts Chem. Res. *1*, 152 (1968).

[143] *W. J. Bailey* and *R. A. Baylouny*, J. org. Chem. *27*, 3476 (1962).



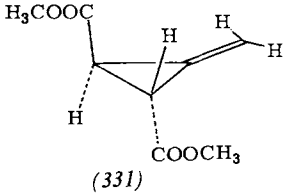
(328) (329)

The rearrangement of the ester *(331)* of Feist's acid is an especially interesting [1,3] sigmatropic transformation. Studies on the optically active substance have demonstrated that the reaction occurs with high stereospecificity [144]. Of the two *a priori* possible symmetry-allowed skeletal processes – [1,3] suprafacial migration with inversion at the migrating atom, and [1,3] antarafacial shift with retention – the latter is rendered inaccessible by the constraints imposed by the σ skeleton.

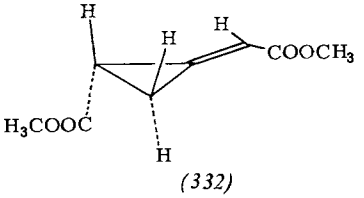


(330)

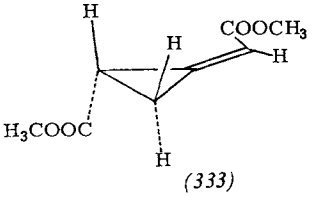
Since substituents are present, the allowed and accessible process may be realized in two electronically identical, but sterically different, ways. Consequently, we may predict that *(331)* must be transformed into *(332)* and/or *(333)*; the evidence is now conclusive [144] that the two isomers actually produced are the predicted ones.



(331)

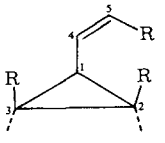


(332)

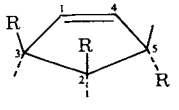


(333)

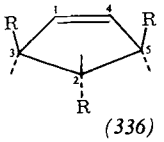
We have mentioned above that the activation energy for the vinylcyclopropane→cyclopentene conversion [145,146] is *ca.* 50 kcal/mole [146]. The bond-breaking process in cyclopropane itself requires an activation energy of 63 kcal/mole [147]; allylic stabilization has been estimated at *ca.* 13 kcal/mole [148]. Consequently, if full use be made of the available allylic stabilization energy in a diradical intermediate, a two step, non-concerted path for the conversion of vinylcyclopropane to cyclopentene is not thermodynamically unreasonable. Some preliminary studies have yielded results consistent with such a mechanism [149]. Nevertheless, in view of the recently established occurrence of symmetry-allowed concerted processes, despite extraordinarily unfavorable geometric constraints, it is worth while to consider the stereochemical consequences of the possible concerted processes for the vinylcyclopropane→cyclopentene change. Consider the maximally labeled derivative *(334)*; the symmetry-allowed reactions are:



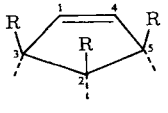
(334)



(335)



(336)



(337)

a) an antarafacial [1,3] shift of bond 1,2 to C-5, with retention at C-2, leading to *(335)*;

b) a suprafacial [1,3] shift of bond 1,2 to C-5, with inversion at C-2, leading to *(336)*.

The isomer *(337)* cannot be produced in a symmetry-allowed process.

Photochemical [1,3] rearrangements, symmetry-allowed as suprafacial shifts, have been observed in a large number of cases [150].

[144] *W. von E. Doering*, personal communication; *cf. E. F. Ullman*, J. Amer. chem. Soc. *82*, 505 (1960).

[145] *C. G. Overberger* and *A. E. Borchert*, J. Amer. chem. Soc. *82*, 1007 (1960).

[146] *M. C. Flowers* and *H. M. Frey*, J. chem. Soc. *1961*, 3547, *R. J. Ellis* and *H. M. Frey*, *ibid. 1964*, 959, 4188; *C. J. Elliot* and *H. M. Frey*, *ibid. 1965*, 345; *A*, *1966*, 553; *C. A. Wellington*, J. physic. Chem. *66*, 1671 (1962); *H. M. Frey* and *D. C. Marshall*, J. chem. Soc. *1962*, 3981; *G. R. Branton* and *H. M. Frey*, *ibid. 1966*, 1342.

[147] *B. S. Rabinowitch*, *E. W. Schlag*, and *K. B. Wiberg*, J. chem. Physics *28*, 504 (1958); *B. S. Rabinowitch* and *E. W. Schlag*, J. Amer. chem. Soc. *86*, 5996 (1960).

[148] *K. W. Egger*, *D. M. Golden*, and *S. W. Benson*, J. Amer. chem. Soc. *86*, 5420 (1964).

[149] *M. R. Willcott* and *V. M. Cargle*, J. Amer. chem. Soc. *89*, 723 (1967); *W. R. Roth*, personal communication.

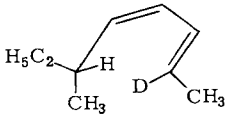
[150] *W. G. Dauben* and *W. T. Wipke*, Pure appl. Chem. *9*, 539 (1964). *J. J. Hurst* and *G. M. Whitham*, J. chem. Soc. *1960*, 2864; *R. C. Cookson*, *V. N. Gogte*, *J. Hudec*, and *N. A. Mirza*, Tetrahedron Letters *1965*, 3955; *W. F. Erman* and *H.C. Kretschmar*, J. Amer. chem. Soc. *89*, 3842 (1967); *R. F. C. Brown*, *R. C. Cookson*, and *J. Hudec*, Tetrahedron *24*, 3955 (1968); *R. C. Cookson*, Chemistry in Britain *5*, 6 (1969); *E. Baggiolini*, *H. P. Hamlow*, *K. Schaffner*, and *O. Jeger*, Chimia *23*, 181 (1969).

Specific thermal [1,5] shifts have been observed in a great number of cases [151]. The simplest case of a [1,5] shift in a 1,3-pentadiene was studied by *Roth* and *König* [152]. They compared the rearrangements of *(338)* and *(339)*, and observed a large kinetic isotope

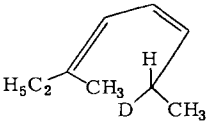


(338) *(339)*

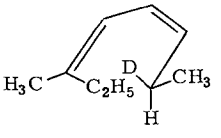
effect of 12.2 at 25 °C, consistent with a highly symmetrical transition state in a concerted process. The activation energy for the rearrangement is in the neighborhood of 35 kcal/mole. Direct confirmation of the concerted, suprafacial character of the [1,5] sigmatropic shift of a hydrogen atom has been most elegantly provided by the same investigators [153], who demonstrated the completely stereospecific conversion of *(340)* into *(341)* and *(342)*.



(340)



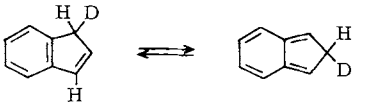
(341)



(342)

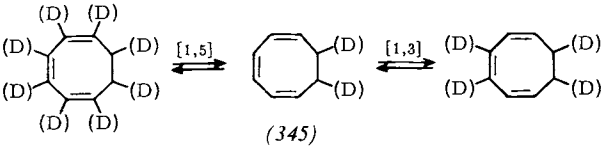
Numerous sequential stereospecific [1,5] shifts have been observed in cyclopentadienes and cycloheptatrienes [154–156].

Roth has beautifully shown the absolute preference for [1,5] over [1,3] shifts in cyclic systems. Thus, a [1,5] shift scrambles the deuterium label in *(343)* over all nonaromatic positions at elevated temperatures [155], despite the necessity of proceeding through the unstable isoindene *(344)*. In sharp contrast, the base-catalyzed reaction proceeds with a stereospecific [1,3] shift [157].



(343) *(344)*

Still another test for the possible occurrence of a thermal [1,3] shift proved negative [158]. The 7,8 dideuterium labeled cycloocta-1,3,5-triene *(345)*, through a series of reversible [1,3] sigmatropic shifts, involving the isomeric cycloocta-1,3,6-triene, would distribute the label statistically over all ring positions. On the other hand, a sequence of [1,5] shifts would place the label in positions 3, 4, 7, and 8 only; the latter result is experimentally observed.



(345)

Photochemical [1,5] shifts of as yet undetermined stereochemistry are known in open, but *not* in cyclic hydrocarbons [159] and in heterocycles [160].

Berson and *Willcott* [161] have observed a remarkable series of isomerizations of methyl-substituted cycloheptatrienes. Their results, summarized in Figure 35, are consistent with a sequence of [1,5] sigmatropic rearrangements and electrocyclic reactions. Our prediction is that the suprafacial [1,5] shifts must proceed

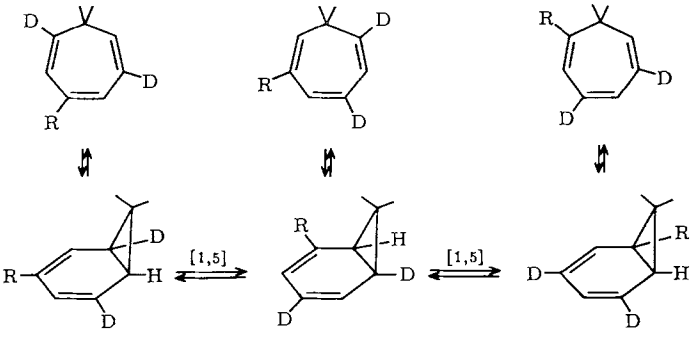


Figure 35. Isomerizations of methyl-substituted cycloheptatrienes through sequences of [1,5] sigmatropic rearrangements and electrocyclic reactions.

with retention at the shifting center. This condition implies that in each shift substituents on the cyclopropane ring pivot 180 °. The beautiful experimental test proposed but as yet not completed by *Berson* and *Willcott* [161] necessitates the pyrolysis of an optically active compound *(346)*. Symmetry-forbidden [1,5]

[151] References to the literature may be found in *D. S. Glass, R. S. Boikess*, and *S. Winstein*, Tetrahedron Letters *1966*, 999. An interesting recently discovered [1,5] shift of a methyl group is described by *R. Grigg, A. W. Johnson, K. Richardson*, and *K. W. Shelton*, Chem. Commun. *1967*, 1192; *cf.* also *V. Boekelheide* and *E. Sturm*, J. Amer. chem. Soc. *91*, 902 (1969).

[152] *W. R. Roth* and *J. König*, Liebigs Ann. Chem. *699*, 24 (1966). See also *H. Kloosterziel* and *A. P. ter Borg*, Rec. Trav. Chim. Pays-Bas *84*, 1305 (1965).

[153] *W. R. Roth* and *J. König*, personal communication.

[154] *V. A. Mironov, E. V. Sobolev*, and *A. N. Elizarova*, Tetrahedron *19*, 1939 (1963); *S. McLean* and *R. Haynes*, Tetrahedron Letters *1964*, 2385.

[155] *W. R. Roth*, Tetrahedron Letters *1964*, 1009.

[156] *A. P. ter Borg, H. Kloosterziel*, and *N. van Meurs*, Rec. Trav. Chim. Pays-Bas *82*, 717, 741, 1189 (1963); *E. Weth* and *A. S. Dreiding*, Proc. chem. Soc. *1964*, 59; *K. W. Egger*, J. Amer. chem. Soc. *89*, 3688 (1967).

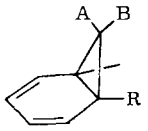
[157] *G. Bergsson* and *A. Weidler*, Acta chem. scand. *17*, 1798 (1963); *A. Weidler, ibid. 17*, 2724 (1963); *A. Weidler* and *G. Bergsson, ibid. 18*, 1484, 1487 (1964); *J. Almy, R. T. Uyeda*, and *D. J. Cram*, J. Amer. chem. Soc. *89*, 6768 (1967), and references therein.

[158] *W. R. Roth*, Liebigs Ann. Chem. *671*, 25 (1964).

[159] For example: *R. Srinivasan*, J. Amer. chem. Soc. *84*, 3982 (1962); *K. J. Crowley*, Proc. chem. Soc. *1964*, 17; *H. Prinzbach* and *E. Druckrey*, Tetrahedron Letters *1964*, 2959.

[160] *E. F. Zwicker, L. I. Grossweiner*, and *N. C. Yang*, J. Amer. chem. Soc. *85*, 2671 (1963); *G. Wettermark*, Photochem. Photobiol. *4*, 621 (1965); *K. R. Huffman, M. Loy*, and *E. F. Ullman*, J. Amer. chem. Soc. *87*, 5417 (1965); *G. Büchi* and *N. C. Yang, ibid. 79*, 2318 (1957).

[161] *J. A. Berson* and *M. R. Willcott, III*, J. Amer. chem. Soc. *87*, 2751, 2752 (1965); *88*, 2494 (1966).



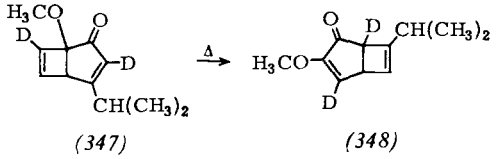
(346)

shifts with inversion – the course which would be followed were the principle of least motion determinative – would result in racemization, while the predicted shifts with retention would lead to no loss of optical activity (Figure 36).



Figure 36. Schematic top view of the possible placements of substituents on a cyclopropane ring migrating around a cyclohexadiene ring by a series of [1,5] sigmatropic shifts, with retention (left) or inversion (right). Note that for clarity the cyclopropane rings are assumed to be perpendicular to the plane of the page, and are not seen.

The Cope and Claisen rearrangements, both [3,3] sigmatropic shifts, are such common reactions that we could not possibly do justice to the many examples studied [162]. These rearrangements are allowed both in a *supra-supra* and an *antara-antara* manner. At first sight it would seem obvious that the transition state for the latter is sterically unattainable. And yet an *antara-antara* Cope rearrangement has been observed; *Mukai* [163]

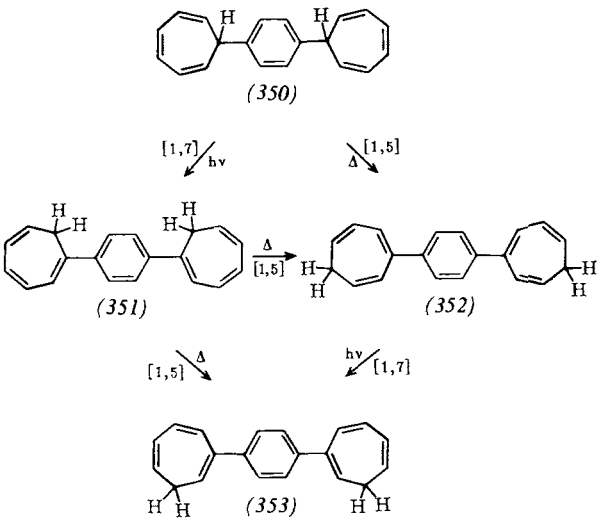


(347) (348) (349)

reported the stereospecific rearrangement of *(347)* to *(348)*. The case provides a striking instance of the manner in which framework restraints may operate to make otherwise difficultly accessible symmetry-allowed reactions possible [*cf.* the transition state *(349)*].

The antarafacial sigmatropic transformation of order [1,7] has been known for some time, in the precalciferol→calciferol interconversion [164].

In cycloheptatriene an antarafacial [1,7] shift is impossible. Consequently, [1,7] shifts within this system must be photochemically induced, or occur with inversion at the shifting site if thermal. A number of



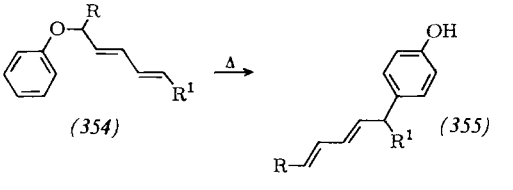
sequences of such light-induced [1,7] rearrangements have been observed [165].

Murray and *Kaplan* [166] have observed the consistent sequence *(350)–(353)* of thermal [1,5] and photochemical [1,7] sigmatropic hydrogen shifts among the isomers of 1,4-di(cycloheptatrienyl)benzene.

Further fascinating examples of [1,7] shifts have been described by *Schmid* [166a].

A symmetry-allowed [3,5] sigmatropic rearrangement must be an excited state reaction if constrained to be suprafacial on both components. So far, there appears to have been observed one case only [167].

The first [5,5] sigmatropic shift has now been realized by *Fráter* and *Schmid* [168], in the facile stereospecific rearrangement of *(354)* to *(355)*.



(354) (355)

[1,2] Shifts in a carbonium ion are very common [169]. Stereospecific hydrogen or methyl shifts in benzenonium cations [170] may be regarded as [1,2] or [1,6] shifts.

[162] *Cf. W. von E. Doering* and *W. R. Roth*, Tetrahedron *18*, 67 (1962); Angew. Chem. *75*, 27 (1963); Angew. Chem. internat. Edit. *2*, 115 (1963); *S. J. Rhoads* in *P. de Mayo:* Molecular Rearrangements. Interscience, New York 1963, Vol. 1, p. 655; *A. Jefferson* and *F. Scheinmann*, Quart. Rev. *22*, 391 (1968).

[163] *T. Miyashi, M. Nitta*, and *T. Mukai*, Tetrahedron Letters *1967*, 3433.

[164] *J. L. M. A. Schlatmann, J. Pot*, and *E. Havinga*, Rec. Trav. Chim. Pays-Bas *83*, 1173 (1964); *M. Akhtar* and *C. J. Gibbons*, Tetrahedron Letters *1965*, 509.

[165] *A. P. ter Borg* and *H. Kloosterziel*, Rec. Trav. Chim. Pays-Bas *84*, 241 (1965); *W. von E. Doering* and *P. P. Gaspar*, J. Amer. chem. Soc. *85*, 3043 (1963); *W. R. Roth*, Angew. Chem. *75*, 921 (1963); Angew. Chem. internat. Edit. *2*, 688 (1963); *L. B. Jones* and *V. K. Jones*, J. Amer. chem. Soc. *90*, 1540 (1968).

[166] *R. W. Murray* and *M. L. Kaplan*, J. Amer. chem. Soc. *88*, 3527 (1966).

[166a] *R. Hug, H.-J. Hansen*, and *H. Schmid*, Chimia *23*, 108 (1969).

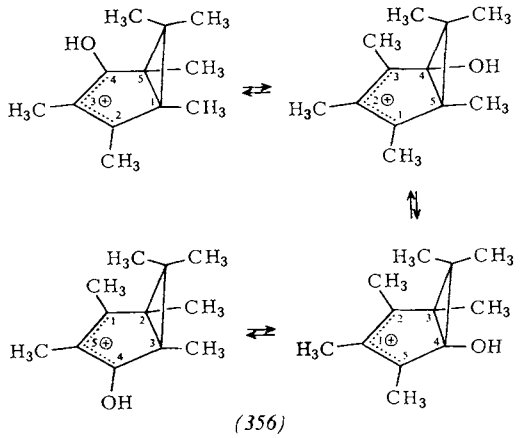
[167] *K. Schmid* and *H. Schmid*, Helv. chim. Acta *36*, 687 (1953).

[168] *Gy. Fráter* and *H. Schmid*, Helv. chim. Acta *51*, 190 (1968).

[169] *Cf.* the reviews by *Y. Pocker*, and by *J. A. Berson* in *P. de Mayo:* Molecular Rearrangements. Interscience, New York 1963, Vol. 1.

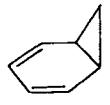
[170] *D. A. McCaulay* and *A. P. Lien*, J. Amer. chem. Soc. *79*, 5953 (1957); *H. Steinberg* and *F. L. J. Sixma*, Rec. Trav. Chim. Pays-Bas *81*, 185 (1962); *C. MacLean* and *E. L. Mackor*, J. chem. Physics *34*, 2208 (1961); *V. A. Koptyug, V. G. Shubin*, and *A. I. Rezvukhin*, Izv. Akad. Nauk SSSR *1965*, 201.

Sigmatropic reactions of order [1,4], *e.g.* migrations in a but-2-en-1-yl cation, have not been observed until recently, when *Swatton* and *Hart* reported the very rapid degenerate rearrangement *(356)* [171].



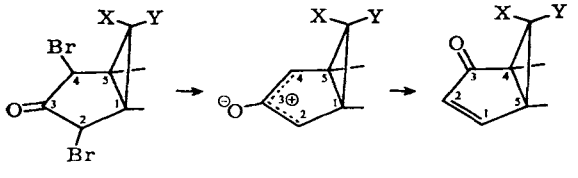
(356)

A [1,4] sigmatropic shift constrained to proceed suprafacially must take place with inversion at the migrating group. Note how this prediction contrasts with that for the [1,5] shift in the sterically very similar *(357)*.



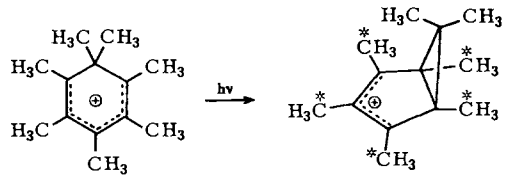
(357)

The predicted inversion in a [1,4] sigmatropic shift has recently been verified by several groups. *Hill* [172], and *Zimmerman* [173] have demonstrated that such a process occurs in the Favorskii reaction of a bicyclo-[3.1.0]hexanone [*(358)*→*(359)*→*(360)*].



(358) *(359)* *(360)*

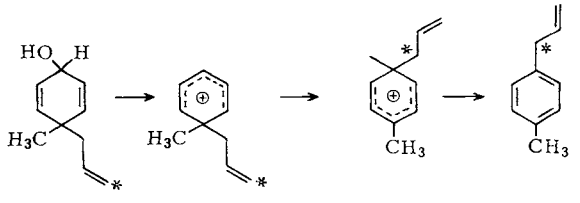
Further, *Hart* [174] has demonstrated that the rearrangement *(356)* previously discovered by him [171] indeed proceeds with inversion. The clearest demonstration of the nature of this rearrangement has been obtained by *Winstein* and *Childs* [175]. They generated various methylated bicyclo[3.1.0]hexenyl cations *(362)* in highly acidic media under conditions such that the nuclear magnetic resonance spectrum of the cation



(361) *(362)*

could be observed directly at various temperatures. The cations were generated by the symmetry-allowed photochemical disrotatory cyclization of the corresponding cyclohexadienyl cations *(361)* and were relatively stable, in consequence of the symmetry-imposed barrier to thermal reversion. As the temperature at which the measurements were made was raised, in the case of the heptamethyl compound *(362)* an averaging process took place; five methyl groups (marked by asterisks) became equivalent, while the other two methyl groups, which at low temperature gave distinct resonances, remained unaffected.

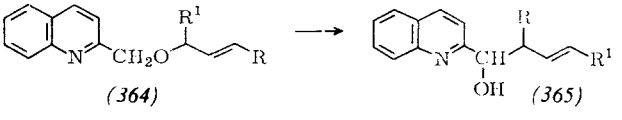
Several examples of [3,4] cationic sigmatropic reactions have recently become available through the elegant researches of *Schmid* [176]. In these dienol-ben-



(363)

zene, as well as the analogous dienone-phenol, rearrangements, the [3,4] sigmatropic reactions are competitive with equally allowed [1,2] and [3,3] shifts.

There also may be at hand some examples of [2,3] anionic sigmatropic reactions, in the Wittig rearrangement – the base-catalyzed transformation of benzyl ethers to alcohols. Thus, *Makisumi* and *Notzumoto* [177] observed the base-catalyzed conversion of *(364)* to *(365)*. Similar results on labeled 9-fluorenylallyl eth-



(364) *(365)*

ers were obtained by *Schöllkopf* [178]. The isoelectronic analogue [*(366)*→*(367)*], within formally neutral species, has been found to occur readily, and has been recognized as a very general reaction-type [179].

[171] *D. W. Swatton* and *H. Hart*, J. Amer. chem. Soc. *89*, 5075 (1967).

[172] *T. M. Brennan* and *R. K. Hill*, J. Amer. chem. Soc. *90*, 5614 (1968).

[173] *H. E. Zimmerman* and *D. S. Crumrine*, J. Amer. chem. Soc. *90*, 5612 (1968).

[174] *H. Hart, T. R. Rodgers*, and *J. Griffiths*, J. Amer. chem. Soc *91*, 754 (1969).

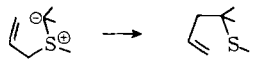
[175] *R. F. Childs* and *S. Winstein*, J. Amer. chem. Soc. *90*, 7146 (1968).

[176] *H.-J. Hansen, B. Sutter*, and *H. Schmid*, Helv. chim. Acta *51*, 828 (1968).

[177] *Y. Makisumi* and *S. Notzumoto*, Tetrahedron Letters *1967*, 6393.

[178] *U. Schöllkopf* and *K. Fellenberger*, Liebigs Ann. Chem. *698*, 80 (1966). See also *H. E. Zimmerman* in *P. de Mayo:* Molecular Rearrangements. Interscience, New York 1963, Vol. 1, p. 372.

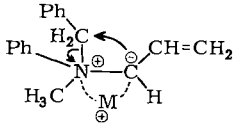
[179] *J. E. Baldwin, R. E. Hackler*, and *D. P. Kelly*, Chem. Commun. *1968*, 537, 538; *G. M. Blackburn, W. D. Ollis, J. D. Plackett, C. Smith*, and *I. O. Sutherland, ibid. 1968*, 186; *R. B. Bates* and *D. Feld*, Tetrahedron Letters *1968*, 417; *B. M. Trost* and *R. LaRochelle, ibid. 1968*, 3327; *J. E. Baldwin* and *R. E. Peavy, ibid. 1968*, 5029; *W. Kirmse* and *M. Kapps*, Chem. Ber. *101*, 994, 1004 (1968).



(366) (367)

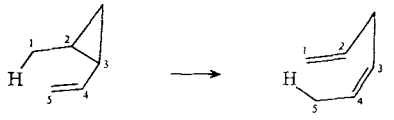
We would expect that [1,2] anionic shifts should proceed with inversion at the migrating atom. Such shifts have been observed[180] in all-carbon systems, but stereochemical information is not available. The Stevens rearrangement involves the migration of an alkyl group from a quaternary ammonium atom to an adjacent carbanionoid center. The reaction is thus isoelectronic with a [1,2] carbanion rearrangement. It is definitely intramolecular[181], and migration proceeds with retention of configuration at the shifting carbon atom[182]. There is considerable argument concerning the mechanism of the reaction[180,182,183]. Ion-pair and diradical mechanisms have been suggested[182,183] which might circumvent the disagreement with the predictions for a concerted process.

The perhaps bizarre alternative suggestion may be put forward that the metal ions always associated with such systems play a determinative role. If a metal ion is strongly associated with the carbanionoid center at the outset of reaction, and with the nitrogen atom when the migration has been concluded, the symmetry-allowed process depicted in *(368)* may be envisaged; in



(368)

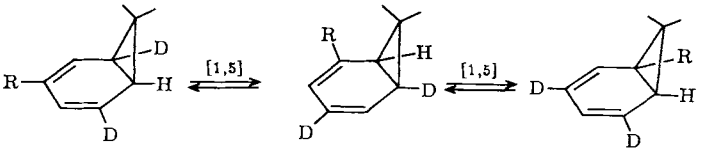
this change, inversion occurs at nitrogen and at the carbanionoid carbon, and a *p* orbital of the metal is involved.



(369)

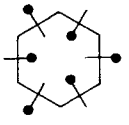
The homo [1,5] sigmatropic shift *(369)* is very well known[184].

The impetus for a general consideration of sequential sigmatropic shifts arose from the experimental observation by *Berson* and *Willcott* of a sequence of [1,5] sigmatropic shifts *(370)* in norcaradienes[161]. Such



(370)

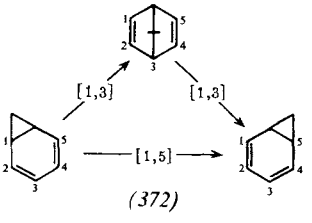
processes must proceed *with retention* at the migrating carbon atom. The consequences of a sequence of motions with retention are sketched in *(371)*. The illustration is essentially a superposition of snapshots of all of



(371)

the possible positions of labels attached to the methylene carbon atom as it migrates around the six-membered ring (*cf.* Figure 36).

Now it is also conceivable, though energetically unlikely, that the methylene group might migrate by a sequence of [1,3] sigmatropic shifts, through norbornadiene intermediates *(372)*.



(372)

In that connection the following question may be asked: given that suprafacial [1,5] sigmatropic shifts must proceed with retention, and that [1,3] shifts must proceed with inversion if constrained to be suprafacial – is it true that a random sequence of [1,3] and [1,5]

[180] *E. Grovenstein, jr.*, and *G. Wentworth*, J. Amer. chem. Soc. *89*, 1852, 2348 (1967), and references therein.

[181] *T. S. Stevens*, J. chem. Soc. *1930*, 2107; *R. A. W. Johnstone* and *T. S. Stevens*, ibid. *1955*, 4487. *R. K. Hill* and *T.-H. Chan*, J. Amer. chem. Soc. *88*, 866 (1966).

[182] *J. H. Brewster* and *M. W. Kline*, J. Amer. chem. Soc. *74*, 5179 (1952); *B. J. Millard* and *T. S. Stevens*, J. chem. Soc. *1963*, 3397; *E. F. Jenny* and *J. Druey*, Angew. Chem. *74*, 152 (1962); Angew. Chem. internat. Edit. *1*, 155 (1962).

[183] *D. J. Cram:* Fundamentals of Carbanion Chemistry. Academic Press, New York 1965, p. 223; *P. T. Lansbury, V. A. Pattison, J. D. Sidler*, and *J. B. Bieber*, J. Amer. chem. Soc. *88*, 78 (1966); *A. R. Lepley, ibid. 91*, 1237 (1969); *J. E. Baldwin*, personal communication.

[184] *D. S. Glass, J. Zirner*, and *S. Winstein*, Proc. chem. Soc. *1963*, 276; *R. J. Ellis* and *H. M. Frey, ibid. 1964*, 221; J. chem. Soc. *1964*, Suppl. 1, 5578; *W. R. Roth*. Liebigs Ann. Chem. *671*, 10 (1964); *W. R. Roth* and *J. König, ibid. 688*, 28 (1965); *W. Grimme*, Chem. Ber. *98*, 756 (1965); *J. K. Crandall* and *R. J. Watkins*, Tetrahedron Letters *1967*, 1717; *R. M. Roberts, R. G. Landolt, R. N. Greene*, and *E. W. Heyer*, J. Amer. chem. Soc. *89*, 1404 (1967); *G. Ohloff*, Tetrahedron Letters *1965*, 3795; *W. R. Roth*, Chimia *20*, 229 (1966). – The reaction is also known in the case of cyclopropyl-carbonyl compounds: *D. E. McGreer, N. W. K. Chiu*, and *R. S. McDaniel*, Proc. chem. Soc. *1964*, 415. A special case of some interest is the "abnormal Claisen rearrangement" studied by *E. N. Marvell, D. R. Anderson*, and *J. Ong*, J. org. Chem. *27*, 1109 (1962); *W. M. Lauer* and *T. A. Johnson, ibid. 28*, 2913 (1963); *A. Habich, R. Barner, W. von Philipsborn*, and *H. Schmid*, Helv. chim. Acta *48*, 1297 (1964); *R. M. Roberts* and *R. G. Landolt*, J. Amer. chem. Soc. *87*, 2281 (1965); *R. M. Roberts, R. N. Greene, R. G. Landolt*, and *E. W. Heyer, ibid. 87*, 2282 (1965); *R. M. Roberts, R. G. Landolt, R. N. Greene*, and *E. W. Heyer, ibid. 89*, 1404 (1967). See also *J. M. Conia, F. Leyendecker*, and *C. Dubois-Faget*, Tetrahedron Letters *1966*, 129; *F. Rouessac* and *J. M. Conia, ibid. 1965*, 3313.

shifts will produce only the same labeling pattern as the previously analyzed sequence of [1,5] shifts [*cf. (371)*]? In this case the answer is yes, as shown by a diagram

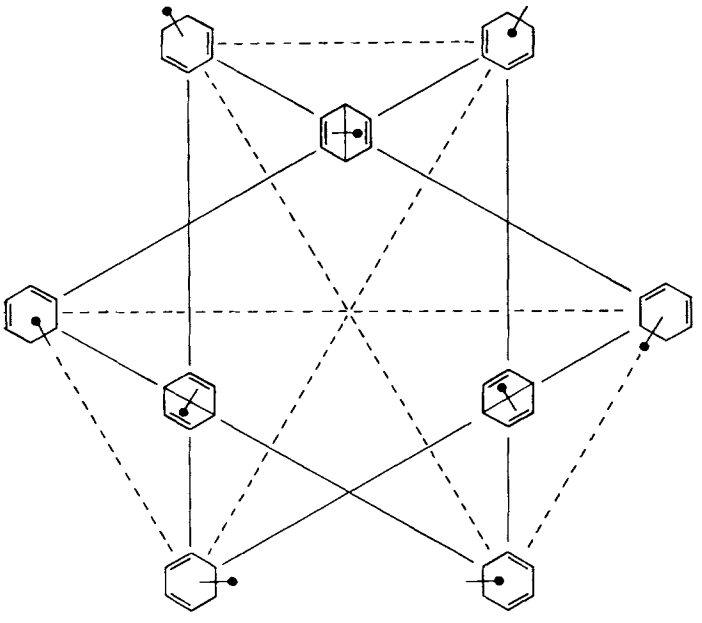
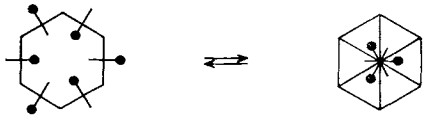


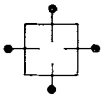
Figure 37. Sigmatropic [1,3] and [1,5] shifts in substituted norcaradienes and norbornadienes. — [1,3] shifts, ···· [1,5] shifts.

(Figure 37) relating all the possible species through all the possible paths. The information contained in Figure 37 is summarized in *(373)* and *(374)*.



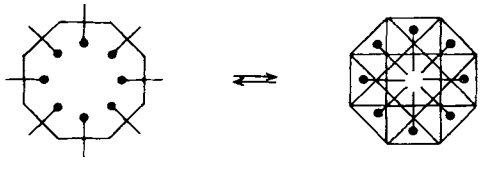
(373) *(374)*

Similar questions may be posed for other [2n.1.0] bicyclic systems. For the [2.1.0] system, only [1,3] shifts are possible; the labeling pattern is summarized in *(375)*.



(375)

For the [6.1.0] system [1,3], [1,5], and [1,7] shifts are all possible. The diagram relating all isomers is very complicated, but its information content may be summarized in *(376)* and *(377)*. Here again any sequence of [1,3], [1,5], or [1,7] shifts which relates two isomers gives the same configuration as any other sequence.



(376) *(377)*

It may be shown that the results derived above represent a general topological property of [2n.1.0] bicyclic systems.

There are two parts to the proof. First, it is clear that a [1,5] shift with retention at a migrating center is indistinguishable from a sequence of *two* [1,3] shifts, each proceeding with inversion at the migrating center. Similarly, a [1,7] shift with inversion is stereochemically indistinguishable from a series of *three* [1,3] shifts, each with inversion. In general,

$$[1, (2q+1)] = [1,3]^q$$

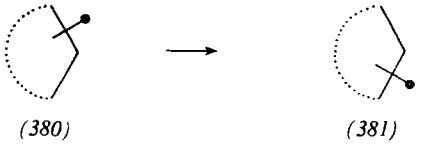
Consequently, it is sufficient to consider a random sequence of [1,3] shifts in constructing a proof.

We will prove that in a bicyclo[(2n−2).1.0] system *every* possible sequence of [1,3] shifts which effects the transformation of *(378)* into *(379)* contains an odd number

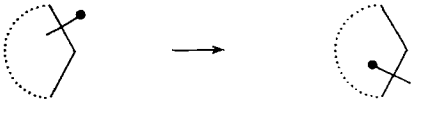


(378) *(379)*

of such shifts if n is even, and an even number of shifts if n is odd. Thus, it will be shown that for n even, there is an odd number of inversions, *i. e.* one net inversion [*(380)*→*(381)*], whereas for n odd, there is net retention [*(382)*→*(383)*]. The cyclic symmetry of the rearrangement then generates the isomer relationships shown in *(384)*.



(380) *(381)*

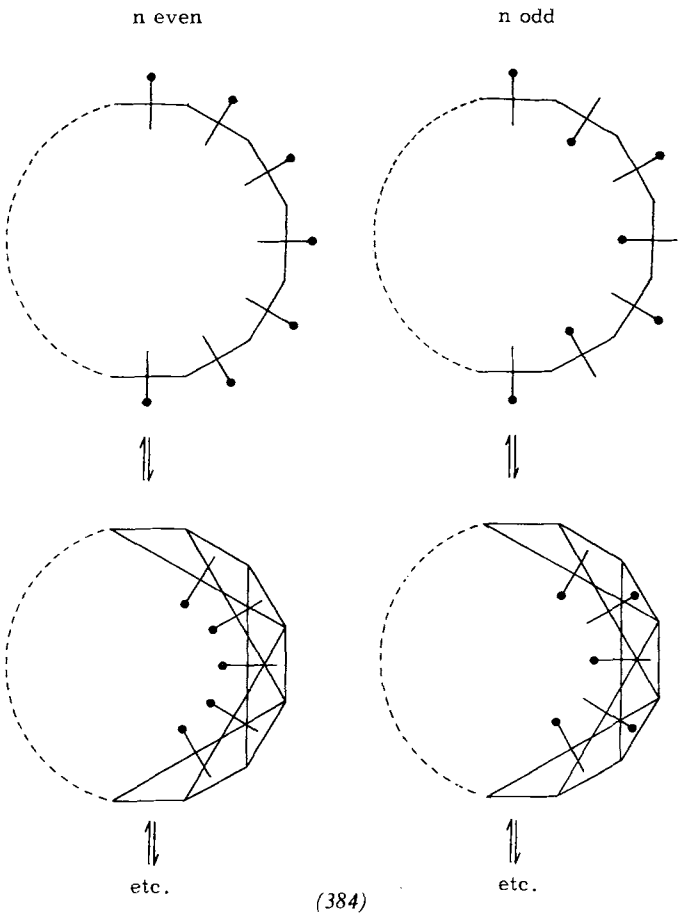


(382) *(383)*

We now construct the mathematical problem equivalent to the rearrangement sequence. Consider a polygon *(385)* with $2n$ vertices, numbered sequentially clockwise from an arbitrary origin. Suppose markers, A and B, are placed at vertices 1 and 2, respectively, of this polygon. A game is then played, with the following set of rules:

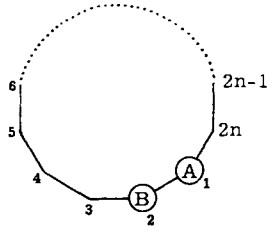
a) A random number of moves of the markers to new vertices is performed sequentially.

b) In each move *either* A *or* B moves two positions clockwise or counterclockwise. Thus, if A is at position k, it can move to $k+2$ or $k-2$.



(384)

c) No hopping is allowed; *i.e.* if A is located at point k and B at $k-1$, the move of A from k to $k-2$ is forbidden and A has only the option of moving to $k+2$.



(385)

Theorem: Given the above rules of the game, *every possible sequence of moves* which begins with A at 1 and B at 2 and terminates with A at 3 and B at 2 comprises an even number of moves if n is odd, and an odd number of moves if n is even.

Before proceeding to the proof of this theorem, one should assure oneself that the above game and theorem are equivalent to the problem presented by the sequential rearrangements. The requisite identifications are that the ring of $2n$ atoms, around which the carbon atom moves, corresponds to the polygon, while the markers A and B represent the bonds from the vertices of the polygon to the migrating atom.

Proof: Define a distance, measured in number of sides of the polygon, between the markers A and B, beginning at B, and *measured clockwise*. Then if B is at 2 and A is at 1, the distance between the two is the maximum: $2n-1$. We now proceed to examine the number of steps it takes to reduce this distance between the markers to 1, with B at 2 and A at 3. First, we will examine the number of moves it takes to reduce the distance to 1, *when B may have moved to any vertex*. The initial move reduces the distance from $2n-1$ to $2n-3$. Every subsequent move can be classified as *effectual* or *ineffectual*. An effectual move makes the distance smaller than the previous minimum, an ineffectual move does not. All ineffectual moves come in pairs: for, if at some point the distance is j, and a move increases the distance to $j+2$, then another move is necessary to return it to j. Only effectual moves reduce the distance between A and B. Since each effectual move reduces the distance by 2, the total number of moves, for any sequence, necessary to reduce the distance from $2n-1$ to 1 is:

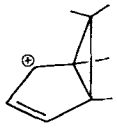
$$(2n-2)/2 = (n-1) + \text{some even number}$$
Effectual *Ineffectual*

So far we have deduced the number of moves necessary to reduce the distance to 1, but B may be at any even-numbered vertex. Now, A and B having been placed at *any* adjacent vertices, an even number of ineffectual moves will suffice to realize the final objective of placing B at position 2, and A at position 3. We have thus shown that the total number of necessary moves is:

$$(n-1) + \text{some even number}$$

Consequently, the required number of moves is odd if n is even, and even if n is odd, which was to be proven.

For cationic sigmatropic rearrangements, the topological relationships can differ significantly from those just shown to be general for neutral species. We consider first the sigmatropic rearrangements of a bicyclo[3.1.0]hexenyl cation *(386)*. In this system [1,2],



(386)

[1,4], and [1,3] shifts may occur; experience indicates that ionic [1,2q] shifts should be much faster than the neutral [1,(2q+1)] rearrangements. Using the previous conventions, and observing the symmetry-imposed conditions that [1,2] shifts must occur with retention, while [1,3] and [1,4] migrations must take place with inversion, we obtain the interrelations shown in Figure 38. The relationships are summarized in *(387)* and *(388)*.

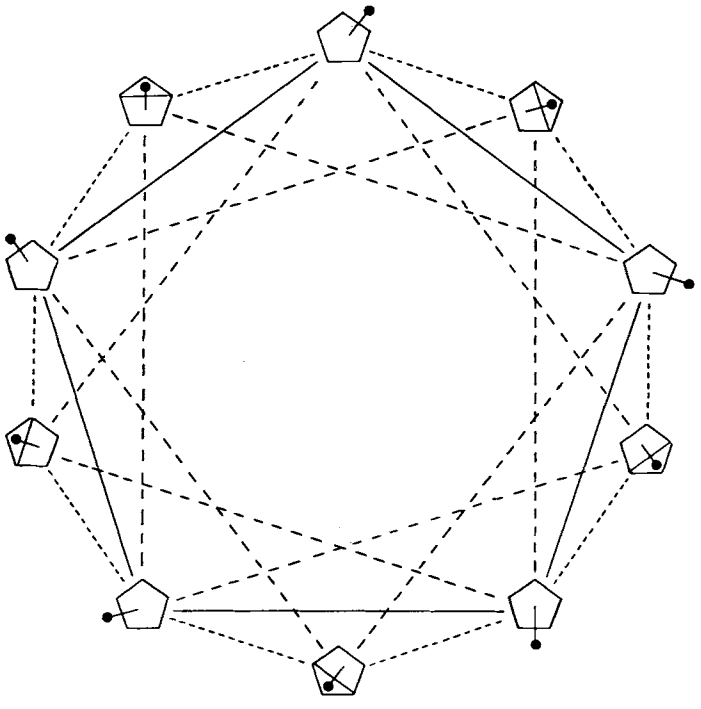
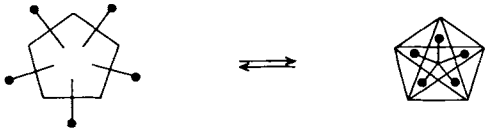


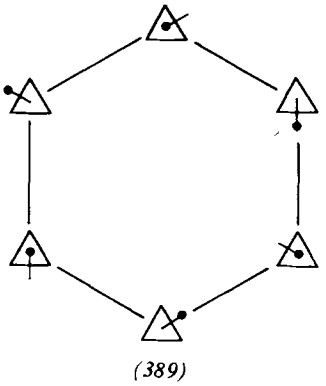
Figure 38. Sigmatropic [1,4], [1,2], and [1,3] shifts in the cation *(386)*. — [1,4] shifts, ····· [1,2] shifts, --- [1,3] shifts.

At this point it might appear that sequential sigmatropic reactions in cyclic polyenyl ions will always have the same consequences as in cyclic polyenes. *This is not*



(387) *(388)*

so. Consider the simplest system in which [1,2] shifts are possible – the rearrangements of the bicyclo-[1.1.0]butyl cation *(389)*. In sharp contrast to those in



(389)

each of the previous cases studied, this sequence produces apparent epimerization, *i.e.* a series of rearrangements can convert *(390)* into *(391)*. It may be readily



(390) *(391)*

seen that similar circumstances will obtain in (7, 11, ...)-membered rings – as well as in the three-membered case (*cf.* Figure 39).

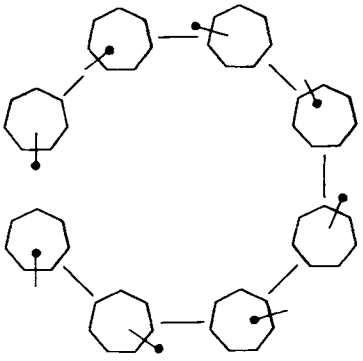


Figure 39. [1,6] Sigmatropic shifts in bicyclo[5.1.0]octadienyl cations.

The bicyclo[(2n+1).1.0] cation cases thus must be divided into two categories. In the first class, the [1,(2n+2)] sigmatropic shift proceeds with *retention* and epimerization must occur as a consequence of $2n+3$ such shifts; such is the case for [1,2], [1,6], [1,10], ... shifts, that is, in general for cases where n is even. The second category comprises those cases in which n is odd, the [1,(2n+2)] sigmatropic shift proceeds with *inversion*, and epimerization can never be realized through any number of symmetry-allowed migrations – as in the cyclic polyene cases.

8. Group Transfers and Eliminations

Consider the concerted reaction in which two hydrogen atoms are transferred from ethane to ethylene *(392)*, in a process suprafacial on both reactants. A



(392)

correlation diagram (Figure 40) is easily constructed for this reaction, utilizing the symmetry plane bisecting the two molecules; the process is clearly symmetry-allowed. In contrast is the diagram (Figure 41) for the

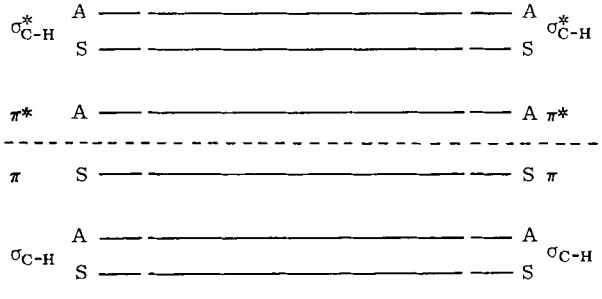


Figure 40. Correlation diagram for the concerted transfer of two hydrogen atoms from ethane to ethylene.



(393)

concerted transfer of two hydrogen atoms from ethane to the termini of butadiene *(393)*; the reaction is symmetry-forbidden.

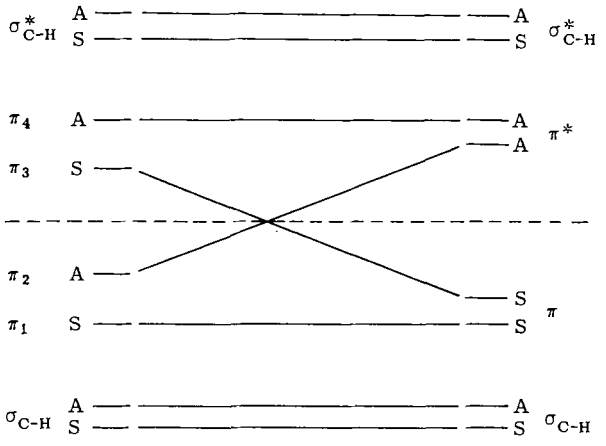
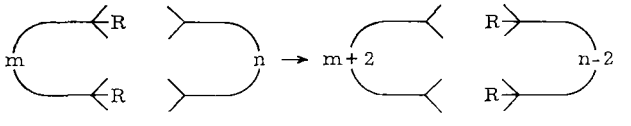


Figure 41. Correlation diagram for the concerted transfer of two hydrogen atoms from ethane to the termini of butadiene.

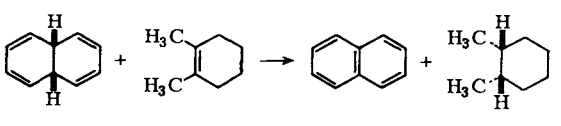
For the general case *(394)*, it is simple to derive the following selection rule: The double-group transfer is symmetry-allowed for ground states when



(394)

$m+n = 4q+2$, for excited states when $m+n = 4q$, where m and n are numbers of π electrons, and q is an integer (0, 1, 2, . . .). The rule applies also to a process antarafacial on both components, and is reversed for a process antarafacial on one component only. The rules must be appropriately modified if the possibility of inversion at R is real (*cf.* Section 11).

The best known example of this type of reaction, with $m = 0$, $n = 2$, is the transfer of hydrogen from diimide to olefins [185]. Hydrocarbon analogues also exist; for example, the reaction *(395)* was observed by *Doering* and



(395)

[185] Reviewed by *S. Hünig, H. R. Müller,* and *W. Thier,* Angew. Chem. *77*, 368 (1965); Angew. Chem. internat. Edit. *4*, 271 (1965); *E. J. Corey, D. J. Pasto,* and *W. L. Mock,* J. Amer. chem. Soc. *83*, 2957 (1961).

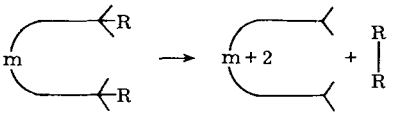
[186] *W. von E. Doering* and *J. W. Rosenthal,* J. Amer. chem. Soc. *89*, 4535 (1967).

Rosenthal [186]. A case with $m = 2$, $n = 4$ has also been observed *(396)* [187].



(396)

The rule derived above also applies to the limiting case with $n = 0$ – the concerted elimination *(397)*. We predicted, thus, that the concerted noncatalytic hydrogenation of a diene, or the reverse elimination, should be



(397)

1,4 rather than 1,2. At the time our predictions were made the literature appeared to contain only two relevant pieces of information:

a) 2,5-Dihydrofuran loses hydrogen in a unimolecular process with $E_a = 48.5$ kcal/mole and a negative entropy of activation, while 2,3-dihydrofuran does not react in this way [188].

b) 3,3,6,6-Tetramethyl-1,4-cyclohexadiene when pyrolyzed in pentane gave a much larger yield of ethane (and *p*-xylene) than could have arisen from a free radical chain reaction [189].

Subsequently, our predictions have been substantiated in a number of studies. *Baldwin* [190] in studying the elimination of hydrogen from an isotopically labeled cyclopentene found a greater than 10:1 preference for 1,4 over 1,2 elimination. *Ellis* and *Frey* [191], *Benson* and *Shaw* [192], and *Kellner* and co-workers [193] have independently studied the pyrolysis of 1,3 and of 1,4-cyclohexadiene. The latter decomposes unimolecularly to benzene and hydrogen with $E_a = 42.7$ kcal/mole; at the same temperatures the 1,3-cyclohexadiene is thermally stable and at higher temperatures it decomposes mainly by radical-chain processes. *Frey* has provided further interesting examples of concerted elimination of hydrogen; on the other hand, his evidence indicates that those processes which lead to the formation of methane or ethane proceed by radical-chain mechanisms [194].

[187] *P. Dowd,* personal communication; *I. Fleming,* personal communication.

[188] *C. A. Wellington* and *W. D. Walters,* J. Amer. chem. Soc. *83*, 4888 (1961).

[189] *W. Reusch, M. Russell,* and *C. Dzurella,* J. org. Chem. *29*, 2446 (1964).

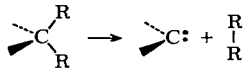
[190] *J. E. Baldwin,* Tetrahedron Letters *1966*, 2953.

[191] *R. J. Ellis* and *H. M. Frey,* J. chem. Soc. *A*, *1966*, 553.

[192] *S. W. Benson* and *R. Shaw,* Trans. Faraday Soc. *63*, 985 (1967); J. Amer. chem. Soc. *89*, 5351 (1967).

[193] *W. D. Walters,* personal communication.

[194] *H. M. Frey* and *D. H. Lister,* J. chem. Soc. *A*, *1967*, 509, 1800; *H. M. Frey* and *R. Walsh,* Chem. Rev. *69*, 103 (1969).



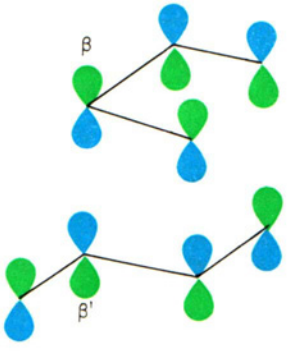
(398)

The concerted loss of two geminal groups *(398)*, provided that it proceeds through a transition state of C_{2v} symmetry (*cf.* Section 10.1), should be an excited state reaction, and thus compete with vicinal elimination [*(397)*, $m=0$] – also a symmetry-allowed excited state process. Both cases are known [195].

9. Secondary Effects

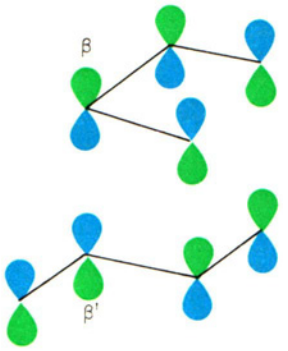
Orbital symmetry arguments may also be used to yield further insight into the origins of secondary conformational effects in concerted cycloaddition reactions.

Consider the Diels-Alder addition of butadiene to itself, as a concerted [$\pi 4_s + \pi 2_s$] cycloaddition reaction. *A priori*, this reaction might take place through either of two alternative transition states, *(399)* or *(400)*. The *endo* approach *(399)* is distinguished from the *exo* *(400)* mainly by the proximity of a β and a β′ orbital in the former. Any secondary interaction among occupied diene and dienophile molecular orbitals will contribute only in a very minor way to the total energy of the transition state, since such an interaction will increase the energy of some levels while decreasing the energy of others. The significant interactions will come from the symmetry-allowed mixing of unoccupied with occupied levels [196]. In the case at hand, inspection of diagrams *(401)* and *(402)* reveals at once that either possibility for such mixing leads to bonding, *i.e.* energy-lowering, interaction of the proximate β and β′ orbitals [197]. Thus, the *endo* transition state *(399)* for this [$\pi 4_s + \pi 2_s$] concerted cycloaddition reaction is stabilized *vis-à-vis* the *exo* alternative *(400)* by symmetry-controlled secondary orbital interactions.



(401)

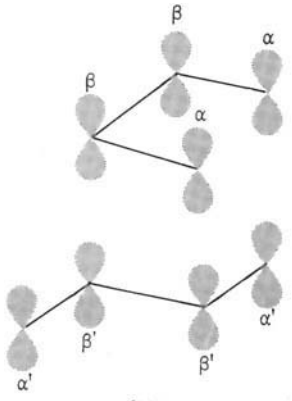
Mixing of highest occupied "diene" orbital (top) with lowest unoccupied "olefin" orbital (bottom)



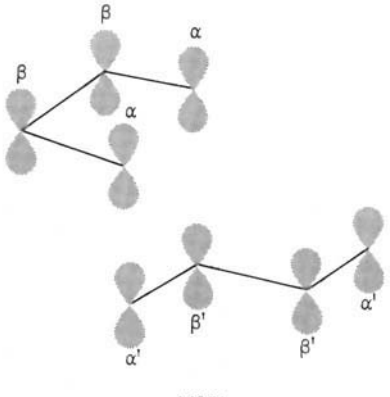
(402)

Mixing of lowest unoccupied "diene" orbital (top) with highest occupied "olefin" orbital (bottom)

The orbital symmetry relationships signalized here provide a simple quantum chemical basis for the large body of experience summarized in the Alder *endo* addition rule [198]. Our treatment differs from previous proposals, which have emphasized the roles of inductive



(399)



(400)

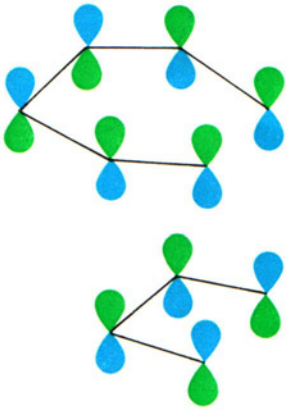
[195] Photolysis of cyclohexadiene: *R. Srinivasan*, J. Amer. chem. Soc. *83*, 2806 (1961); photolysis of ethane and ethylene: *M. Okabe* and *J. R. McNesby*, J. chem. Physics *34*, 668 (1962); cyclohexane: *R. P. Doepker* and *P. Ausloos*, *ibid. 42*, 3746 (1965). In the gas phase photolysis of azomethane, it is well established that the predominant primary process is decomposition to nitrogen and two methyl radicals; however, some evidence has been presented for a minor molecular elimination of ethane: *R. E. Rebbert* and *P. Ausloos*, J. phys. Chem. *66*, 2253 (1962).

[196] This has also been stressed by *K. Fukui* in *P.-O. Löwdin* and *B. Pullman:* Molecular Orbitals in Chemistry, Physics, and Biology. Academic Press, New York 1964, p. 525.

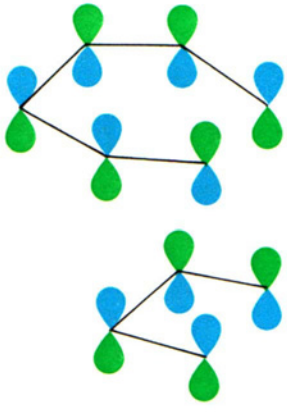
[197] The role of other secondary interactions has been stressed by *L. Salem*, J. Amer. chem. Soc. *90*, 543, 553 (1968).

[198] *K. Alder* and *G. Stein*, Angew. Chem. *50*, 514 (1937); *K. Alder*, Liebigs Ann. Chem. *571*, 157 (1951); *K. Alder* and *M. Schumacher*, Fortschr. Chem. org. Naturstoffe *10*, 1 (1953). For exceptions to the rule, *cf. J. A. Berson*, *Z. Hamlet*, and *W. A. Mueller*, J. Amer. chem. Soc. *84*, 297 (1962).

forces [199], electrostatic forces consequent upon charge transfer between diene and dienophile [200], and maximum accumulation of unsaturation [198]. In particular it is now clear that in some cases the orbital interactions among unsaturated centers involved in a concerted cycloaddition reaction will be such as to raise rather than lower, the energy of the *endo* transition state, and lead to a preference for *exo* addition, insofar as



(403)

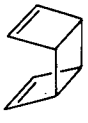


(404)

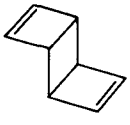
symmetry factors are dominant; inspection of the relevant orbital diagrams *(403)* and *(404)* for the symmetry-allowed $[\pi 6_s+\pi 4_s]$ combinations indicates that it is such a case.

This prediction was made prior to the discovery of [6+4] cycloadditions, and has since been confirmed [201]. By contrast, the symmetry-allowed $[\pi 8_s+\pi 2_s]$ and $[\pi 2_s+\pi 2_s+\pi 2_s]$ cycloadditions should resemble the [4+2] process and proceed by preference through *endo* transition states; there is already evidence for that preference in an example of the latter process [202].

The dimerization of cyclobutadiene is a special case of much interest, considered in the light of orbital symmetry relationships. If, as seems likely, there is substantial double bond localization in that highly reactive molecule, one can delineate, *a priori*, the possibilities of $[\pi 2_s+\pi 2_s]$, $[\pi 2_s+\pi 4_s]$, and $[\pi 4_s+\pi 4_s]$ cycloadditions. Our selection rules require a preference for the concerted $[\pi 2_s+\pi 4_s]$ process, and indeed evidence that this path is favored has been brought forward [203]. Examination



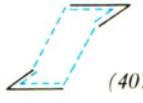
(405)



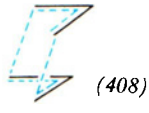
(406)

of secondary orbital interactions along the lines set down here reveals further that the *endo* process, leading to the *syn* dimer *(405)*, should be favored over the alternative *exo* combination, which would give the *anti* dimer *(406)*. The formation of both *syn* and *anti* dimers in reactions initiated with a variety of possible cyclobutadiene precursors has been reported, but in those experiments in which there was the greatest likelihood of the transitory existence of a free cyclobutadiene, the predicted *endo* process was observed [204].

The [3,3] sigmatropic shift in 1,5-hexadienes has been shown to proceed more easily through a four-center



(407)



(408)

chair-like transition state *(407)* than through the boat-like alternative *(408)* [205]. We suggest that orbital symmetry relationships may play a major role in determining that preference. A correlation diagram for the molecular orbitals involved in the rearrangement is illustrated in Figure 42. The levels are classified as symmetric or antisymmetric with respect to the mirror plane *m* in the boat-like transition state, or a two-fold rotation axis in the chair-like form. The scheme shown is for the former case, and the diagram for the latter is qualitatively similar. The correlation of reactant bonding levels with product bonding levels, characteristic of a symmetry-allowed thermal reaction, should be noted. At the half-way mark in the reaction the level ordering is recognizable as that of two strongly interacting allyl radicals. The actual behavior of the levels along the

[199] *A. Wassermann*, J. chem. Soc. *1935*, 825, 1511; *1936*, 432; Trans. Faraday Soc. *35*, 841 (1939).

[200] *R. B. Woodward* and *H. Baer*, J. Amer. chem. Soc. *66*, 645 (1944).

[201] *R. C. Cookson, B. V. Drake, J. Hudec*, and *A. Morrison*, Chem. Commun. *1966*, 15; *K. Houk*, Dissertation, Harvard (1968).

[202] *R. C. Cookson, J. Dance*, and *J. Hudec*, J. chem. Soc. *1964*, 5416.

[203] *G. Wittig* and *J. Weinlich*, Chem. Ber. *98*, 471 (1965).

[204] *R. Criegee*, Angew. Chem. *74*, 703 (1962); Angew. Chem. internat. Edit. *1*, 519 (1962), and references therein: *P. S. Skell* and *R. J. Peterson*, J. Amer. chem. Soc. *86*, 2530 (1964), and references therein; *L. Watts, J. D. Fitzpatrick*, and *R. Pettit*, *ibid. 88*, 623 (1966); *E. Hedaya, R. D. Miller, D. W. McNeil, P. F. D'Angelo*, and *P. Schissel*, J. Amer. chem. Soc. *91*, 1875 (1969).

[205] *W. von E. Doering* and *W. R. Roth*, Tetrahedron *18*, 67 (1962); Angew. Chem. *75*, 27 (1963); Angew. Chem. internat. Edit. *2*, 115 (1963); *R. K. Hill* and *N. W. Gilman*, Chem. Commun. *1967*, 619; for some recent theoretical work see *M. Simonetta, G. Favini, C. Mariani*, and *P. Gramaccioni*, J. Amer. chem. Soc. *90*, 1280 (1968). Similar preferences in the aromatic Claisen rearrangement have been elegantly studied by *Gy. Fráter, A. Habich, H.-J. Hansen*, and *H. Schmid*, Helv. chim. Acta *52*, 335 (1969).

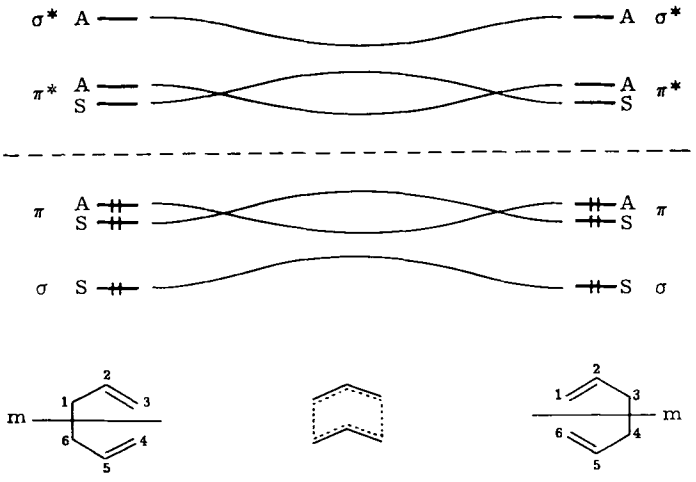


Figure 42. Correlation diagram for the [3,3] sigmatropic rearrangement of 1,5-hexadiene.

reaction coordinate is abstracted from extended Hückel calculations.

If the correlation diagrams are qualitatively similar for the boat and chair reactions, where does the observed preference come from? An explanation requires the construction of two further correlation diagrams (Figure 43), for the alternative hypothetical processes in which two allyl radicals approach each other from infinity, in parallel planes, oriented with respect to each other in the one case in a *quasi* boat relationship, and

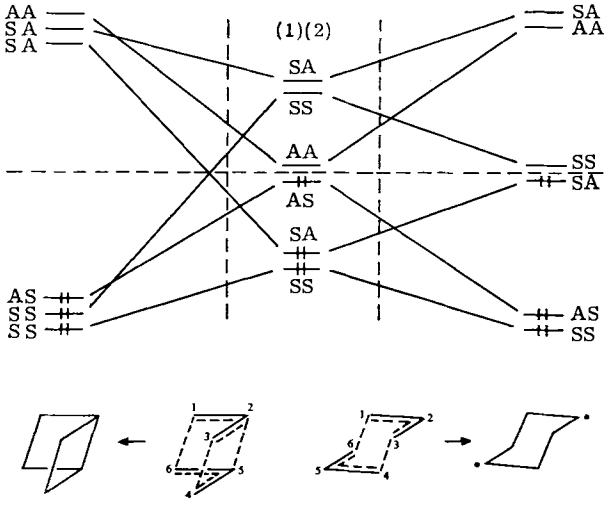


Figure 43. Correlation diagram for the approach of two allyl radicals from infinity in a *quasi* boat or a *quasi* chair relationship. (1) and (2) at the top of the center column refer to the symmetry elements present (see text).

in the other in a *quasi* chair fashion. In each of these processes there are two symmetry elements:

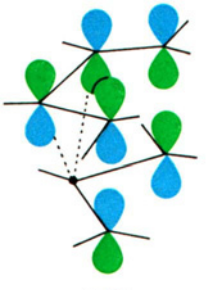
a) in both, a mirror plane m_1, which passes through C-2 and C-5, and bisects the angles C(1)-C(2)-C(3) and C(6)-C(5)-C(4);

b) in the boat approach, a second mirror plane, m_2, parallel to and half-way between the planes of the approaching radicals, and in the chair approach a two-fold axis of symmetry, lying on the intersection of m_2 and the plane defined by C(1)-C(3)-C(4)-C(6).

To complete the correlations one must specify the end products of these hypothetical motions; these are a bicyclohexane in the boat approach, and a 1,4-cyclohexylidene biradical in the chair pathway. Among the occupied levels the critical difference in the two pathways is in the behavior of the occupied S_1A_2 level, which in the boat-like approach correlates to an antibonding σ orbital while in the chair-like process it goes over to a non-bonding biradical level. The crucial point of the argument now is that a reaction proceeding as in Figure 42 must pass at the half-way point through some point in a correlation diagram resembling one or the other of those shown in Figure 43, and that this point will be approximately the same horizontal distance, marked by dashed vertical lines, along the reaction coordinate in the two alternate pathways of Figure 43. Further, at any such point the chair-like transition state is at lower energy as a result of the difference in correlation properties of the occupied S_1A_2 orbital. The central conclusion is that orbital interactions involving C-2 and C-5 have a net antibonding, energy-raising effect. In this sense, the argument represents a further development of the simple orbital repulsion effect suggested by *Doering* and *Berry* [205].

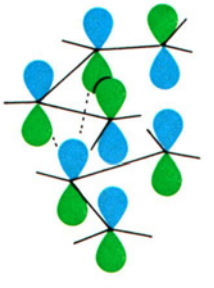
It should be emphasized that the effects discussed here are, not unexpectedly, small ones, and that in systems possessing special geometrical restraints which necessitate a boat-like transition state, [3,3] sigmatropic changes take place with no special difficulty [206].

To present a final illustration of the procedure, in a case in which the result is not yet known, we consider the [4+2] cycloaddition of a butadiene to an allyl cation. The two significant interactions are shown in *(409)* and *(410)*. The secondary interactions in *(409)* must be negligible, while those in *(410)* are antibonding; a preference for the *exo* transition state is expected [206a].



(409)

Mixing of highest occupied diene orbital (top) with lowest unoccupied allyl orbital (bottom)



(410)

Mixing of lowest unoccupied diene orbital (top) with highest occupied allyl orbital (bottom)

[206] *J. M. Brown*, Proc. chem. Soc. *1965*, 226; *W. von E. Doering* and *W. R. Roth*, Tetrahedron *19*, 715 (1963); *R. Merényi*, *J. F. M. Oth*, and *G. Schröder*, Chem. Ber. *97*, 3150 (1964); *H. A. Staab* and *F. Vögtle*, Tetrahedron Letters *1965*, 54.

[206a] Since the above was written, the prediction has been confirmed: *H. M. R. Hoffmann* and *D. R. Joy*, J. chem. Soc. *B 1968*, 1182.

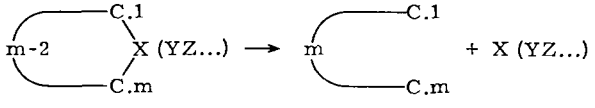
10. Divertissements!

In the previous sections, we have discussed and exemplified orbital symmetry control of the major general types of concerted organic reactions. We turn now to a discussion of two special types, each of which possesses fascinating unique features, and further illustrates the power of the principle of orbital symmetry conservation in understanding and predicting the detailed course of chemical transformations.

10.1. Cheletropic Reactions

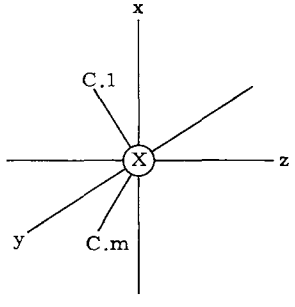
We define as *cheletropic reactions* those processes in which two σ bonds which terminate at a single atom are made, or broken, in concert.

Let us consider the cheletropic reaction *(411)*, in which a small molecule X(YZ. . .) and a polyene containing



(411)

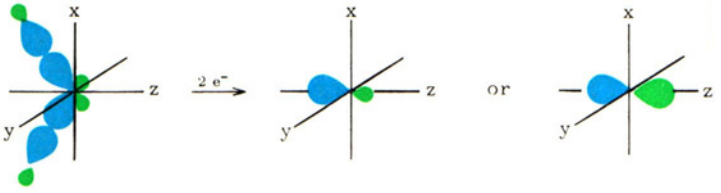
an *m*-electron π system are produced. We shall examine the geometrical aspects of the reaction, with reference to an invariant coordinate system *(412)*, whose origin is always at X, and whose z axis bisects the line



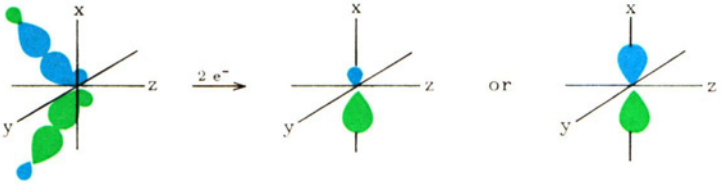
(412)

between C.1 and C.m. Thus, the σ bonds being broken lie in the xz plane, and their four electrons are distributed as usual, in pairs, in the two generalized orbitals *(413)* and *(414)*. Now, in general, two electrons must be delivered from these orbitals to each of the developing products, with conservation of orbital symmetry. A crucial point now emerges: the transfer of two electrons from the breaking σ bonds to new orbitals in the product molecule X(YZ. . .) may take place in either of two sharply distinct ways.

a) Two electrons from the symmetric orbital [*(413)* ≡*(415)*] may take up new positions in a z-symmetric lone pair orbital of X(YZ. . .), or enter a π system antisymmetric with respect to the xy plane.



(415)

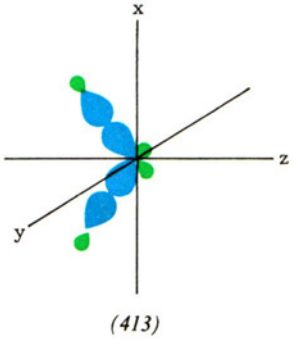


(416)

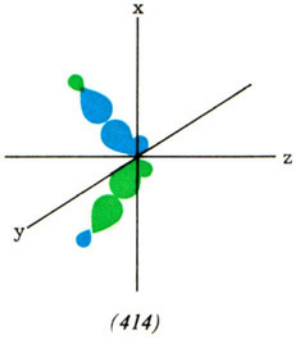
b) Two electrons from the antisymmetric orbital [*(414)* ≡*(416)*] may take up new positions in an x-symmetric lone pair orbital of X(YZ. . .), or enter a π system antisymmetric with respect to the yz plane.

In the light of this analysis, it is clear that the geometrical displacements at C.1 and C.m are dependent upon the detailed geometry of departure of X(YZ. . .), and in particular, on the sense of the displacements of the atoms YZ. . . which are attached to X. To illustrate this important point, we consider the departure of a bent molecule Y-X-Z, which as it develops must acquire a symmetric lone pair at the central atom X. The reaction may take place in either of two ways, depicted in *(417)* and *(418)*.

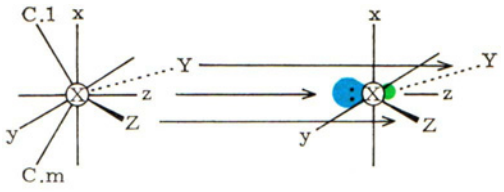
a) *Cf. (417)*: X acquires its needed lone pair from the symmetric σ orbital *(415)*, as X, Y, and Z depart co-lin-



(413)

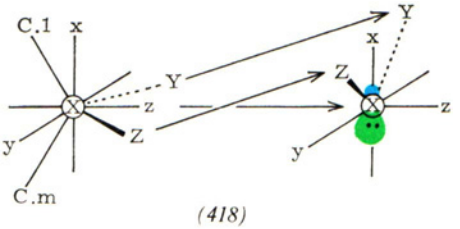


(414)



(417)

early, all remaining in the yz plane. We shall designate such processes as *linear* cheletropic reactions. It



(418)

may be noted that in a formal sense, the product electron pair is participating in a *suprafacial* fashion, in that the two bonds from which the two electrons came lie on the same side of the nodal surface (approximated by the plane xy) of the product orbital which the pair occupies.

b) *Cf. (418)*: X acquires its needed lone pair from the antisymmetric σ orbital *(416)*, as X departs co-linearly, remaining in the yz plane, while Y and Z undergo displacements in both the x and z directions, with the result that the product molecule lies in the xy plane. We shall designate such processes as *non-linear* cheletropic reactions. In this case the product electron pair at X is participating in an *antarafacial* fashion, in that the two bonds from which the electrons came lie on opposite sides of the nodal surface (approximated by the plane yz) of the product orbital which the pair occupies.

It is now clear that in linear cheletropic reactions of the type *(411)*, two electrons must be delivered from the antisymmetric σ orbital [*(416)* ≡*(420)* ≡*(423)*] to the highest occupied π orbital of the polyene *(419)*. Consequently, the displacements at C.1 and C.m must be disrotatory when $m = 4q$ [*(420)*→*(421)*], and conrotatory when $m = 4q+2$ [*(423)*→*(424)*].

By contrast, if the fragmentation *(411)* follows the non-linear cheletropic path, two electrons must be delivered to the highest occupied π orbital of the polyene *(419)* from the symmetric σ orbital [*(415)* ≡*(422)* ≡*(425)*]. In this case, therefore, the displacements at C.1 and C.m must be conrotatory if $m = 4q$ [*(422)*→*(421)*], and disrotatory when $m = 4q+2$ [*(425)*→*(424)*].

The selection rules are summarized in Figure 44. In these cheletropic transformations there undoubtedly

	Allowed Ground State Reactions	
m	Linear	Non-linear
4*q*	Disrotatory	Conrotatory
4*q*+2	Conrotatory	Disrotatory

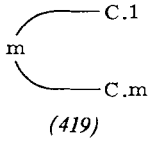
Figure 44. Selection rules for cheletropic reactions.

exists, for each ground state reaction, an excited state process characterized by reversed stereochemical features. However, the extruded small molecule X(YZ)... will frequently possess many occupied lone pair orbitals, and the accompanying possibility of numerous $n \rightarrow \pi^*$ states raises the possibility in any given case that excited state processes with the *same* stereochemical characteristics as the corresponding ground state transformation may be available.

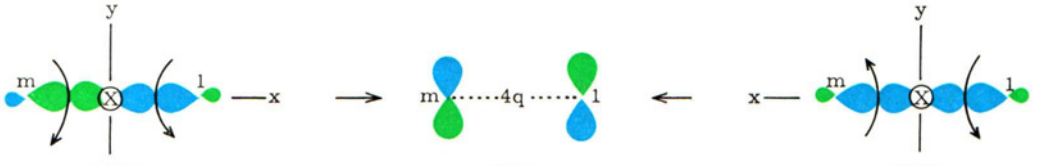
Linear cheletropic fragmentations leading to the production of nitrogen or carbon monoxide represent reactions well-suited for the construction of formal correlation diagrams, which have been drawn by *Lemal* [207], and by *Baldwin* [208], as well as by us. For car-

[207] *D. M. Lemal* and *S. D. McGregor*, J. Amer. chem. Soc. *88*, 1335 (1966).

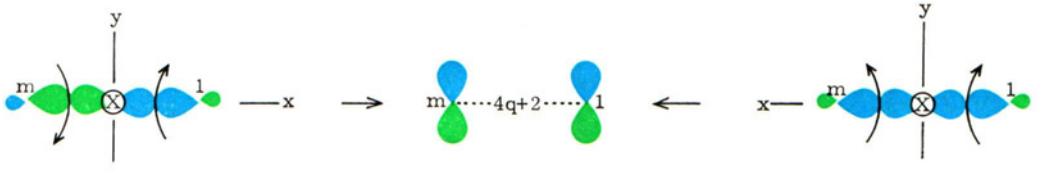
[208] *J. E. Baldwin*, Canad. J. Chem. *44*, 2051 (1966).



(419)

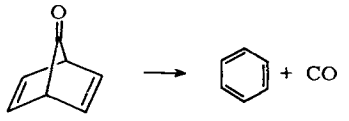


(420) (421) (422)



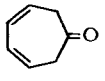
(423) (424) (425)

bon monoxide elimination no direct stereochemical results are available. It is clear, however, that cyclopent-3-en-1-ones ($m=4$) undergo decarbonylation readily, apparently in a concerted manner [208]. In this connection, the failure of attempts to prepare norbornadien-7-one *(426)*, may be contrasted with the stability of norbornanones [209].



(426)

A case with $m=6$ is represented by 3,5-cycloheptadienone *(427)*, which in one of the few known condensed-phase decarbonylations, undergoes photolysis to hexatriene and carbon monoxide [210].

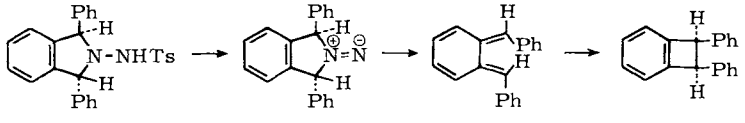


(427)

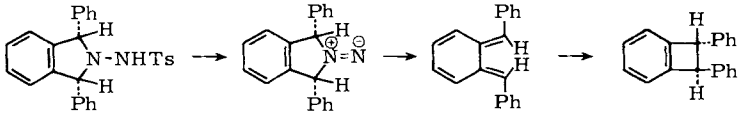


(428)

The elimination of nitrogen from diazenes *(428)* has been carefully studied by *Lemal* [207]. The process is stereospecific and disrotatory, as predicted; the linear disrotatory path is clearly one involving less strain than the non-linear conrotatory alternative in this case.



(429)



(430)

Remarkable sequences [*(429)*, *(430)*] comprising disrotatory nitrogen eliminations, followed by conrotatory electrocyclic reactions have been revealed by *Carpino* [211].

The reversible, facile addition of sulfur dioxide [212] to dienes is well known [213]. The expected disrotatory course for the elimination of sulfur dioxide from a butadiene sulfone has been established [214]. The corresponding photochemical process is not completely stereospecific, but a clear preference for the conrotatory path is shown [215]. Sulfur dioxide also readily undergoes 1,6-addition to 3-*cis*-hexatrienes; the reverse process has recently been shown to proceed in a conrotatory fashion, and must therefore be classified as a linear cheletropic reaction [216].

Cheletropic reactions in which a three-membered ring is produced or destroyed, *e.g.* fragmentations of type *(411)* in which $m = 2$, are of special interest in that geometric factors require that they take place in a disrotatory, or suprafacial manner. Consequently, these transformations must occur by the non-linear cheletropic path.

The well-known [217] stereospecific combination of singlet carbenes with olefins to give cyclopropanes undoubtedly falls in the non-linear cheletropic class [218].

Cyclopropenones and cyclopropanones lose carbon monoxide thermally under mild conditions [219,220], and even more readily on irradiation [219,221]. Stereochemical information on the decarbonylation is lacking. It has, however, been clearly demonstrated that nitrogen is stereospecifically extruded in a disrotatory fashion from alkyl-substituted three-membered ring

[209] See, for example, *S. Yankelevich* and *B. Fuchs*, Tetrahedron Letters *1967*, 4945.

[210] *O. L. Chapman* and *G. W. Borden*, J. org. Chem. *26*, 4185 (1961); *O. L. Chapman, D. J. Pasto, G. W. Borden*, and *A. A. Griswold*, J. Amer. chem. Soc. *84*, 1220 (1962); *D. I. Schuster, B. R. Sckolnick*, and *F.-T. H. Lee, ibid. 90*, 1300 (1968).

[211] *L. A. Carpino*, Chem. Commun. *1966*, 494.

[212] For molecular orbital descriptions of sulfur dioxide and sulfones, see *W. Moffitt*, Proc. Roy. Soc. *A 200*, 409 (1950).

[213] *H. Staudinger* and *B. Ritzenhaler*, Ber. dtsch. chem. Ges. *68*, 455 (1935); *G. Hesse, E. Reichold*, and *S. Majmudar*, Chem. Ber. *90*, 2106 (1957); *M. P. Cava* and *A. A. Deana*, J. Amer. chem. Soc. *81*, 4266 (1959). The last group has also described some interesting selective photochemical eliminations of sulfur dioxide: *M. P. Cava, R. H. Schlessinger*, and *J. P. Van Meter*, J. Amer. chem. Soc. *86*, 3173 (1964).

[214] *W. L. Mock*, J. Amer. chem. Soc. *88*, 2857 (1966); *S. D. McGregor* and *D. M. Lemal, ibid. 88*, 2858 (1966).

[215] *J. Saltiel* and *L. Metts*, J. Amer. chem. Soc. *89*, 2232 (1967).

[216] *W. L. Mock*, J. Amer. chem. Soc. *89*, 1281 (1967); *W. L. Mock, ibid. 91*, 5682 (1969).

[217] *P. S. Skell* and *R. C. Woodworth*, J. Amer. chem. Soc. *78*, 4496 (1956); *81*, 3383 (1959); *P. S. Skell* and *A. Y. Garner, ibid. 78*, 5430 (1956); *W. von E. Doering* and *P. LaFlamme, ibid. 78*, 5447 (1956); *H. M. Frey, ibid. 80*, 5005 (1958); *W. R. Moore, W. R. Moser*, and *J. E. LaPrade*, J. org. Chem. *28*, 2200 (1963).

[218] For this reaction, semiempirical calculations yield results in striking concordance with the analysis of non-linear cheletropic processes presented here. *Cf. R. Hoffmann*, J. Amer. chem. Soc. *90*, 1475 (1968).

[219] *R. Breslow, T. Eicher, A. Krebs, R. A. Peterson*, and *J. Posner*, J. Amer. chem. Soc. *87*, 1320 (1965); *R. Breslow, L. J. Altman, A. Krebs, E. Mohacsi, I. Murata, R. A. Peterson*, and *J. Posner, ibid. 87*, 1326 (1965); *R. Breslow* and *G. Ryan, ibid. 89*, 3073 (1967).

[220] *N. J. Turro, P. A. Leermakers, H. R. Wilson, D. C. Neckers, G. W. Byers*, and *G. F. Vesley*, J. Amer. chem. Soc. *87*, 2613 (1965).

[221] *D. C. Zecher* and *R. West*, J. Amer. chem. Soc. *89*, 153 (1967).

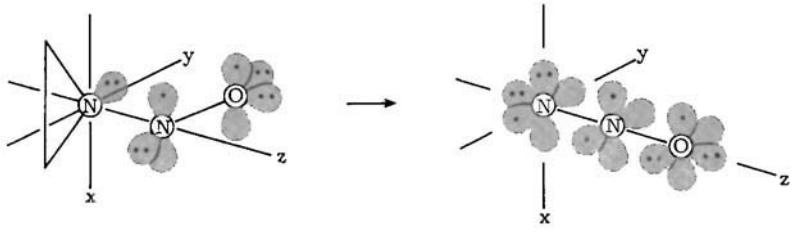
diazenes *(431)* [222]; this change must follow the non-linear path, with x-displacement of N-2 in the plane of the aziridine ring as reaction proceeds.



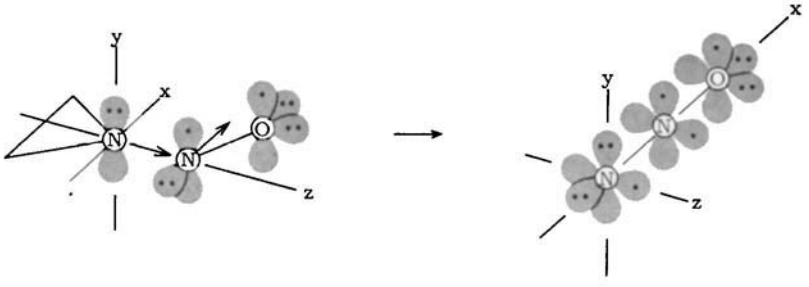
(431)

Sulfur dioxide is readily lost from episulfones in a stereospecific disrotatory manner [223,224]. In order to circumvent the problem which seemed to be posed by the fact that linear cheletropic fragmentation is symmetry-forbidden in this case, it has been suggested [224] that the reaction might proceed in a non-concerted way, through a discrete intermediate. It is now clear that the available evidence is also consistent with the view that the elimination follows the concerted symmetry-allowed non-linear cheletropic path [*cf. (418)*].

The observed ready elimination of nitrous oxide *(433)* from *N*-nitrosoaziridines [225] probably also follows the non-linear cheletropic path [*(432)*→*(433)*]; note that the $4\pi_y$ system remains intact throughout the reaction, and that an x-symmetric lone pair at nitrogen in *(433)* is derived from the bonding antisymmetric σ orbital of the aziridine ring. However, an interesting alternative should be considered. If the nitroso compound be allowed to achieve the conformation *(434)*, the unshared electron pair at the pyramidal aziridine nitrogen atom may become one of the z-symmetric lone pairs of nitrous oxide *(435)*, while the electron pair from the bonding antisymmetric σ orbital of the aziridine ring enters the $4\pi_x$ system. In view of the fact that the uncoupling of two electrons from the $4\pi_y$ system of *(432)* may require *ca.* 23 kcal/mole, as estimated from the barrier to rotation in *N*-nitrosoamines [226], it seems unlikely that the molecule will make use of this alternative symmetry-allowed process to destroy itself.

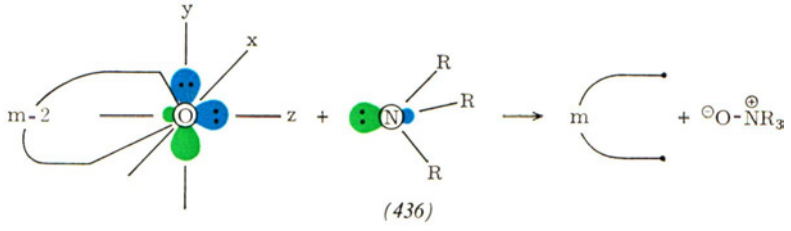


(434) *(435)*



(432) *(433)*

The hypothetical abstraction reaction *(436)* provides a further example of a cheletropic change. If the abstraction takes place in a *linear* fashion, the lone pair of the amine and the two oxygen lone pairs are transformed into the N-O bond and the z and y-axis unshared pairs of the *N*-oxide *(437)*. The remaining x-axis lone pair of the *N*-oxide must be taken from the antisymmetric σ orbital of the breaking carbon-oxygen bonds. Therefore, two electrons from the corresponding symmetric σ orbital must be delivered to the polyene product.



(436)

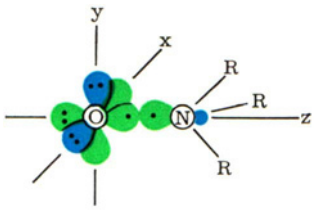
[222] *J. P. Freeman* and *W. H. Graham*, J. Amer. chem. Soc. *89*, 1761 (1967). However, the corresponding aryl-substituted case proceeds in a non-stereospecific manner (personal communication from *L. A. Carpino*).

[223] *N. P. Neureiter* and *F. G. Bordwell*, J. Amer. chem. Soc. *85*, 1210 (1963); *N. Tokura*, *T. Nagai*, and *S. Matsumara*, J. org. Chem. *31*, 349 (1966); *L. A. Carpino* and *L. V. McAdams III*, J. Amer. chem. Soc. *87*, 5804 (1965); *N. P. Neureiter*, *ibid. 88*, 558 (1966); *L. A. Paquette*, Accounts Chem. Res. *1*, 209 (1968).

[224] *F. G. Bordwell*, *J. M. Williams, jr.*, *E. B. Hoyt, jr.*, and *B. B. Jarvis*, J. Amer. chem. Soc. *90*, 429 (1968).

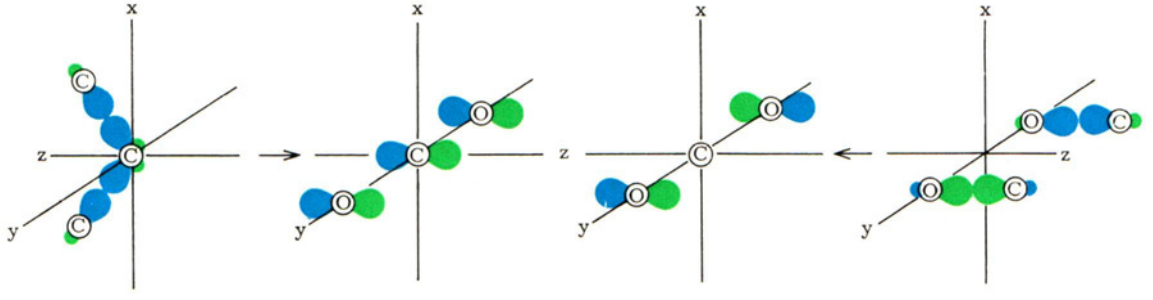
[225] *R. D. Clark* and *G. K. Helmkamp*, J. org. Chem. *29*,1316 (1964).

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



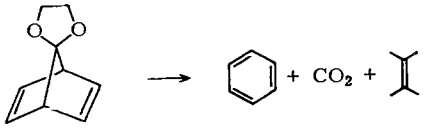
(437)

Consequently, the reaction must occur in a disrotatory sense when $m=4q+2$, or conrotatory when $m=4q$. If, on the other hand, the amine attacks in a *non-linear* manner, *i.e.* in the xz plane, but in the x direction, the stereochemical consequences are precisely reversed. A possible analogue of the linear reaction is available in the stereospecific abstraction of sulfur from the *cis*- and *trans*-butene episulfides by phosphines [227].



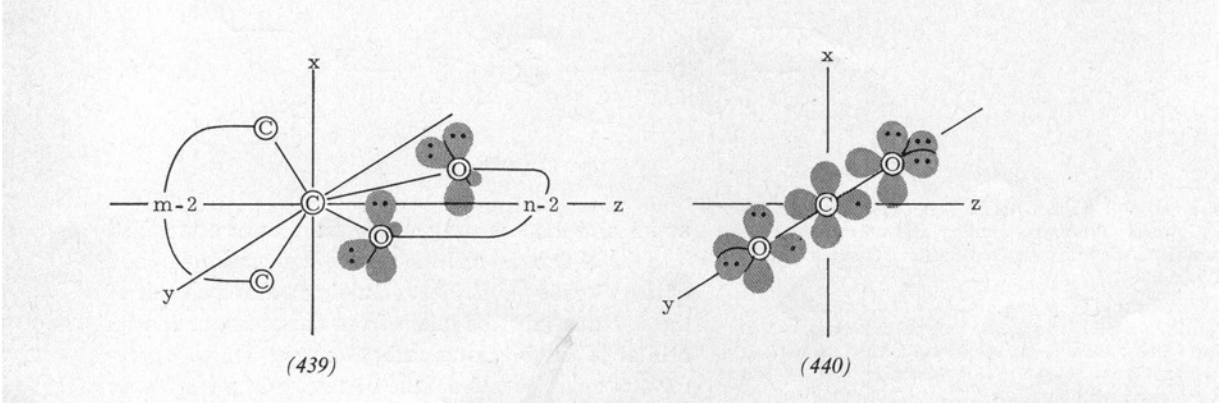
(441) (442) (443) (444)

A fascinating concatenation of a cheletropic fragmentation with a vicinal elimination is presented by the decomposition of a spiroketal to carbon dioxide and two olefins. As yet, the only known instances of the reaction involve ethylene ketals derived from substituted



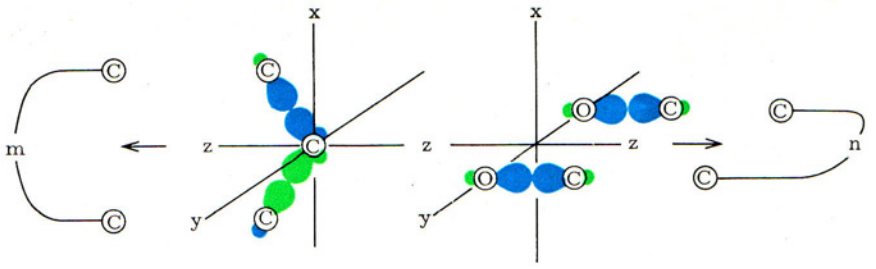
(438)

norbornadienones (438) [228]. It is most interesting to examine the stereochemical aspects of the process in the general case (439); m and n represent the numbers of electrons in the π systems of the product polyenes. In addition to the four electrons which constitute the skeletal σ bonds, carbon dioxide (440) requires twelve electrons: eight of these populate two perpendicular 4π systems, in the xy and yz planes, respectively, while four occupy two y-symmetric lone pair orbitals. If the reaction under discussion follows the linear cheletropic path, it is clear that the eight lone pair electrons at the oxygen atoms of (439) pass smoothly into the y-symmetric lone pair orbitals and the $4\pi_{xy}$ system of carbon dioxide (440), with conservation of orbital symmetry. Further, the orbitals of the orthogonal $4\pi_{yz}$ system can only be filled by transferring two electrons from the symmetric C–C–C σ orbital (441) to the lowest occupied symmetric π_{yz} orbital (442), and two from the antisymmetric O–C–O σ orbital (444) to the highest occupied π_{yz} orbital (443). Therefore, the electrons occupying the antisymmetric C–C–C σ orbital (446) must be delivered to the highest occupied orbital of the polyene (445), while those in the symmetric O–C–O σ orbital (447) take up their new positions in the highest occupied orbital of the polyene (448). Consequently, the geometric displacements associated with the carbon-carbon bond cleavages will be disrotatory when $m=4q$, or conrotatory when $m=4q+2$; by contrast, the carbon-oxygen scissions will be associated with disrotatory displacements when $n=4q+2$, or conrotatory when $n=4q$. If the reaction follows the *non-linear* cheletropic path, the stereochemical consequences attendant upon the carbon-carbon bond cleavages will of course be reversed. Finally, it may be noted that if there is a minimum in the potential surface for the reaction, representing the intermediacy of a singlet carbene species (449), the analysis in terms of orbital symmetry conservation is unchanged.



(439) (440)

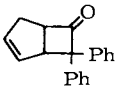
[227] *D. B. Denney* and *M. J. Boskin*, J. Amer. chem. Soc. *82*, 4736 (1960).
[228] *D. M. Lemal*, *E. P. Gosselink*, and *S. D. McGregor*, J. Amer. chem. Soc. *88*, 528 (1966).



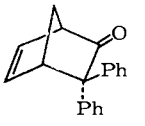
(445) (446) (447) (448)



(449)



(450)



(451)

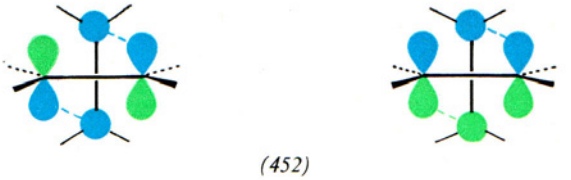
It might appear that in respect to cheletropic reactions, the principle of orbital symmetry conservation is rather generous than discriminate. But that is not so. Cheletropic reactions are unusual in that the stereochemical imperatives imposed by orbital symmetry control upon one of the reactant sites leave no imprint upon the products. Consequently, verification of the predictions which can be made about the detailed course of cheletropic reactions cannot be achieved simply by examining the stereochemistry of the products, and awaits more sophisticated scrutiny.

10.2. Cycloaddition Reactions of Ketenes

The combination of ketenes with olefins to give cyclobutanes has long been known [229]. In recent years, the reaction has been subjected to very searching scrutiny, and the evidence is now conclusive that it is concerted. Thus, the reaction proceeds with a high negative entropy of activation [230], the dependence of rate on solvent polarity is modest [230,231], and stereometric relations in the reactants are maintained in the products [232] – the most striking instance being the formation of distinct adducts from the reactions of dichloroketene with the *cis*- and *trans*-cyclooctenes [233]. Most compelling is the observation that the reaction of ketenes with dienes – even those so constrained as to favor terminal addition – gives only cyclobutanes, and no cyclohexenes [234]. For example, cyclopentadiene and diphenylketene react to give *(450)*; no *(451)* is produced.

A concerted combination of ethylenes to give a cyclobutane must follow the $[\pi 2_s + \pi 2_a]$ path, and in the case at hand the facts demonstrate beyond question that the olefinic reactant participates in a suprafacial way. Is there a special factor in the structure of ketenes which disposes them to play an antarafacial role in cycloaddition reactions?

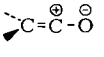
We have seen that the $[\pi 2_s + \pi 2_a]$ process involves orthogonal approach of the reacting species (*cf.* Section 6) – *i.e.* that the π systems must orient themselves as in



(452)

(452) – and we recognize that the path is not normally a readily accessible one, in the absence of special factors (*cf.* Figure 25, Section 6.1). For normal olefins, insurmountable difficulties would appear to be presented by steric hindrance factors, and by transition-state strain associated with framework distortions necessary to maintain effective orbital overlap.

Ketenes are powerful electrophiles. Chemically, the spearhead of their reactivity is the carbon atom of their especially reactive carbonyl group. This dominant aspect of the structure of ketenes, succinctly expressed in the valence-bond structure *(453)*, suggests that we analyze the combination of a vinyl cation *(454)* – *i.e.* a *vinylium* ion – with an olefin from the viewpoint of or-



(453)



(454)

bital symmetry conservation. The relevant orbital diagrams are *(455)* and *(456)*, and the significant differences *vis-a-vis* those for the simple olefin-olefin combination *(452)* are the substantially more favorable situation in respect to steric oppositions, and more especially, the presence of the orthogonal vacant *p* orbital in

[229] *Cf. H. Staudinger:* Die Ketene. Enke, Stuttgart 1912.

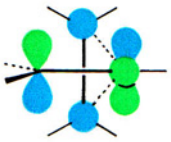
[230] *R. Huisgen, L. A. Feiler,* and *P. Otto,* Tetrahedron Letters *1968*, 4485.

[231] *W. T. Brady* and *H. R. O'Neal,* J. org. Chem. *32*, 612 (1967).

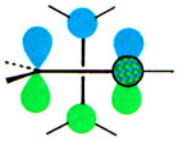
[232] *G. Binsch, L. A. Feiler,* and *R. Huisgen,* Tetrahedron Letters *1968*, 4497; *J. C. Martin, V. W. Goodlett,* and *R. D. Burpitt,* J. org. Chem. *30*, 4309 (1965); *R. Huisgen, L. Feiler,* and *G. Binsch,* Angew. Chem. *76*, 892 (1964); Angew. Chem. internat. Edit. *3*, 753 (1964).

[233] *R. Montaigne* and *L. Ghosez,* Angew. Chem. *80*, 194 (1968); Angew. Chem. internat. Edit. *7*, 221 (1968).

[234] *R. Huisgen* and *P. Otto,* Tetrahedron Letters *1968*, 4491.



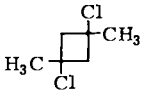
(455)



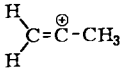
(456)

the vinylium ion [green in *(455)* and checkered in *(456)*]. *It is at once apparent that the latter special feature contributes two strong bonding interactions* [dotted lines in *(455)*] *which are absent from the* $[\pi 2_s+\pi 2_a]$ *reaction path for simple olefins.* It should be noted that the view presented is such that the *top* of the vacant *p* orbital is seen, and that it is the bottom of that orbital which is bonding to the occupied π system of the simple olefinic reactant [*cf. (455)*]. To put the matter in another way, the normal symmetry-allowed combination of a cation with an ethylene, in this unique situation sets the stage for and is coalescent with the $[\pi 2_s+\pi 2_a]$ cycloaddition reaction.

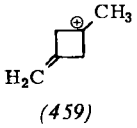
In the light of the analysis just presented, it is clear that a vinylium ion must be regarded as constituted *par excellence* for participation as the $\pi 2_a$ component in the concerted $[\pi 2_s+\pi 2_a]$ cycloaddition. Consequently, it is most gratifying to find that the predicted reaction has in fact been observed, though not hitherto recognized as such. Thus, *Griesbaum* [235] found that allene reacts with hydrogen chloride at −70 °C to give a mixture of the stereoisomeric dichlorodimethylcyclobutanes *(457)*; it is now clear that an initially-produced cation *(458)* combines with a molecule of allene by the



(457)

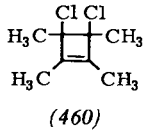


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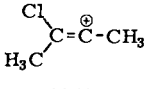


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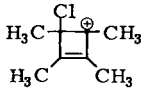
$[\pi 2_s+\pi 2_a]$ route to give *(459)*, which reacts with chloride ion and hydrogen chloride to afford the observed products. Further, the very useful, but surprising – indeed hitherto baffling – synthesis of 1,2-dichloro-1,2,3,4-tetramethylcyclobutene *(460)*, by treatment of 2-butyne with chlorine in the presence of boron trifluoride [236,237], is now readily explicable: $[\pi 2_s+\pi 2_a]$ combination of 2-butyne with the β-chlorovinylium ion *(461)* leads directly to the cyclobutenyl cation *(462)*, whose discharge by chloride ion yields *(460)*. These striking examples leave no doubt that vinylium ions possess in high degree the predicted capacity for concerted combination with $\pi 2_s$ systems.



(460)

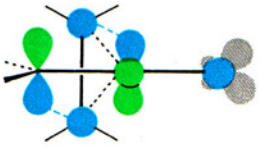


(461)

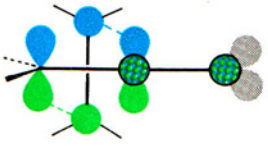


(462)

And now we can answer emphatically in the affirmative the inquiry which launched the discussion just concluded. Ketenes, in their capacity as vinylium ylides *(453)*, are in fact ideally constituted to play an antarafacial role in reaction with $\pi 2_s$ systems, and it is that symmetry-allowed role which they exhibit in the many observed concerted combinations with olefinic systems. Of course, ketenes are not simple vinylium ions, but



(463)



(464)

detailed analysis reveals that the circumstances are not significantly altered in the more complicated case. Thus, for ketenes the relevant orbital diagrams are *(463)* and *(464)*. In this case the place of the vacant *p* orbital of the simple vinylium ion is taken by the unoccupied $\pi^*_{C=O}$ orbital of the ketene molecule [*cf. (463)*]; it is the exceptionally low-lying position of this orbital which accounts in molecular orbital terms for the high electrophilic reactivity of ketenes. As in the simpler case, there is no net change in bonding through interaction of the extra π system with the π* orbital of the $\pi 2_s$ component [*cf. (456)* and *(464)*]. Finally, it should be pointed out explicitly that interaction of the $\pi_{C=C}$ system of the ketene molecule with the antisymmetric lone pair orbital at the oxygen atom is essentially irrelevant to the matter at hand. This interaction, which is small in terms of energy in any event, creates three new allylic orbitals (Figure 45). Of these, two are occupied; the lower simply takes the place of the usual two-orbital π system [*cf. (464)* and *(456)*] and the electrons in the middle orbital return to their original lone pair status as reaction proceeds.

In the dimerization of ketenes – also regarded as concerted [238] – one of the ketene molecules exercises its unique potentiality as a $\pi 2_a$ component, while the other acts in normal $\pi 2_s$ fashion. In that connection it should be noted that the participation of a ketene as a $\pi 2_s$ component is not facilitated by the presence of the orthogonal $\pi_{C=O}$ system, nor is the interaction with the lone

[235] *K. Griesbaum, W. Naegele,* and *G. G. Wanless,* J. Amer. chem. Soc. *87*, 3151 (1965); *K. Griesbaum,* Angew. Chem. *78*, 953 (1966); Angew. Chem. internat. Edit. *5*, 933 (1966).

[236] *R. Criegee* and *A. Moschel,* Chem. Ber. *92*, 2181 (1959).

[237] *I. V. Smirnov-Zamkov,* Doklady Akad. Nauk SSSR *83*, 869 (1952); *I. V. Smirnov-Zamkov* and *N. A. Kostromina,* Ukr. Khim. Zhur. *21*, 233 (1953).

[238] *R. Huisgen* and *P. Otto,* J. Amer. chem. Soc. *90*, 5342 (1968).

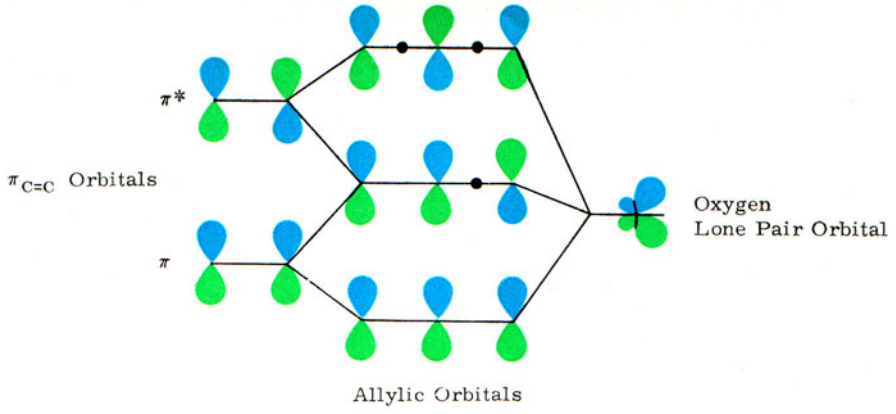


Figure 45. Allylic orbitals in the ketene molecule. — Note that as a consequence of the relative stability of the occupied atomic oxygen orbital, the node in the middle allylic orbital is not at the central atom, as it would be in a three-carbon system, and must be located between carbon and oxygen.

pair at oxygen expected to have a major effect. Thus, in participating in cycloaddition reactions as $\pi 2_s$ components, ketenes should not differ markedly from normal alkyl ethylenes. Consequently, in the reactions of ketenes with dienes, the normal symmetry-allowed $[\pi 4_s + \pi 2_s]$ reaction is not expected to be a ready one. Further, the $[\pi 4_s + \pi 2_a]$ reaction is of course symmetry-forbidden, and the presence of an orthogonal vacant *p* orbital, or low-lying $\pi^*_{C=O}$ system, cannot facilitate the $[\pi 4_a + \pi 2_a]$ process. Taken together, these circumstances account for the formation of cyclobutanones to the exclusion of cyclohexenones when ketenes react with simple dienes.

11. Generalized Selection Rules for Pericyclic Reactions

In our development of the theme of orbital symmetry control of concerted chemical changes, we have laid the basis for a general consideration of all *pericyclic* reactions – that is, reactions in which all first-order changes in bonding relationships take place in concert on a closed curve. Thus, we have discussed in detail the special characteristic features of several clearly differentiable reaction types. But we have also made it clear that the different classes have much in common. In particular, we have pointed out that electrocyclic reactions and sigmatropic changes can as well be treated as concerted intramolecular cycloaddition processes. Now, we develop further the important generalization that all pericyclic reactions may be categorized as concerted cycloaddition processes, and must obey the selection rules for such changes.

The selection rules for two-component cycloadditions [*cf.* Figure 22, Section 6] may easily be generalized by induction to include any number of components. In that way we derive the following general rule for all pericyclic changes:

A ground-state pericyclic change is symmetry-allowed when the total number of $(4q+2)_s$ *and* $(4r)_a$ *components is odd.*

Obviously, if the designated total is *even*, the reaction is symmetry-forbidden. Odd-electron systems generally conform to the pattern for even-numbered systems containing one more electron, and there is in general, corresponding to every ground-state reaction, a related excited-state process for which the rule is simply reversed.

In order to complete the generalized description of pericyclic reactions, it is necessary at this point to introduce one further, and final, convention. Clearly, when q or $r = 0$, a $4r$ component necessarily represents a single atomic orbital, and a $4q+2$ component may do so. That is to say, such a single orbital component may be vacant or occupied. Like any other component, single orbital components may participate in either a suprafacial or an antarafacial manner, and they require a special designation – a presubscript ω – consistent with the characterization of σ and π components, thus:

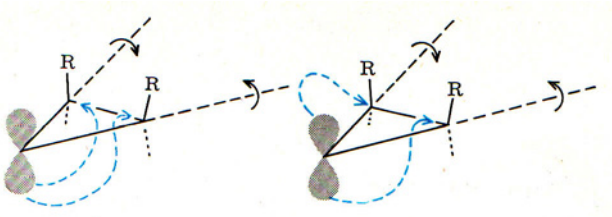
$$\omega 0_s \quad \omega 0_a \quad \omega 2_s \quad \omega 2_a$$

With the tools now at hand, it is a simple matter to classify any pericyclic reaction, and to determine whether it is symmetry-allowed. We shall now recapitulate the examples mentioned earlier, and exemplify the procedure in some new instances. Note that the dashed lines in all of the analyses represent bonding interactions in the transition state.

a) The conrotatory electrocyclic opening of cyclobutenes [*cf.* Figures 23 and 24, Section 6] may be regarded either as a $[\pi 2_s + \sigma 2_a]$ or a $[\pi 2_a + \sigma 2_s]$ process, and the general rule shows at once that it is symmetry-allowed.

b) The suprafacial [1,3] sigmatropic shift with inversion at the migrating center [*cf.* Figure 34, Section 7] may also be regarded as a symmetry-allowed $[\pi 2_s + \sigma 2_a]$ or a $[\pi 2_a + \sigma 2_s]$ change.

c) The disrotatory electrocyclic transformation of a cyclopropyl cation to an allyl cation may be regarded either as an $[\omega 0_s + \sigma 2_s]$ *(465)* or as an $[\omega 0_a + \sigma 2_a]$ *(466)* process, and is symmetry-allowed. Note that in a formal sense, when a single ω component is involved in a pericyclic reaction, the ω orbital moves to a new position, and one of the dashed lines used in the analysis vanishes in the product.



$[\omega 0_s+\sigma 2_s]$ (465) $[\omega 0_a+\sigma 2_a]$ (466)

d) The [1,2] sigmatropic shift within a cation cannot take place with inversion of the migrating group, since the $[\omega 0_a+\sigma 2_s]$ *(467)* and $[\omega 0_s+\sigma 2_a]$ *(468)* processes are symmetry-forbidden. Note that antarafacial bonding



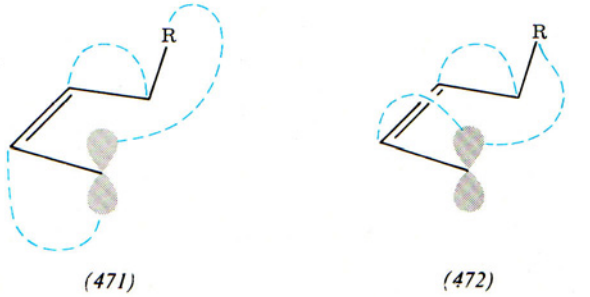
$[\omega 0_a+\sigma 2_s]$ (467) $[\omega 0_s+\sigma 2_a]$ (468)

interaction between two atoms joined by a non-participating bond and bridged by a single atom is physically impossible. Thus, the $[\omega 0_s+\sigma 2_s]$ processes depicted in *(469)* and *(470)* both represent the symmetry-allowed but physically unrealizable antarafacial [1,2] sigmatropic shift with inversion at the migrating center.



(469) (470)

e) The suprafacial [1,4] sigmatropic shift with inversion at the migrating center may be regarded, *i.a.*, as a symmetry-allowed $[\pi 2_a+\omega 0_a+\sigma 2_a]$ process *(471)*. All of the



(471) (472)

alternative formal classifications *(473)*, each of which represents a symmetry-allowed reaction, require inversion at R, and no allowed suprafacial process exists in which R migrates with retention; for example, the

$[\pi 2_s+\omega 0_a+\sigma 2_s]$
$[\pi 2_s+\omega 0_s+\sigma 2_a]$ *(473)*
$[\pi 2_a+\omega 0_s+\sigma 2_s]$

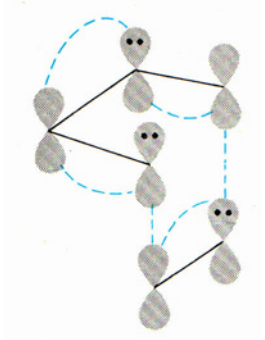
$[\pi 2_s+\omega 0_s+\sigma 2_s]$ pericyclic reaction depicted in *(472)* is obviously symmetry-forbidden.

f) The non-linear cheletropic extrusion of sulfur dioxide from an episulfone [*cf.* *(418)*, Section 10.1] is a symmetry-allowed $[\sigma 2_s+\sigma 2_a]$ reaction *(474)*, and the reverse process would be a $[\pi 2_s+\omega 2_a]$ change *(475)*.



(474) (475)

g) The Diels-Alder reaction is obviously a symmetry-allowed $[\pi 4_s+\pi 2_s]$ change, but it could be analyzed as an allowed $[\omega 0_s+\omega 2_s+\omega 0_a+\omega 2_a+\omega 0_s+\omega 2_s]$ process *(476)*.



(476)

The example is included partly in a sportive spirit, but it does have the serious purposes of indicating that (i) the participation of any number and kind of ω components in a pericyclic reaction presents no occasion for difficulty in analyzing the process in terms of the general rule, and (ii) polarization of the bonds involved in a pericyclic reaction in no way alters the orbital symmetry control to which it is subject.

It should be emphasized that use of the general selection rule for pericyclic reactions must always be subject to the following precautions.

a) The geometry of each individual case must be examined on its merits in order to ascertain whether the process is physically realizable. We have already exemplified, in d) above, and in our discussion of the rearrangement of the ester of Feist's acid [*cf.* *(331)*, Section 7.1], situations in which formally symmetry-allowed processes are geometrically impossible.

b) In cases in which the reacting components are directly joined by non-participating bonds, forced ancillary off-circuit antibonding interactions may render an otherwise allowed reaction symmetry-forbidden. Thus, prismane cannot be converted to three isolated, non-interacting, ground state ethylene moieties by a $[\sigma 2_s+\sigma 2_a+\sigma 2_a]$ process. The geometric constraints imposed by the non-participant σ framework require that the ethylene moieties produced in such a reaction inter-

act strongly in an antibonding way, and the orbital symmetry-imposed electronic configuration of the array is in fact that of a doubly excited state of the actual product benzene [*cf.* Section 6.4]. Any case in which similar circumstances may be suspected should be subjected individually to complete analysis in the light of the principle of orbital symmetry conservation.

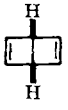
12. Violations

There are none!

Nor can violations be expected of so fundamental a principle of maximum bonding. All the more is it then important to give consideration to some reactions which might appear on casual inspection to contravene orbital symmetry conservation.

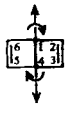
First, it should be emphasized explicitly here that a given symmetry-allowed concerted reaction need not necessarily represent the manner in which reacting molecules will actually comport themselves. Quite possibly another path, involving reactive *intermediates* of relatively low energy may be followed. The other side of this coin is that molecules may in some cases combine, or decompose, to give the very products which would result from symmetry-forbidden concerted processes. In these cases it is clear that the actual reaction path is a non-concerted one, involving discrete intermediates; indeed, the principle of orbital symmetry conservation is very useful in defining conditions in which such processes may be expected. Such are often the circumstances in the combination of ethylenes to give cyclobutanes. The direct, concerted $[\pi 2_s + \pi 2_s]$ combination is of course symmetry-forbidden, and the allowed $[\pi 2_s + \pi 2_a]$ reaction is realizable only in special circumstances. Nevertheless, there are a substantial number of instances, lacking the special prerequisites for the $[\pi 2_s + \pi 2_a]$ reaction, in which the combination of two ethylenic molecules leads to a cyclobutane [239]. And in such cases, the available evidence is compelling in favor of the view that discrete diradical or ionic intermediates are involved [240]; further, it is of obvious significance that such reactions are observed only when the reactant olefins are ornamented by substituents so constituted as to provide effective stabilization of the requisite intermediate.

It remains only to address a few final comments to the matter of symmetry-forbidden reactions which may occur in a concerted fashion. In principle, of course, given sufficient energy, and means of constraining molecules in energy-rich configurations, we could bring about any symmetry-forbidden reaction. A very powerful Maxwell demon could make a molecule of cyclobutane by grasping a molecule of ethylene in each hand, and – not without an impressive exhibition of his strength – forcing the two together face-to-face. He could seize a molecule of cyclobutene at its methylene groups, and tear it open in a disrotatory fashion to obtain butadiene. But without such demoniac intervention, molecules will very rarely comport themselves in like fashion – since reaction paths with lower energy surfaces than those associated with symmetry-forbidden processes will almost always be available. None the less, the possibility remains that molecules may be constructed within which no other such alternatives exist; then, provided that the molecule be sufficiently energized, the symmetry-forbidden path would necessarily be followed. Derivatives of *cis*-bicyclo[2.2.0]hexadiene *(477)* quite possibly exemplify such a process. These substances do undergo conversion to the corresponding

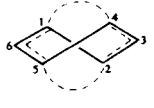


(477)

benzenoid isomers, with an activation energy in the neighborhood of 37 kcal/mole [241]. The simple disrotatory cleavage of the central bond is symmetry-forbidden, but *(477)* is already strained to the extent of *ca.* sixty kilocalories relative to benzene [242], and the addition of a further thirty-seven kilocalories may sufficiently energize the molecule as to overcome the prohibition against disrotatory cleavage. But even in this case, the possibility is not entirely excluded that events may take another course, and that the transformation may proceed through a discrete intermediate. For example, if the breaking of the central bond of *(477)* is accompanied by a quasi-conrotatory skewing distortion [*cf. (478)*] – a boat→twist-boat transformation – the result *(479)* is an array containing two skewed allyl radical systems [C(5)-C(6)-C(1) and C(2)-C(3)-C(4)], joined orthogonally at their termini. Were all bonding between C-1 and C-4 to be lost concurrently with these



(478)



(479)

motions, the related symmetry-derived antibonding components in the transition state for conversion to benzene would vanish, and the process could continue

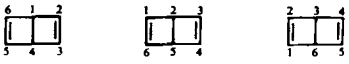
[239] An excellent review is available: *J. D. Roberts* and *C. M. Sharts*, Organic Reactions *12*, 1 (1962).

[240] *P. D. Bartlett, L. K. Montgomery*, and *B. Seidel*, J. Amer. chem. Soc. *86*, 616 (1964); *L. K. Montgomery, K. Schueller*, and *P. D. Bartlett, ibid. 86*, 622 (1964); *P. D. Bartlett* and *L. K. Montgomery, ibid. 86*, 628 (1964); *P. D. Bartlett*, Science *159*, 833 (1968).

[241] *J. F. M. Oth*, Angew. Chem. *80*, 633 (1968); Angew. Chem. internat. Edit. *7*, 646 (1968); Rec. Trav. Chim. Pays-Bas, *87*, 1185 (1968); *H. C. Volger* and *H. Hogeveen*, Rec. Trav. Chim. Pays-Bas *86*, 830 (1967).

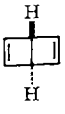
[242] *W. Schäfer*, Angew. Chem. *78*, 716 (1966); Angew. Chem. internat. Edit. *5*, 669 (1966).

to completion by appropriate symmetry-allowed combinations of the isolated allyl radicals. Even if some 1,4 bonding is retained – and of course, were that the case, some 2,5 bonding would be generated – the corresponding symmetry-derived antibonding components in the transition state *(479)* will be smaller than those in the transition state for the simple symmetry-forbidden disrotatory cleavage; it is of special interest that if *(479)* should represent the transition state for the conversion of bicyclohexadienes to aromatic compounds, the former should be susceptible of isomerization in the sense *(480)*→*(481)*→*(482)*.



(480) *(481)* *(482)*

Finally, we emphasize the fact that *cis*-bicyclo-[2.2.0]hexadienes owe their remarkable durability to symmetry-imposed barriers, and, to introduce a light note, suggest that our fellow chemists estimate how long the isomer *(483)* – put together, perhaps, by our versatile demon – would survive.



(483)

13. Other Theoretical Work

In view of the fact that the principle of conservation of orbital symmetry has been found to be an exceptionally powerful predictive and interpretive tool, it is not surprising that a number of alternative theoretical approaches have been set forth. In all cases the central conclusions, of necessity, agree in all respects with our own. Reference should be made to the interesting contributions of *Fukui* [243], *Salem* [244], *Zimmerman* [245], *Dewar* [246], *Oosterhoff* and *van der Lugt* [247], and, of course, *Longuet-Higgins* and *Abrahamson* [248].

It is also appropriate here to mention some earlier studies relevant to and antecedent to our own. Correlation diagrams for the simplest chemical reactions are no novelty; some interesting applications are presented by *Laidler* [249]. Such diagrams were extensively used by *Griffing* [250], but were incorrectly interpreted. In an important paper by *Herzfeld* [251] it was shown that for a set of $2p$ orbitals the number of nodes in a molecular system is conserved as atoms are brought near each other, and that when the orbitals are alike no two states of different energy can have the same number of nodes. *Bader* [252] presented a novel and interesting discussion of some elementary reactions.

We have already mentioned the suggestion of *Oosterhoff* [253] that orbital symmetry might play a role in electrocyclic reactions. The advantages of a six-electron transition state were pointed out by *Syrkin* [254]. His papers, and those by *Balaban* [255] and *Mathieu* and *Valls* [256] are a rich source of references for possible concerted reactions.

Numerous reviews summarizing various aspects of the application of the principle of conservation of orbital symmetry have already appeared [257].

The frontier-electron theory was developed by *Fukui*, who has continued an intensive exploration of various methods of calculation pertinent to problems of chemical reactivity [258]. In some of our work we have utilized extended Hückel calculations [259] to confirm qualitative conclusions. The virtue of these approximate calculations lies in the fact that they may be applied to σ as well as π systems. The method was originally developed in collaboration with *Lipscomb* and owes much to previous work of *Longuet-Higgins* on boron hydrides.

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Of special interest are several recent applications of orbital symmetry conservation in novel directions. The derivation of selection rules for the isomerization and substitution reactions of transition metal complexes [260], the suggestion that orbital symmetry is determinative in chemiluminescent reactions [261], and the analysis of the role of orbital symmetry in excited state energy transfer [262] merit particular attention.

14. Conclusion

We have now explicated the principle of conservation of orbital symmetry, and exemplified its use. It may perhaps be appropriate here to emphasize that the central content of the principle lies in the incontrovertible proposition that a chemical reaction will proceed the more readily, the more *bonding* may be maintained throughout the transformation. Consequently, we cannot doubt that the principle will endure, whatever the language in which it may be couched, or whatever greater precision may be developed in its application and extension.

Nor can it be doubted that extension will be made – both of a fundamental and of a detailed nature. Since every elementary step in *any* chemical reaction is a concerted process, correlative ideas must be applicable to *all* reactions. The exploration of applications in inorganic chemistry has barely been begun. And within the realm already delineated, only the imagination sets limits upon the number and variety of new and fascinating molecules which may be designed to favor reactions as yet undiscovered, but now known to be feasible.

Received: January 7, 1969 [A 710 IE]
German version: Angew. Chem. *81*, 797 (1969)

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Classification of Partition Reactions of Inorganic Cations

By H. Specker and A. Kettrup [*]

In partition reactions of inorganic cations, it is necessary to establish the composition of the extracted compounds. The methods used and the limits of their application are described and illustrated for the extraction of cobalt thiocyanates. The results obtained allow new analytical applications, e.g. the fractional extraction of Hg, Bi, Cd, In, and Zn.

1. Introduction

The aim of the present article is to describe the methods that provide information about the composition of an extracted species, as well as their application limits, using the extraction of cobalt thiocyanates as an example.

A general picture will also be given of the extraction of inorganic compounds with ketones and triesters of phosphoric acid as solvents. Extractions with diesters of phosphoric acid and with amines will not be discussed, since these systems were reviewed comparatively recently [1–3].

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[1] *D. F. Peppard* in: Advances in Inorganic Nuclear Chemistry Academic Press, New York 1966, Vol. 9.

[2] *D. Dyrssen, J.-O. Liljenzin*, and *J. Rydberg*: Solvent Extraction Chemistry. North-Holland Publ. Co., Amsterdam 1967.

[3] *A. Kettrup* and *H. Specker*, Fortschr. chem. Forsch. *10*, 237 (1968).

2. Methods of Determining the Compositions of Extracted Compounds

All the methods described below were originally developed for determination of the compositions of complexes in single-phase, particularly aqueous systems. The question of primary interest is that of the number n of ligands (*e.g.* halide ions) bound per central atom. In extractions with solvents that are capable of coordination, we also wish to know the number r of solvent molecules bound. If a definite compound, *e.g.* a halogenometalate

$$(A^+)_z[ML_n]^{z-} \cdot rS$$

is extracted over a wide concentration range, two series of measurements with suitable variations are generally sufficient to give the numbers of halide and solvent ligands.

The photometrically determined extinction value is very often used as a measure of the concentration of the complex formed in normal solution equilibria;

however, any other physical property that is definitely associated with the compound formed, *e.g.* the electric conductivity, may also be used. In partition measurements, the equilibrium reached in the extraction is fixed by the phase separation. In this case, provided that the total concentration of the element in question in the organic phase can be taken as equal to the concentration of the extracted complex and the blank extraction is not high, the inorganic components can be determined by a simple analysis of the organic phase. However, this will be possible in only a few cases.

2.1. Molar Ratio Method

The molar ratio method depends on the stoichiometric, *i.e.* quantitative reaction of the components forming the compound [4]. This means that in normal solution equilibria the complex formation constant K_n and in extractions the partition constant K_D, must be very large. In this method the concentration of one component of the complex, *e.g.* of the metal (C_M), is kept constant, while the concentration of the other, in this case of the ligand (C_L), is increased from one experiment to the next. In partition methods, the system is allowed to reach partition equilibrium after each addition of L, and the concentration of the complex in the organic phase is measured. This method gives satisfactory results when the partition constants are high; it has been used successfully to determine the number of solvent ligands in the system $UO_2(NO_3)_2 \cdot 2$ tributyl phosphate [5].

2.2. Logarithmic Method

This method for the investigation of solution equilibria, in particular of very weak complexes, which was first described by *Bent* and *French* [6], can be derived as follows. For a reaction

$$aM + nL \rightleftharpoons M_aL_n$$

we obtain

$$K = [M_aL_n]/([M]^a \cdot [L]^n)$$

Similarly, the heterogeneous partition constant (w = water, org = organic solvent) is given by

$$K_D = [M_aL_n\bullet_r]_{org} / \left([M]^a_w \cdot [L]^n_w \cdot [S]^r_{org}\right)$$

Introduction of the partition coefficient D gives

$$K_D = D / \left([L]^n_w \cdot [S]^r_w\right)$$

and hence, taking logarithms, we obtain

$$\log D = \log K_D + n \cdot \log [L]_w + r \cdot \log [S]_{org}$$

n, which will be referred to simply as the number of halide ligands, is determined by varying the halide concentration C_L while the concentrations of all other components, including that of the metal C_M, are kept constant. It is assumed that the components react to only a small extent. The equilibrium concentration can then be replaced by the total concentration: $[L] = C_L$, $[S] = C_S$, *etc.* Collection of the constant terms gives

$$\log D = A + n \cdot \log C_L.$$

n is the gradient of the straight line obtained by plotting the logarithm of the partition coefficient for M (metal) against the logarithm of the concentration C_L. The number r of solvent ligands can similarly be obtained by a series of measurements in which only the solvent concentration C_S in an inert solvent is progressively varied. Then

$$\log D = B + r \cdot \log C_S$$

Umland [7] applied the logarithmic method to two-phase systems for the determination of n for metal quinolinolates ("oxinates"). *Irving* [8], and even earlier *McKay* [9], used this method based on the above derivation for the first time to determine the numbers of coordinately bound solvent molecules (tributyl phosphate) in lanthanide nitrates and in uranyl nitrate respectively. According to *McKay*, in the determination of r, the solvent concentrations must be kept low in order to remain in the "ideal" range, *i.e.* $C_{TBP} < 0.186$ mole/l in the case of tributyl phosphate. The partition coefficients in this range are generally small, and are often very difficult to determine unless tracer methods can be used. This method for the determination of the number r of solvent ligands has therefore been confined so far to partition systems containing highly active esters of phosphoric acid. It can also be seen from the equations that the heterogeneous partition constants K_D can be calculated in this way, as was suggested by *Umland* [10].

2.3. Straight-Line Method

The straight-line method was developed by *Asmus* [11] for the investigation of medium-strong to weak complexes; the little-known method of *Edmonds* and *Birnbaum* [12] has a mathematically equivalent form.

[4] *J. H. Yoe* and *A. L. Jones*, Ind. Engng. Chem., internat. Edit. *16*, 111 (1944).

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[12] *S. M. Edmonds* and *N. Birnbaum*, J. Amer. chem. Soc. *63*, 1471 (1941).

We applied the straight-line method for the first time to two-phase systems (purely empirically at first, and then mathematically) for the determination of the empirical formulas of extracted halogenometalate complexes and of the coefficients n and r [13]. In this method, increasing quantities of the component L (*e.g.* halide) are added to a constant preset quantity of M (cation); a quantity that is proportional to the quantity of complex ML_n formed is then measured. The results of the measurements are used to find functions that appear as straight lines in a suitably chosen system of coordinates only if a parameter is identical with n, or with n or r in the case of an extraction system. In a greatly simplified form, with all the constants and known quantities collected and represented by P' and P'' *Asmus*'s final equation can be written in the form:

$$\frac{1}{{}_{v}n(r)} = P' \cdot \frac{1}{m} - P''$$

where v is the volume (in ml) of the component L or solvent added, and m is the quantity that is proportional to the concentration of ML_nS_r (generally the extinction).

To determine n, increasing quantities of L are added to the aqueous solution, the extraction is carried out, and m is measured in the extract. To determine r, increasing quantities of the active solvent, *e.g.* tributyl phosphate, are added to the inert solvent, *e.g.* isooctane, while keeping all other parameters constant, and $1/v^r$ (r = 1,2,3,4....) is plotted as usual against $1/m$. K_D can be calculated here, like K_n in the single-phase systems, from the gradient $\tan\alpha$ of the straight line and the intercept Q on the ordinate [13]. The straight-line method is illustrated schematically in Figure 1.

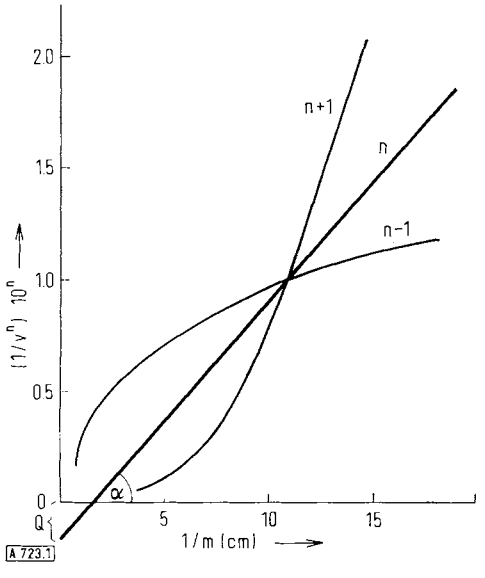


Fig. 1. Schematic illustration of *Asmus*'s straight line method.

[13] *H. Specker, G. Werding,* and *G. Schiewe,* Z. analyt. Chem. *206,* 161 (1964).

[14] *J. Ostromisslenski,* Ber. dtsch. chem. Ges. *44,* 286, 1189 (1911).

[15] *P. Job,* C.R. hebd. Séances Acad. Sci. *180,* 928 (1925).

2.4. Continuous Variation Method

The most widely used method of determining the composition of a compound ML_n is the method devised by *Ostromisslensky* [14] and *Job* [15] on the basis of the principle of "continuous" variations. Equimolar solutions of the components M and L are mixed in quantities such that the total volume, and hence the total concentration C, remains constant:

$$(C_M + C_L) = C$$

$$C_M = C(1-x) \text{ and } C_L = C \cdot x$$

where $0 \leq x \leq 1$ (mole fraction of the component L). The concentration of the compound ML_n reaches a maximum when the ratio of the initial concentrations is exactly

$$C_L/C_M = x/(1-x) = n$$

This method is particularly suitable when $n = 1$; if n = 2,3, or even 4, it can be used only if one complex is formed and if its formation constant is sufficiently high. The improper use of this method has been referred to by several authors, particularly *Woldbye* [16], *Jones* [17], and *Asmus* [18].

In two-phase systems, the Job method is also subject to these limitations, but occasionally offers greater advantages. It has been used by *Pilipenko* [19] and by *Umland* [20] to determine the compositions of extracted chelates, and its theoretical validity for this purpose has been verified by *Irving* [21]. This method was later used successfully for the investigation of metal halides and halogenometalates [5]. It has also been used to find the number r of solvent ligands. Figure 2 illustrates the use of this method for the determination of r in the system ferric thiocyanate – tributyl phosphate, in one case with variation of iron in the aqueous phase and of tributyl phosphate in the organic, and in the

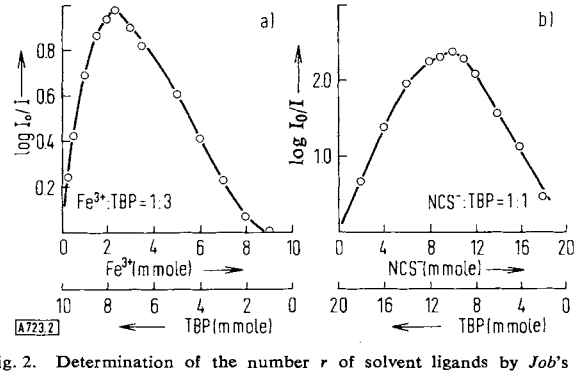


Fig. 2. Determination of the number r of solvent ligands by *Job*'s method in the system $Fe(NCS)_3$-tributyl phosphate (TBP). a) Fe^{3+} and TBP in continuous variation; b) NCS^- and TBP in continuous variation; ordinates in a) and b): extinction of the organic phase.

[16] *F. Woldbye,* Acta chem. scand. *9,* 299 (1955).

[17] *M. Jones,* J. Amer. chem. Soc. *81,* 4485 (1959).

[18] *E. Asmus* and *P. Meyer,* Z. analyt. Chem. *190,* 390 (1962).

[19] *A. T. Pilipenko,* Ž. analitičeskoj Chim. *8,* 286 (1953).

[20] *F. Umland* and *W. Hoffmann,* Z. analyt. Chem. *168,* 268 (1959).

[21] *H. M. Irving* and *T. B. Pierce,* J. chem. Soc. (London) *1959,* 2565.

other with variation of thiocyanate in the aqueous phase and of tributyl phosphate in the organic. Both series of measurements lead to the conclusion that the extracted compound has the composition $Fe(NCS)_3 \cdot 3$ TBP.

2.5. Comparison of Spectra

The composition of the extracted compound can always be deduced from the absorption spectra when they agree with the spectra of metal halides or halogenometalates in solution or even with the spectra of single-phase equilibrium mixtures. Comparison of the absorption spectra of extracts and of model solutions can frequently also be used when the organic phase contains several compounds in equilibrium with one another instead of predominantly one compound. The methods described earlier can be used only with reservations, if at all, in such cases. If a series of recorded absorption spectra show one or more isosbestic points, *i.e.* points at which the extinction remains the same when the spectra change, there are only two absorbing compounds in equilibrium with each other. This special case frequently facilitates the interpretation of the spectra, and hence the calculation of the equilibrium.

2.6. Detection of Mononuclear Complexes

The most suitable method for determining whether mononuclear or polynuclear complexes are formed in solution is the logarithmic method (Section 2.2) proposed by *Bent* and *French* [6]. To find the number a of central atoms M in a dissolved complex having the empirical formula M_aL_n, the metal concentration C_M is varied in the presence of a constant high excess concentration of the component L and of all the other reactants present. The coefficient a is found as the gradient of the straight line obtained on plotting

$$\log C_{M_aL_n} = f(\log C_M)$$

For mononuclear complexes, therefore, it is always found that $\tan \alpha = a = 1$. The equation is also applicable to two-phase systems. The logarithm of the concentration of the complex in the extract is again plotted against the logarithm of the predetermined metal concentration in the aqueous phase (or more accurately the equilibrium concentration), and the slope of the straight line is determined:

$$\log C_{complex} = a \cdot \log C_M + \text{const.} \quad (C_M \gg C_{complex})$$

The partition coefficient D or $\log D$ may be plotted instead of $\log C_{complex}$. A line parallel to the abscissa is then obtained only if the extracted compound is mononuclear. The partition coefficient is then independent of the given concentration C_M of the central atom [22].

[22] *I. Nelidow* and *R. M. Diamond*, J. physic. Chem. *59*, 710 (1955).

Except in the typical polyacids and heteropolyacids, polynuclear complexes or polymers occur only at higher metal concentrations; the occurrence of these compounds is then synonymous in many cases with the formation of autocomplexes. Thus we have detected autocomplexes in the extraction of cobalt thiocyanates at high concentrations under certain conditions.

3. Determination of the Complex Constants in Solution

The formation constant of a complex is easy to determine if there is only one complexing equilibrium in solution. Suitable methods are the logarithmic method, the straight line method, and other known methods. It is equally easy to determine the constant K_D of a partition reaction having a single, definite course if the concentrations can be used instead of activities in the calculations. More complicated methods are required, on the other hand, to determine the constants of successive complexes quantitatively for step equilibria in a solution or in partition processes.

It is rarely possible to carry out a detailed quantitative treatment of such difficult situations in two-phase systems. We have tried to record the absorption spectra of cobalt thiocyanates in the pure extraction solvents (tributyl phosphate, cyclohexanone, isobutyl methyl ketone) in very different cation and anion concentration ranges, in order to apply the results to extracts and to compare them. The choice of methods for the investigation of the stepwise complex formation was limited by the almost total overlap of the spectra of successive cobalt complexes. The methods available are firstly *Bjerrum*'s method of corresponding solutions (calibration curve method) [23], secondly a variant of the spectroscopic method described by *Newman* and *Hume* [24], and thirdly two mutually complementary evaluation methods based on the presence of isosbestic points [25, 26]. The use of all the methods mentioned so far will be illustrated below for the extraction of cobalt thiocyanates.

4. Cobalt Thiocyanates in the Partition System

The analytical application of cobalt thiocyanate extraction has been known for 100 years [27]. Despite their ready accessibility for analytical and photometric investigations the composition of the blue cobalt halides extracted is not yet definitely known; this is true even of the aqueous solutions. Our measurements

[23] *J. Bjerrum*, Kgl. dansk. Vidensk. Selsk., *21*, 4 (1944).

[24] *L. Newman* and *D. N. Hume*, J. Amer. chem. Soc. *79*, 4551 (1957).

[25] *G. Werding*, Dissertation, Universität Münster 1963.

[26] *W. Libus*, *A. Ugniewska*, and *S. Minc*, Roczniki Chem. (Ann. Soc. chim. Polonorum) *34*, 29 (1960).

[27] *H. W. Vogel*, Ber. dtsch. chem. Ges. *8*, 1553 (1875).

have failed to confirm *Lehné*'s opinion [28], based on the spectra (ε_{max} = 150 l·mole^{-1} cm^{-1}, λ = 620 nm), that only $[Co(NCS)_4]^{2-}$ is present in aqueous 8.4 M ammonium thiocyanate solution. The spectra show clearly that $[Co(NCS)_3]^-$ must also be present at this concentration.

The classical method for the analysis of the organic phase leads to two definite results, when the "blank value" is taken into account, with an excess of cobalt ion and with an excess of ammonium thiocyanate (see Table 1). With an excess of cobalt, only $Co(NCS)_2$ is extracted with the three solvents mentioned, whereas with an excess of thiocyanate, TBP extracts the trithiocyanatocobaltate and the other solvents extract the tetrathiocyanatocobaltate. The blank extraction was reproducibly suppressed in every case by addition of an inert solvent (isooctane).

Table 1. Ratio NCS^- : Co^{2+} found by analysis of the organic phases.

	Tributyl phosphate	Cyclo-hexanone	Isobutyl methyl ketone
Constant NCS^- conc. (mole/l) (excess)	0.75	0.75	0.75
Increasing Co^{2+}conc. (mole/l)	0—0.1	0—0.07	0—0 09
NCS^-/Co^{2+} = n (corr.)	3.1	4.0	3.8
Constant Co^{2+} conc. (mole/l) (excess)	0.75	0.75	1.50
Increasing NCS^- conc. (mole/l)	0—0.07	0—0.07	0—0.025
NCS^-/Co^{2+} = n (corr.)	1.86	1.94	2.1

The molar ratio method does not give the desired result because of the limitations mentioned above. S-shaped curves of very little value are obtained. This method simply confirmed that the extraction does not proceed stoichiometrically and that several compounds are extracted at the same time. For the same reason, the logarithmic method also failed to give a definite result. Even *Asmus*'s straight line method was of no assistance in extractions from aqueous solutions containing thiocyanate, owing to the simultaneous extraction of several compounds. If, by analogy with the photometric determination of cobalt, the extraction is carried out with tributylammonium thiocyanate and *n*-butanol at pH = 6, only one thiocyanato complex is extracted, as is shown by the constant spectrum (ε_{max} = 625 nm). In this special case the conditions for both the straight line method and the logarithmic method are satisfied. It is clear from Figures 3 and 4 that the complex extracted is tetrathiocyanatocobaltate, and not the hexathiocyanato compound, as was originally assumed.

Like the analysis of the mixture, the determination of the number r of solvent ligands is difficult because of the succession of step equilibria. It is however possible to determine the coordinately bound solvent molecules either with an extremely large excess of ammonium thiocyanate or with an excess of cobalt. Under these conditions the compounds $[Co(NCS)_4]^{2-}$ and

[28] *M. Lehné*, Bull. Soc. chim. France *1951*, 76.

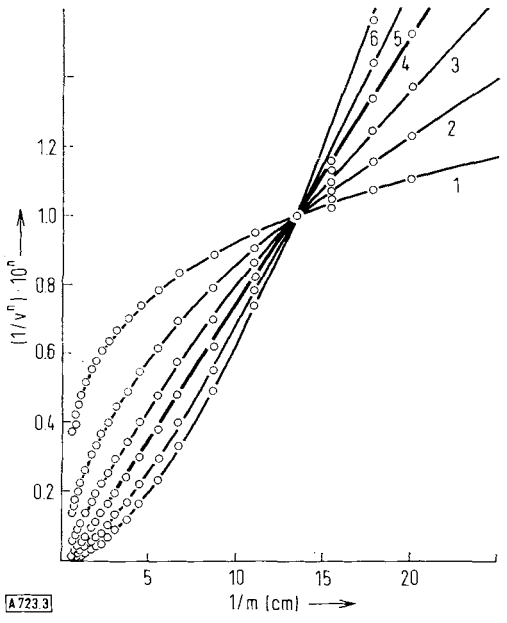


Fig. 3. Determination of the number n of thiocyanate ligands by the straight line method in the two-phase system: $(C_4H_9)_3NH^+$—Co^{2+}—NCS^-—H_2O/*n*-butyl acetate.

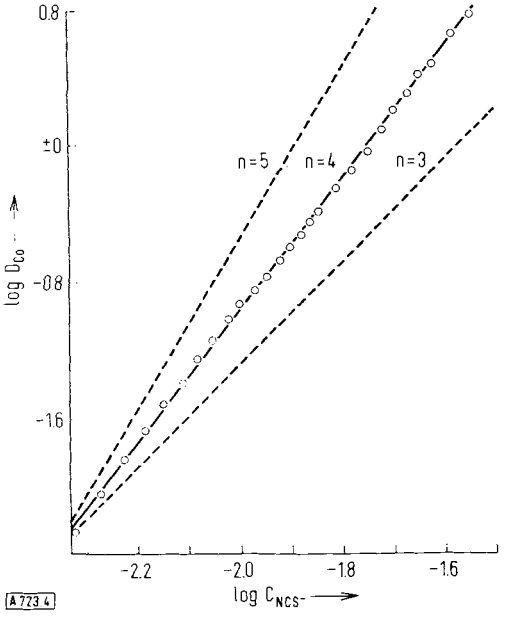


Fig. 4. Determination of the number n of thiocyanate ligands by the logarithmic method in the two-phase system: $(C_4H_9)_3NH^+$—Co^{2+}—NCS^-—H_2O/*n*-butyl acetate.

$Co(NCS)_2$ respectively are present. For the compound $NH_4[Co(NCS)_3]$, which is always present in the equilibrium when the concentrations of the components are comparable, r can only be estimated from the intermediate values. It was possible to show in preliminary experiments and from the absorption spectra that at a cobalt: thiocyanate molar ratio of 1:4 in the aqueous phase the trithiocyanatocobaltate is present in the tributyl phosphate extract to the extent of 85 %. The determination of the number of solvent ligands, however, was still confined to the tributyl phosphate-cobalt thiocyanate system, since very accurate analysis of the organic phases was not possible in the systems with cyclohexanone and isobutyl methyl ketone.

The results obtained by the logarithmic method with a large excess of thiocyanate are shown in Figure 5. The concentration of the active solvent (tributyl phosphate) was varied from 0 to 0.3 M in isooctane and plotted against the partition coefficient. All the series of experiments gave a slope of 4, *i.e.* the compound $(NH_4)_2[Co(NCS)_4]$ is coordinated with four molecules of tributyl phosphate.

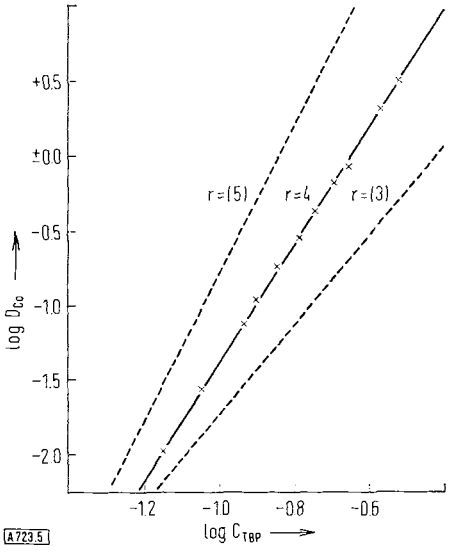


Fig. 5. Use of the logarithmic method for the determination of the number r of solvent ligands on tetrathiocyanatocobaltate.

The extracted compound $Co(NCS)_2$ has also been investigated by the logarithmic method. With low starting concentrations [0.1 mole/l of $Co(NCS)_2$], the slope is clearly 2, showing that the compound $Co(NCS)_2 \cdot 2$ TBP is present. At higher starting concentrations in the aqueous phase [1.6 mole/l of $Co(NCS)_2$] and under otherwise identical conditions the slope of the straight line is 3; intermediate concentrhtions give slopes of 2 to 3. It is very probable in this case that an autocomplex having the composition $Co_2(NCS)_4 \cdot 3$ TBP is being extracted, but we have not yet been able to obtain definite confirmation of this.

These extraction systems were also investigated by *Asmus*'s straight line method, which fully confirmed the results of the logarithmic method.

The continuous variation method was also used to obtain further confirmation of the numbers r of solvent ligands found so tar. The conditions for the use of this method are also satisfied, since one series of experiments can be carried out with an excess of cobalt and another with an excess of thiocyanate. The experiments with an excess of cobalt confirmed the compound $Co(NCS)_2 \cdot 2$TBP, while the experiments with an excess of thiocyanate confirmed the compound $(NH_4)_2[Co(CNS)_4] \cdot 4$TBP. The determination of the number r of solvent ligands on extraction of trithiocyanatocobalt was more difficult. This compound is never present alone in the extract. However, we were able to calculate from a large number of spectra that at a cobalt: thiocyanate ratio of 1:4 in the aqueous phase the trithiocyanato compound is present in the tributyl phosphate phase to the extent of 85 %. Under these conditions the logarithmic method gives a slope of 2.93. This leads to $r = 3$ for the number of solvent ligands, and to the compound $NH_4[Co(NCS)_3] \cdot 3$TBP.

To sum up, therefore, good agreement can be obtained by several methods even for the very complicated cobalt thiocyanate system.

The formation constants K_3 and K_4 in the following reactions were also calculated:

$$Co(NCS)_2 + NH_4NCS \overset{K_3}{\rightleftharpoons} NH_4[Co(NCS)_3]$$

$$NH_4[Co(NCS)_3] + NH_4SCN \overset{K_4}{\rightleftharpoons} (NH_4)_2[Co(NCS)_4]$$

Since we had available a large volume of experimental data and many absorption spectra, *Bjerrum*'s method of corresponding solutions, *Newman* and *Hume*'s method, and the method based on isosbestic points were used

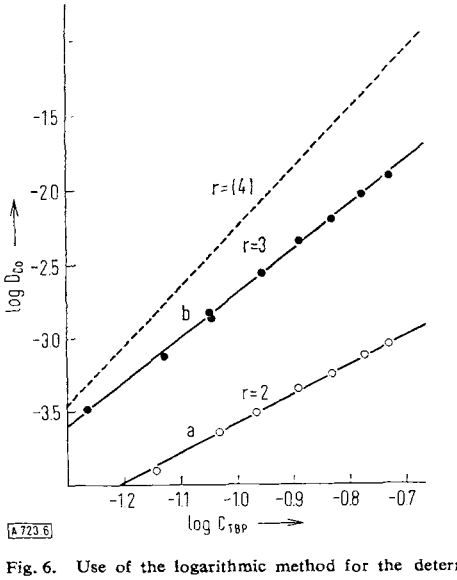


Fig. 6. Use of the logarithmic method for the determination of the number r of solvent ligands in the system Co^{2+}—NCS^-—H_2O/tributyl phosphate-isooctane. a) from 0.1 M $Co(NCS)_2$ solution; b) from 1.6 M $Co(NCS)_2$ solution.

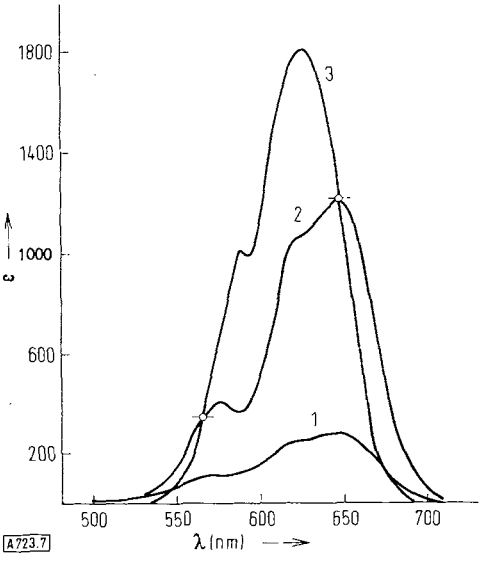


Fig. 7. Absorption spectra of cobalt thiocyanates in tributyl phosphate. Curve 1: spectrum of $Co(NCS)_2$; curve 2: spectrum of $NH_4[Co(NCS)_3]$; curve 3: spectrum of $(NH_4)_2[Co(NCS)_4]$. o = isosbestic points.

for the solvents tributyl phosphate, cyclohexanone, and isobutyl methyl ketone.

The results are shown in Table 2. The complex constants K_4 are greater by factors of 30 to 50 in cyclohexanone and in isobutyl methyl ketone than in tributyl phosphate. This provides quantitative confirmation that different compounds[29] are extracted by different solvents. The number of inorganic ligands

Table 2. Complex constants of cobalt thiocyanates in organic solvents.

	K_n	Tributyl phosphate	Cyclo-hexanone	Isobutyl methyl ketone
Bjerrum method	K_3	$2.5 \cdot 10^4$	$3.4 \cdot 10^4$	$2.4 \cdot 10^4$
	K_4	$1.9 \cdot 10^2$	$6.5 \cdot 10^3$	$7.1 \cdot 10^3$
Newman-Hume method	K_3	$2.4 \cdot 10^4$	$3.3 \cdot 10^4$	$2.5 \cdot 10^4$
	K_4	$2.0 \cdot 10^2$	$6.1 \cdot 10^3$	$7.0 \cdot 10^3$
Isosbestic point method	K_3	$3 \cdot 10^4$	—	—
	K_4	$1.9 \cdot 10^2$	—	—

is smaller with highly active solvents, *i.e.* inorganic ligands can be displaced by solvent molecules.

The percentage distribution of the thiocyanato complexes can also be calculated as a function of the ammonium thiocyanate concentration from the K_n values. In equilibrium with the aqueous phase, the compound $NH_4[Co(NCS)_3]$ occurs to extents of up to 85, 53, and 47 % respectively in tributyl phosphate, cyclohexanone, and isobutyl methyl ketone.

5. Investigation of Other Extraction Systems

As has been repeatedly mentioned, the application of the methods discussed to the system cobalt thiocyanate-organic solvent presents special difficulties. In studies on the extraction of other metals, which are based on the periodic system, the conditions for the use of these methods are much more favorable. The composition of the extracted species is shown in Table 3.

Table 3. List of compounds extracted (Cyclo = cyclohexanone, TBP = tributyl phosphate).

Central atom	Solvent (S)	Compound extracted	Ref.
CuI	TBP	$[Cu_2I_3]^- \cdot 3S$	[30]
Ag	Cyclo	$[Ag_2I_3]^- \cdot 2S$	[30]
	TBP	$[Ag_2I_3]^- \cdot 2S$	[30]
AuIII	TBP	$[AuCl_4]^- \cdot 3S$	[30, 31]
Zn	Cyclo	$ZnI_2 \cdot 2S$, $Zn(NCS)_2 \cdot 4S$, $[ZnI_3]^- \cdot 3S$, $[Zn(NCS)_3]^- \cdot 3S$	[32]
	TBP	$ZnCl_2 \cdot 2S$, $ZnI_2 \cdot 2S$, $Zn(NCS)_2 \cdot 4S$, $[Zn(NCS)_3]^- \cdot 3S$	[32]
Cd	Cyclo	$CdI_2 \cdot 2S$, $[CdI_3]^- \cdot 3S$	[32]
	TBP	$CdCl_2 \cdot 2S$, $CdI_2 \cdot 2S$, $Cd(NCS)_2 \cdot 4S$, $[Cd(NCS)_3]^- \cdot 3S$	[32]
Hg	Cyclo	$HgI_2 \cdot 2S$, $HgCl_2 \cdot 2S$, $Hg(NCS)_2 \cdot 4S$, $[HgI_3]^- \cdot S$, $[HgCl_3]^- \cdot S$, $[Hg(NCS)_3]^- \cdot 3S$	[32]
	TBP	$HgI_2 \cdot 2S$, $HgCl_2 \cdot 2S$, $Hg(NCS)_2 \cdot 4S$, $[HgI_3]^- \cdot S$, $[HgCl_3]^- \cdot S$, $[Hg(NCS)_3]^- \cdot 3S$	[32, 33]
Ga	Cyclo	$[GaCl_4]^- \cdot 2S$	[34]
	TBP	$[GaCl_4]^- \cdot 2S$, $Ga(NCS)_3 \cdot 3S$, $[Ga(NCS)_4]^- \cdot 2S$	[34]
In	Cyclo	$[InI_4]^- \cdot 2S$	[34]
	TBP	$[InCl_4]^- \cdot 2S$, $[InI_4]^- \cdot 2S$, $In(NCS)_3 \cdot 3S$, $[In(NCS)_4]^- \cdot 2S$	[34]
Tl	Cyclo	$[TlCl_4]^- \cdot 2S$, $[TlI_4]^- \cdot xS$, $TlI_3 \cdot xS$	[34]
	TBP	$TlCl_3 \cdot S$	[34]
Sc	TBP	$Sc(NO_3)_3 \cdot 3S$	[36]
Sn	TBP	$SnCl_4 \cdot 2S$	[37]
Ti	TBP	$TiCl_4 \cdot TBP$, $TiCl_4 \cdot 2TBP$	[38]
Zr	TBP	$Zr(OH)_2Cl_2 \cdot 2(TBP \cdot HCl)$, $[ZrO(NCS)_2 \cdot 2TBP]_x$, $Zr(NO_3)_4 \cdot 2S$	[39, 40]
Hf	TBP	$Hf(OH)_2Cl_2 \cdot 2(TBP \cdot HCl)$, $[HfO(NCS)_2 \cdot 2TBP]_x$	[39]
Bi	Cyclo	$BiI_3 \cdot 3S$	[29]
	TBP	$BiI_3 \cdot 3S$	[29]
V	TBP	$HVO_2Cl_2 \cdot 2S$	[41]
Cr	TBP	$HCrO_3Cl \cdot 2S$, $H_2Cr_2O_7 \cdot 2S$	[32, 41]
Mo	TBP	$MoO_2Cl_2 \cdot 2S$	[32, 41]
W	TBP	$WO_2Cl_2 \cdot 2S$	[32, 41]
U	TBP	$UO_2(NO_3)_2 \cdot 2S$, $UO_2Cl_2 \cdot 2S$	[43, 47]
Re	TBP		[48]
Fe	Cyclo	$Fe(NCS)_3 \cdot 3S$	[5]
	TBP	$FeCl_3 \cdot 3S$, $[FeCl_4]^- \cdot 2S$, $Fe(NCS)_3 \cdot 3S$	[29, 44]
Co	Cyclo	$Co(NCS)_2 \cdot xS$, $NH_4[Co(NCS)_3] \cdot xS$, $(NH_4)_2[Co(NCS)_4] \cdot xS$	[42]
	TBP	$CoCl_2 \cdot xS$, $[CoCl_3]^- \cdot xS$, $[Co(Cl_4)_4]^- \cdot xS$, $Co(NCS)_2 \cdot 2S$, $Co(NCS)_2 \cdot 3TBP$, $[Co(NCS)_3]^- \cdot 3S$, $[Co(NCS)_4]^{2-} \cdot 4S$	[42]
Ru	TBP	$Ru(NO)(NO_3)_4 \cdot 3S$, $Ru(NO)(NO_3)_3 \cdot 4S$	[45]
Rh	TBP		[49]
PtII	TBP	$H[PtCl_5] \cdot 3S$	[49]
Lanthanides (M)	TBP	$M(NCS)_3 \cdot 3S$, $M(NO_3)_3 \cdot 3S$	[35, 36]
Actinides (M)	TBP	$M(NO_3)_3 \cdot 3S$, $M(NO_3)_4 \cdot 2S$; $MO_2(NO_3)_2 \cdot 2S$	[9, 46]

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6. Analytical Uses

If the compound extracted is known, the equilibrium constants of partition reactions can be calculated. These K_D values in the dilute solution range are an accurate expression of the extracting powers of organic solvents, particularly if extracted compounds of the same formula type are compared, *e.g.* the complexes of the iodides of Group II triad metals with tributyl phosphate. Using total ionic strengths $I < 0.01$ and identical initial concentrations of the metal salt solution, the halide solution, the mineral acid, and the solvent, the quantities obtained are thermodynamic constants at a given temperature, and are preferable to partition coefficients obtained at arbitrary concentrations. These results can be transferred to the analytical concentration range ($I > 0.01$) only if the activity coefficients of all the components of a partition system are known. This is only rarely true of aqueous solutions, and is never true for organic solvents.

The partition coefficients found in the ideal solution range nevertheless agree well with the partition behavior of metals at high concentrations of the components of the aqueous and organic phases, and can therefore be used for the classification of inorganic partition reactions.

The constants were calculated by the logarithmic method (intercept on the ordinate) and by *Asmus*'s straight line method (intercept on the ordinate and slope) [11].

A selection of the K_D values obtained is given in Table 4; they reflect the observed partition behavior very satisfactorily. To supplement these results, the enthalpies of partition of some systems were measured [50, 51]. The partition constants and enthalpies of partition can, as one would expect, be correlated.

Table 4. K_D value and enthalpy of partition as a measure of the partition behavior of an element (TAP = triamyl phosphate; MIBK = isobutyl methyl ketone; for TBP and Cyclo, see Table 3.

	K_D-value		$-\Delta H_{293}$ (kcal/mole^{-1})
	Linear method	Log method	
$BiI_3 \cdot 3TBP$	$6 \cdot 10^8$	$4.3 \cdot 10^8$	6.8 ± 0.1
$BiI_3 \cdot 3TAP$	$4.5 \cdot 10^7$	$1.5 \cdot 10^7$	—
$BiI_3 \cdot 3$ Cyclo	$2.8 \cdot 10^4$	—	4.9 ± 0.15
$Li[BiI_4] \cdot 2MIBK$	$5 \cdot 10^1$	—	3.4 ± 0.1
$Fe(NCS)_3 \cdot 3TBP$	$1 \cdot 10^9$	$7.3 \cdot 10^8$	8.3 ± 0.2
$HgI_2 \cdot 2TBP$	$5.8 \cdot 10^{11}$	$7.3 \cdot 10^{11}$	10.1 ± 0.2
$HgI_2 \cdot 2$ Cyclo	—	$8.2 \cdot 10^8$	7.0 ± 0.1
$HgI_2 \cdot 2MIBK$	$1.1 \cdot 10^8$	$2.4 \cdot 10^8$	5.9 ± 0.1
$CdI_2 \cdot 2TBP$	—	$8 \cdot 10^4$	5.5 ± 0.2
$ZnI_2 \cdot 2TBP$	—	$1.5 \cdot 10^{-2}$	4.7 ± 0.2
$UO_2(NO_3)_2 \cdot 2TBP$	—	—	6.2 ± 0.2

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Analytical uses can be predicted from the partition constants. An impressive example of this is the fractional extraction of mercury, bismuth, cadmium, zinc, and indium, which is shown in Figure 8.

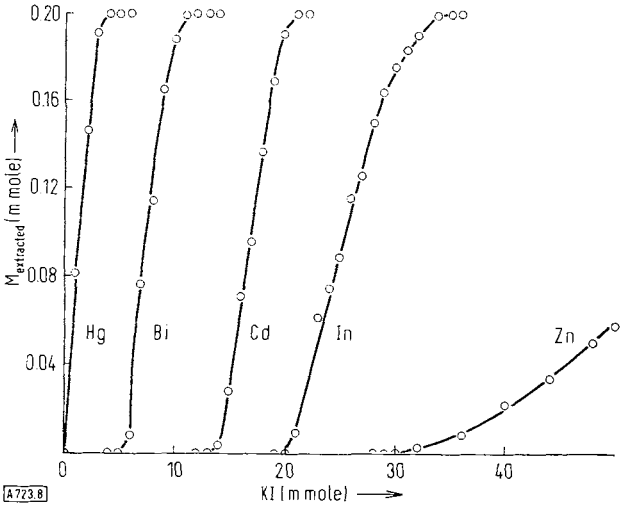


Fig. 8. Extraction sequence of some iodides with cyclohexanone as the solvent. Quantities present: 0.2 mmole of Hg^{2+}, Bi^{3+}, Cd^{2+}, In^{3+}, and Zn^{2+}.

HgI_2 and $[HgI_3]^-$ are extracted with high partition constants; this is the basis of a very selective extractive separation of mercury from nearly all other elements [52]. Trace elements in bismuth can be concentrated in the same way [53]. This principle is also used for the concentration of traces in pig iron and steels in the extraction of the chlorides with tributyl phosphate [54]. The problem of the determination of very low tin contents ($<10^{-3}$ %) in steels has also been solved in this way [37]. In principle, the partition constants can be used to find the practical partition coefficients, and hence the degree of partition [13], if only one compound is extracted with a high partition constant and if the anionic ligand is introduced in the aqueous phase or the active solvent in the organic phase.

We thank the Deutsche Forschungsgemeinschaft and the Stifterverband für die Deutsche Wissenschaft (Hibernia AG and Scholven-Chemie) for their support of our work over several years.

Received: December 3, 1968 [A 723 IE]
German version: Angew. Chem. *81*, 888 (1969)
Translated by Express Translation Service, London.

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Elemento-Organic Amines and Imines

By O. J. Scherer[*]

Amines with mixed substituents containing two or three El–N bonds[**] are relatively stable if one or two of these bonds are $(CH_3)_3$ Si–N bonds. IR and ^1H–NMR studies indicate that the (p → d)π bond components of the element-nitrogen bonds steadily decrease from silicon, phosphorus, and sulfur toward their higher homologs. Because of the differences in the polarities of the element-nitrogen bonds, these substances can be used for selective insertion and cleavage reactions. The reaction of metalated N-silyl-aminoarsines with methyl chloride as well as the reaction of metalated N-trimethyl(IVa)-element-substituted amino-tert-butylphosphines with halogenotrimethyl(IVa)element compounds open new, simple routes for the conversion of elemento-organic amine systems into imine systems. The problem of reversible and irreversible $(CH_3)_3$El ligand migration (1,3 shift) is discussed for trimethyl(IVa)element-substituted benzamidines, diaminophosphines, aminoiminophosphoranes, sulfinamides, and aminosulfimines.

1. Introduction

Whereas compounds of nitrogen with its five neighboring elements have mostly been known for a long time and have been extensively studied, compounds of nitrogen with the other nine elements in the portion of the periodic system shown were very much an unexplored field until about ten years ago.

C	N	O
Si	P	S
Ge	As	Se
Sn	Sb	Te
Pb	Bi	Po

The often extreme sensitivity of element-nitrogen compounds of this type to moisture and oxygen, their not infrequent extreme thermal instability, and their toxicity (particularly that of the heavier homologs) may have been major causes of the striking neglect of this field of study.

To permit the investigation and discussion of the thermal stabilities, reactivities, bonding, and ligand migration reactions of elemento-organic nitrogen compounds containing different hetero atoms, it was first necessary to synthesize many model substances [1].

It was found very useful in many cases to attach one or two trimethylsilyl groups to the nitrogen atom, possibly because the bulky trimethylsilyl ligand provides favorable steric conditions, and may also strengthen the σ bond by (p → d)π bonding [2] with the "lone" pair of electrons on the nitrogen.

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[**] El = a higher IVa, Va, or VIa element; by IVa, Va, and VIa elements are meant elements of the IV, V, and VI main groups of the periodic system.

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2. Bis(organoelement)-Substituted Amines with Two Different Hetero Atoms

2.1. IVa/IVa Elements

If two hydrogen atoms in ammonia or a primary amine are imagined to be replaced by the organoelement ligands X and Y, we formally obtain the following class of compounds:



R = H, alkyl, aryl
X,Y = organoelement ligand

Compounds of this type [*e.g. (2), (4), (9)*, and *(10)*] with different group IVa elements are best synthesized by double decomposition of lithium *N*-methyl-*N*-trimethyl(IVa)elementamides [*e.g. (1), (3)*, and *(5)*] with halogenotrimethyl(IVa)element compounds. The "lithium methylamide" derivatives can be prepared

Table 1. Physical properties of the compounds *(2)*, *(4)*, *(9)* and *(10)*.

Compound		B.p. (°C/torr)	Ref.
(2a)	$(CH_3)_3SiN(CH_3)Si(CH_3)_3$	147/760	[3, 13]
(2b)≡(4a)	$(CH_3)_3SiN(CH_3)Ge(CH_3)_3$	42/12	[4b]
(2c)≡(10a)	$(CH_3)_3SiN(CH_3)Sn(CH_3)_3$	59–61/11	[3, 5, 9]
(2d)	$(CH_3)_3SiN(CH_3)Pb(CH_3)_3$	42–43/0.5	[3]
(4b)	$(CH_3)_3GeN(CH_3)Ge(CH_3)_3$	172/735	[4b]
(4c)	$(CH_3)_3GeN(CH_3)Sn(CH_3)_3$	28/2	[4b, 5]
(4d)	$(CH_3)_3GeN(CH_3)Pb(CH_3)_3$	49/2	[4b]
(9a)	$R'Si(CH_3)_2N(CH_3)Si(CH_3)_3$ [a]	46–48/0.1	[5]
(9b)	$R'Si(CH_3)_2N(CH_3)Ge(CH_3)_3$ [a]	50–52/0.1	[5]
(9c)	$R'Si(CH_3)_2N(CH_3)Sn(CH_3)_3$ [a]	63–66/0.1	[5, 7]
(9d)	$R'Si(CH_3)_2N(CH_3)Pb(CH_3)_3$ [a]	66–68/0.1	[5]
(10b)	$[(CH_3)_3SiN(CH_3)]_2Sn(CH_3)_2$	61–63/0.5	[3, 9]
(10c)	$[(CH_3)_3SiN(CH_3)]_3SnCH_3$	83–85/0.5 [b]	[9]
(10d)	$[(CH_3)_3SiN(CH_3)]_4Sn$	129–132/0.5 [c]	[9]

[a] $R' = (CH_3)_3Si-NCH_3$. [b] M.p. = 22–23 °C. [c] M.p. = 90–92 °C.

[2] a) *E.g. D. P. Craig, A. Maccoll, R. S. Nyholm, L. E. Orgel*, and *L. E. Sutton*, J. chem. Soc. (London) *1954*, 332; b) *E. A. V. Ebsworth*: Volatile Silicon Compounds. Pergamon Press, Oxford 1963, p. 101; c) *U. Wannagat*, Advances inorg. Chem. Radiochem. *6*, 225 (1964).

both by metalation [eq. (a)] and by cleavage of element-nitrogen bonds [eq. (b) and (c)] (for examples see Table 1).

$(CH_3)_3Si-N(CH_3)-H + RLi \rightarrow (CH_3)_3Si-N(CH_3)-Li + RH$ (a) [3]
$R = CH_3$, n-C_4H_9 *(1)*

(1) + $(CH_3)_3ElCl \rightarrow (CH_3)_3Si-N(CH_3)-El(CH_3)_3 + LiCl$
El = Sn *(2c)*, Pb *(2d)* *(2)* (a') [3]

$[(CH_3)_2Ge-N(CH_3)]_3 + 3\ CH_3Li \rightarrow 3\ (CH_3)_3Ge-N(CH_3)-Li$ (b) [4]
(3)

(3) + $(CH_3)_3ElCl \rightarrow (CH_3)_3Ge-N(CH_3)-El(CH_3)_3 + LiCl$
(4) [4]
El = Si *(4a)*, Ge *(4b)*, Sn *(4c)*, Pb *(4d)*

$(CH_3)_3Sn-N(CH_3)-Sn(CH_3)_3 + CH_3Li \rightarrow (CH_3)_3Sn-N(CH_3)-Li + (CH_3)_4Sn$ (c) [5]
(5)

(5) + $(CH_3)_3ElCl \rightarrow$ *(2c)*, *(4c)* + LiCl [5]
El = Si, Ge

$(CH_3)_3Si-NC(CH_3)_3-Li$ has also been allowed to react with $(CH_3)_3ElCl$ compounds (El = Ge, Sn, Pb) in accordance with eq. (a') [6].

Owing to the ease with which *N*-methyl-*N*-trimethylsilylamine can be obtained from chlorotrimethylsilane and methylamine, *(1)* has been the most widely used compound for syntheses of this type.

(1) + $(CH_3)_2SiCl_2 \rightarrow (CH_3)_3Si-N(CH_3)-Si(CH_3)_2-Cl + LiCl$ [5, 7]
(6)

(6) + 2 $RNH_2 \rightarrow (CH_3)_3Si-N(CH_3)-Si(CH_3)_2-N(R)-H + RNH_2 \cdot HCl$
R = H, CH_3 *(7)* [5, 7]

(7) + n-$C_4H_9Li \rightarrow (CH_3)_3Si-N(CH_3)-Si(CH_3)_2-N(R)-Li + n$-$C_4H_{10}$
R = H [8a], CH_3 [5, 7] *(8)*

(8) + $(CH_3)_3ElCl \rightarrow (CH_3)_3Si-N(CH_3)-Si(CH_3)_2-N(R)-El(CH_3)_3 + LiCl$
(9)

R = CH_3, El = Ge *(9b)* [5], Sn *(9c)* [7], Pb *(9d)* [5];
R = H, El = Ge [8a]

n *(1)* + $(CH_3)_{4-n}SnX_n \rightarrow (CH_3)_{4-n}Sn[N(CH_3)-Si(CH_3)_3]_n + n\ LiX$ [9]
$n = 1 \rightarrow 4$; X = Cl, Br *(10)*

Organo(IVa)element derivatives of ammonia, *e.g. (7)*, R = H, are difficult to prepare, since the compounds R_3El-NH_2 required as starting materials are thermally stable only if R is a bulky ligand. With R = CH_3, El = Si [10] or Ge [11], the monoorgano(IVa)element derivative $(CH_3)_3El-NH_2$ immediately condenses to give $[(CH_3)_3El]_2NH$ and NH_3, whereas the tin analog gives only the tertiary amine [12].

$3(CH_3)_3SnNH_2 \rightarrow 2\ NH_3 + [(CH_3)_3Sn]_3N$

The simplest member of the silicon series [13] is triethylsilylamine. The metalation of this compound with *n*-butyllithium and substitution of the product with chlorotrimethylgermane [14] presents no difficulties.

$(C_2H_5)_3Si-NH_2 + n$-$C_4H_9Li \rightarrow (C_2H_5)_3Si-NH-Li + n$-$C_4H_{10}$
(11)

(11) + $(CH_3)_3GeCl \rightarrow (C_2H_5)_3Si-NH-Ge(CH_3)_3 + LiCl$
(12)

As is shown in Section 4, *(12)* is the key substance for the synthesis of elemento-organic amines containing three different hetero atoms.

Nearly all elemento-organic amines with two different hetero atoms are water-clear, moisture-sensitive liquids that can be purified by vacuum distillation. The lead compounds *(2d)*, *(4d)*, and *(9d)*, which exhibit remarkable thermal stability, also deserve special mention, since comparable plumbylamines with an alkyl group in place of the ligand $(CH_3)_3El$ are extremely unstable, even when the lead atom carries bulky groups [15]. The sensitivity to water, as expected, increases rapidly from the silicon compound to the lead compound. Among the *N*-silylated stannylamines *(10)* the water sensitivity is least for *(10d)*, which can even be handled in air for short periods. This special behavior is probably due to steric effects, the tin atom being shielded from nucleophilic attack by the four *N*-methyl-*N*-trimethylsilylamino groups.

Comparison of the ^1H-NMR spectra of the compounds *(2)*, *(4)*, and *(9)* reveals the following relations (see Table 2):

$\delta(CH_3)_3Si$ [*(2)*], $\delta(CH_3)_3Ge$ [*(4)*], and $\delta(CH_3)_2Si$ [*(9)*]

unlike $\delta CH_3(N^1)$, are displaced to higher fields on transition from El = Si to its higher homologs. Whereas the hetero atom has no appreciable influence on $J_{^{13}CH(Si)}$ and $J_{^{13}CH(Ge)}$, $J_{^{13}CH(N^1)}$ decreases slightly from El = Si to El = Pb. These results indicate that the (p $\rightarrow$ d)π strengthening of the El–N bond decreases from silicon to its higher homologs. If the $(CH_3)_3Si-N(CH_3)$ group is attached instead of CH_3 to the silicon atom in class *(2)*, the hetero atom El in

[3] *O. J. Scherer* and *M. Schmidt*, J. organometallic Chem. *3*, 156 (1965).

[4] a) *I. Ruidisch* and *M. Schmidt*, Angew. Chem. *76*, 686 (1964); Angew. Chem. internat Edit. *3*, 367 (1964); b) *I. Schumann-Ruidisch* and *B. Jutzi-Mebert*, J. organometallic Chem. *11*, 77 (1968).

[5] *D. Biller*, Diplomarbeit, Universität Würzburg 1966.

[6] *I. Schumann-Ruidisch*, *W. Kalk*, and *R. Brüning*, Z. Naturforsch. *23b*, 307 (1968).

[7] *O. J. Scherer*, *D. Biller*, and *M. Schmidt*, Inorg. nuclear Chem. Letters *2*, 103 (1966).

[8] a) *O. J. Scherer* and *D. Biller*, Angew. Chem. *79*, 410 (1967); Angew. Chem. internat. Edit. *6*, 446 (1967); b) unpublished.

[9] *O. J. Scherer* and *P. Hornig*, J. organometallic Chem. *8*, 465 (1967).

[10] *R. O. Sauer*, J. Amer. chem. Soc. *66*, 1707 (1944).

[11] *I. Ruidisch* and *M. Schmidt*, Angew. Chem. *76*, 229 (1964); Angew. Chem. internat. Edit. *3*, 231 (1964).

[12] a) *K. Jones* and *M. F. Lappert*, Proc. chem. Soc. (London) *1962*, 358; J. chem. Soc. (London) *1965*, 1944; b) *K. Sisido* and *S. Kozima*, J. org. Chemistry *29*, 907 (1964); c) *W. L. Lehn*, J. Amer. chem. Soc. *86*, 305 (1964); d) *O. J. Scherer*, *J. F. Schmidt*, and *M. Schmidt*, Z. Naturforsch. *19b*, 447 (1964).

[13] *R. Fessenden* and *J. S. Fessenden*, Chem. Reviews *61*, 361 (1961).

[14] *O. J. Scherer* and *D. Biller*, Z. Naturforsch. *22b*, 1079 (1967).

[15] *W. P. Neumann* and *K. Kühlein*, Tetrahedron Letters *1966*, 3419.

Table 2. ^{1}H–NMR data (in Hz) for the bis[organo(IVa)element]-substituted amines *(2)*, *(4)*, *(9)*, and *(10)* (in CCl_4, TMS as internal standard). All the coupling constants given in the tables are absolute values obtained from the band splitting. The signs [77] of the coupling constants are neglected.

Compound	$\delta(CH_3)_3Si$	$\delta(CH_3)_2Si$	$\delta\,CH_3(N^1)$	$\delta\,CH_3(N^2)$	$\delta\,CH_3$(El)	$J_{^{13}CH(Si)}$	$J_{^{13}CH(N^1)}$	$J_{^{13}CH(El)}$	J_{ElCH}	J_{ElNCH}	Ref.
(2a)	− 3.0		−148.5			120.0	137.5				[3,4b]
(2b)≡*(4a)*	− 1.5		−153.0		−16.3	119.2	136.0	127.0			[4b]
(2c)≡*(10a)*	0		−156.0		−13.0	118.0	133.0	129.5	53.4 / 55.8 [a]	43.6 / 45.5 [b]	[3, 9]
(2d)	+ 2.5		−168.5		−56.0	120.0	133.0	136.5	65.5 [c]	78.0 [d]	[3]
(4b)	−13.8 [e]		−157.5			127.0 [f]	135.5				[4b]
(4c)	−11.6 [e]		−166.0		−10.8	126.8 [f]	134.5		53.5 / 56.0 [a]	46.8 / 49.0 [b]	[4b]
(4d)	−10.0 [e]		−181.0		−55.0	126.0 [f]	133.5		64.8 [c]	95.0 [d]	[4b]
(9a)	− 4.0	−5.8	−145.5	−145.5	− 4.0						[5]
(9b)	− 4.0	−3.6	−149.5	−145.5	−16.0						[5]
(9c)	− 4.0	−1.0	−156.0	−145.5	−13.0				53.0 / 56.0 [a]	42.0 / 45.0 [b]	[5, 7]
(9d)	− 3.6	+0.6	−170.5	−145.0	−57.0				66.0 [c]	76.0 [d]	[5]
(10b)	− 1.5		−156.0		−20.0	117.5	133.0	129.5	57.5 / 60.0 [a]	47.0 / 49.5 [b]	[9]
(10c)	− 3.0		−158.0		−28.5	117.5	133.5	131.0	70.1 / 73.5 [a]	50.4 / 52.8 [b]	[9]
(10d)	− 6.0		−158.0			118.0	134.5			63.8 / 66.8 [b]	[9]

[a] = $J_{^{117,119}Sn-C-H}$; [b] = $J_{^{117,119}Sn-N-C-H}$; [c] = $J_{^{207}Pb-C-H}$; [d] = $J_{^{207}Pb-N-C-H}$; [e] = $\delta(CH_3)_3Ge$; [f] = $J_{^{13}CH(Ge)}$.

(9) now has a pronounced influence only on $\delta(CH_3)_2Si$ and $\delta CH_3(N^1)$, while $\delta(CH_3)_3Si$ and $\delta CH_3(N^2)$, the signals of the ligands situated farther away from El, show practically no measurable change.

In the *N*-silylated stannylamines *(10)*, δCH_3(Si) and δCH_3(Sn) show an almost linear displacement to lower fields as the number *n* of methyltrimethylsilylamino groups is increased, whereas δCH_3(N) is practically unaffected by *n*. The increases in the coupling constants $J_{^{117,119}Sn-C-H}$ and $J_{^{117,119}Sn-N-C-H}$ are greatest for the transitions $n = 2 \rightarrow 3$ and $n = 3 \rightarrow 4$ respectively. It should be mentioned that $J_{^{117,119}Sn-N-C-H}$ for *(10d)* $n = 4$, is greater than $J_{^{117,119}Sn-C-H}$ for *(2c)* and *(10b)*, $n = 2$. The values of 63.8 and 66.8 Hz are considerably higher than those of the class of unsilylated compounds $[(C_2H_5)_2N]_nSn(CH_3)_{4-n}$ [16].

The elemento-organic amines containing different hetero atoms differ in the polarities of the element-nitrogen bonds; a selective "insertion reaction" of a 1,2-dipole should therefore be favored. It is known from examples in the literature [17] that even the Si–N bond, which is the least polar in this group, reacts smoothly with most 1,2-dipoles. *N*-Methyl-*N*-trimethylsilyl-*N*-trimethylstannylamine *(2c)* and methyl or phenyl isocyanate react under mild conditions (low temperature, high dilution, and a slight excess of *(2c)*) to form 1:1 adducts *(13)* [18].

$$(CH_3)_3Si-\underset{\displaystyle CH_3}{\underset{|}{N}}-Sn(CH_3)_3 + R-N=C=O \qquad R = CH_3,\ C_6H_5$$

(2c)

$$\rightarrow (CH_3)_3Si-\underset{\displaystyle CH_3}{\underset{|}{N}}-\underset{\displaystyle O}{\underset{\|}{C}}-\underset{\displaystyle R}{\underset{|}{N}}-Sn(CH_3)_3$$

(13)

Whereas insertion of the isocyanate into the Si–N bond cannot be absolutely ruled out in the case of $R=CH_3$, the absence of $J_{^{117,119}Sn-N-C-H}$ coupling for *(13)*, $R=C_6H_5$, indicates addition to the more polar Sn–N bond for this substance at least. A moderate excess of isocyanate leads to mixtures of products as a result of further "insertion reactions" while a larger excess leads to trimerization of the isocyanate [18]. Benzonitrile, which does not react with the Si-N bond of $(CH_3)_3Si-N(CH_3)-H$ [19], forms a benzamidine derivative with $(CH_3)_3Sn-N(CH_3)_2$ [20]. *(2c)* gives no indication [19] of reaction in accordance with eq. (d), even under more forcing conditions (several hours at higher temperatures).

$$(CH_3)_3Si-\underset{\displaystyle CH_3}{\underset{|}{N}}-Sn(CH_3)_3 + C_6H_5-C\equiv N \qquad \text{(d)}$$

(2c)

$$\not\rightarrow C_6H_5-C\begin{matrix}\overset{\displaystyle N-Sn(CH_3)_3}{\|}\\ \underset{\displaystyle N-Si(CH_3)_3}{|}\\ \underset{\displaystyle CH_3}{}\end{matrix}$$

(14)

The difference in the reactions of $(CH_3)_3Sn-N(CH_3)_2$ and *(2c)* is due either to steric effects or to decreased basicity in the latter compound as a result of the $(p \rightarrow d)\pi$ bond to the silicon atom.

2.1.1. Elemento-Organic Benzamidines

Elemento-organic benzamidines *(16)* [19–23] containing different group IVa elements are obtained by addition of lithium *N*-alkyl-*N*-trimethylsilylamides to

[16] *M. R. Kula*, *C. G. Kreiter*, and *J. Lorberth*, Chem. Ber. *97*, 1294 (1964).

[17] Cf. *e.g. H. Ulrich*: Cycloaddition Reactions of Heterocumulenes. Academic Press, London 1967, Vol. 9, p. 187ff.

[18] *O. J. Scherer*, *D. Biller*, and *G. Bonse*, unpublished.

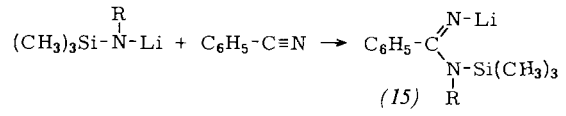
[19] *O. J. Scherer* and *P. Hornig*, Chem. Ber. *101*, 2533 (1968).

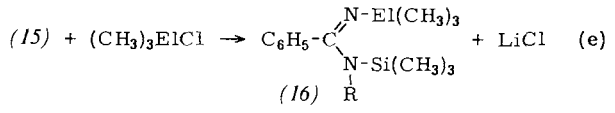
[20] *T. A. George*, *K. Jones*, and *M. F. Lappert*, J. chem. Soc. (London) *1965*, 2157.

[21] *C. Krüger*, *E. G. Rochow*, and *U. Wannagat*, Chem. Ber. *96*, 2138 (1963).

[22] *W. P. Neumann* and *E. Heymann*, Liebigs Ann. Chem. *683*, 24 (1965).

[23] *W. P. Neumann* and *K. Kühlein*, Tetrahedron Letters *1966*, 3423.

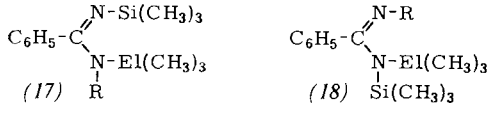




El = Si; R = CH_3 *(16a)*, C_2H_5 *(16b)*, El = Ge *(16c)*, Sn *(16d)*, Pb *(16e)*, R = CH_3

benzonitrile followed by reaction with chlorotrimethyl(IVa)element compounds [eq. (e)][19].

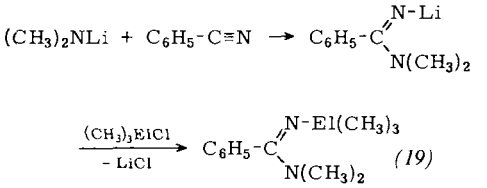
The compounds *(16)* are moisture-sensitive liquids that can be distilled in an oil-pump vacuum. They are rapidly split at the element-nitrogen bond by water and alcohol to form the free base (which was identified as the hydrochloride). Owing to the proximity of the two nitrogen atoms to each other, these compounds are ideal models for the investigation of ligand migration reactions. The isomers *(17)* and *(18)* of *(16)* must also be considered.



(17) *(18)*

(16) can be discussed only if one assumes the occurrence of either metal-proton coupling across five bonds or shortening of the coupling path by additional coordinate bonding of Sn and Pb to the singly-bonded amidine nitrogen atom. This coupling can be explained much more simply if *(16d)* and *(16e)* are formulated as the isomers *(17)*.

An answer to the question of the predominant isomer is provided by the *N'*-trimethyl(IVa)element-substituted *N,N*-dimethylbenzamidines *(19)*, which can be obtained from lithium dimethylamide, benzonitrile, and $(CH_3)_3ElCl$ (El = Si, Ge, Sn)[19].



El = Si *(19a)*, Ge *(19b)*, Sn *(19c)*

The fact that no coupling with the CH_3N group ($J_{117,\,119Sn-N-C-H} = 0$) is observed in the ^1H–NMR spectrum of *(19c)* may be taken as strong evidence that the benzamidines *(16c)*–*(16e)* are in the isomeric form *(17)*. This is supported by the fact that for all $(CH_3)_3El$ groups bound to the imine nitrogen atom,

Table 3. ^1H–NMR data (in Hz) for the benzamidine derivatives *(16)* and *(19)* (in CCl_4, TMS as internal standard) [19]. δC_6H_5(m) is omitted.

Compound	$\delta CH_3(N)$	$\delta CH_3-CH_2(N)$	$\delta CH_3(Si)$	$\delta CH_3(El)$	$J_{117,\,119Sn-C-H}$	$J_{117,\,119Sn-N-C-H}$	$J_{207Pb-C-H}$	$J_{207Pb-N-C-H}$
(16a)	−153.0		0.0 (35 °C) +16.5/ −12.0 (−30 °C)					
(16b)		−53.0 (t) −174.5 (q)	0.0 (35 °C)					
(16c)	−154.0		+16.5	−25.5				
(16d)	−154.0		+15.5	−17.5	55.0/57.0	28.5/29.7		
(16e)	−161.0		+17.5	−64.5			69.0	32.0
(19a)	−171.5		+17.0					
(19b)	−169.0			+ 6.0				
(19c)	−169.5			+ 9.5	52.5/55.0			

The ^1H–NMR spectra of *(16a)* and *(16b)* (Table 3) exhibit in addition to the expected phenyl and *N*-methyl resonances, a broad signal in the trimethylsilyl region at 35 °C (even at high dilution), which splits into two singlets of equal area at about −30 °C. This observation points to a reversible intramolecular migration (1,3 shift) of the two trimethylsilyl ligands.

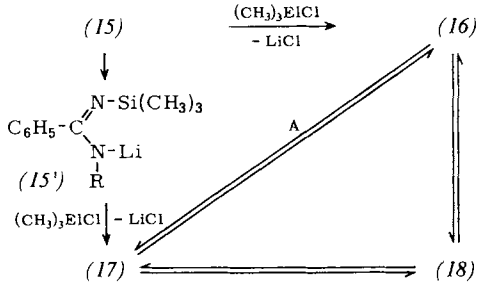
Despite frequent modification of the preparation conditions, silicon derivatives always contain small quantities of a "by-product"; on the basis of its IR and ^1H–NMR spectra and its element analysis, it is concluded that this product has the structure of the isomer *(18)* [19]. The two isomers are not in equilibrium with each other, at least after the reaction at room temperature, as is shown by the fluctuation of the quantity of *(18)*.

Unlike the bis-silylated compounds *(16a)* and *(16b)*, the compounds *(16c)*, *(16d)*, and *(16e)* are entirely in the form of one isomer. Since the ^1H–NMR spectra of *(16d)* and *(16e)* also exhibit $J_{117,119Sn-N-C-H}$ and $J_{207Pb-N-C-H}$ coupling respectively, the structure the resonance is distinctly displaced toward higher fields. The difference between the chemical shifts of trimethylelement ligands attached to the amine and to the imine nitrogen atoms of the benzamidine is about 30 Hz (Table 3).

The ligand arrangement required in *(17)* does not conflict with the reaction path proposed in eq. (e) if one considers the reaction scheme 1 for the formation of *(16a)*–*(16e)*.

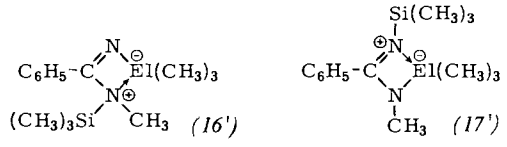
a) Adduct *(15)* does not react, as required by eq. (e), in the form *(15)*, but in the form *(15')*, to give *(17)*. This explanation is not convincing, since *(15)* and $(CH_3)_3SiCl$ on the one hand and lithium methylamide, benzonitrile, and chlorotrimethylsilane (but not chlorotrimethylstannane) on the other give mixtures of isomers [19]. The formation of *(15')* by insertion of benzonitrile into the Si–N bond of $(CH_3)_3Si-N(CH_3)-Li$ was ruled out by the reaction of $(CH_3)_3Si-N(CH_3)-H$ with benzonitrile.

b) Though reaction (e) takes place as indicated, *(16c)*–*(16e)* unlike *(16a)* and *(16b)*, undergo an irreversible ligand ex-



Scheme 1. El = Si—Pb; R = CH_3, C_2H_5.

change (step A in Scheme 1). The tendency of the elements Ge, Sn, and Pb (unlike Si) to increase their coordination number above four may be the driving force for the rearrangement of *(16)* into *(17)*. Unlike in *(16')*, a gain in energy due to further limiting resonance structures is possible in the modified form *(17')* of *(17)*

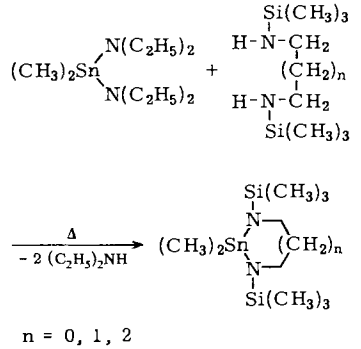


The tendency of silicon to achieve the greatest possible (p → d)π bond strengthening would also oppose the substitution on the imine nitrogen.

Nothing definite can be said at present about the mechanism of this ligand exchange reaction. The ability of the organo-(IVa)element substituents to migrate is probably strongly influenced by the mutual proximity of the two nitrogen atoms and the ease of displacement of the π electrons inside the amidine skeleton. Since *(16a)* and *(16b)* give isomer mixtures, it must be assumed that here at least the rearrangement from *(16)* to *(17)* does not proceed *via (18)*, but that a synchronous mechanism must be considered for the ligand migration (cf. Section 2.2.1).

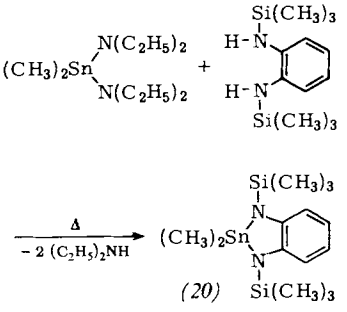
2.1.2. Heterocycles

Bis[organo(IVa)element] combinations in which one hetero atom forms part of a ring while the other is exocyclic can be obtained by synthetic variants of transamination with cyclization [24a].



n = 0, 1, 2

It is interesting to note that with CH_3 instead of the $(CH_3)_3Si$ group, only the six-membered analogs can be prepared [24a] (polymerization occurs with the five-membered rings [24]). This is a very clear illustration of the stabilizing influence of the trimethylsilyl ligand. The *N*-silylated stannabenzimidazolidine *(20)* is obtained by this method from *N,N'*-bis(trimethylsilyl)-*o*-phenylenediamine and bis(diethylamino)dimethylstannane [24a].



2.2. IVa/Va Elements

Phosphorus-nitrogen compounds with a $(CH_3)_3Si$ group on the nitrogen are obtained almost exclusively by cleavage of bis-silylated amines with phosphorus halides [25]. Attempts to prepare these compounds in the same way as their analogs with IVa elements, *i.e.* from lithium *N*-methyl-*N*-trimethylsilylamide *(1)* and methylphosphorus halides, have been unsuccessful [26]. Reactions of *(1)* with methylhalogeno and trihalogeno compounds of arsenic, antimony, and bismuth, on the other hand, have been successful [27a].

$$n\,(CH_3)_3Si{-}NCH_3{-}Li + (CH_3)_{3-n}ElX_n \;\underset{(1)}{\rightarrow}\; [(CH_3)_3Si{-}NCH_3]_n\,El(CH_3)_{3-n} + n\,LiX \qquad (21)$$

El = As, n = 1–3, X = Cl, Br; El = Sb, n = 1–3, X = Cl, Br; El = Bi, n = 1–3, X = Br

As-(*N*-Methyltrimethylsilylamino)dimethylarsine*(21a)* is also formed by cleavage of an As–N bond of *N,N*-bis(dimethylarsino)methylamine with methyllithium and reaction of the lithium *N*-methyl-*N*-dimethylarsinoamide *(22)*, formed in accordance with eq. (f) with chlorotrimethylsilane [27b]. Methyllithium cleaves the As–N bond of *(21a)* only under more forcing conditions (approx. 70 °C) [3].

$$(CH_3)_2As{-}N(CH_3){-}As(CH_3)_2 + CH_3Li \rightarrow \underset{(22)}{(CH_3)_2As{-}N(CH_3){-}Li} + As(CH_3)_3 \qquad (f)$$

$$(22) + (CH_3)_3SiCl \rightarrow (CH_3)_2As{-}N(CH_3){-}Si(CH_3)_3 + LiCl \qquad (21a)$$

A new, simple route to the relatively little-investigated class of iminoarsoranes is provided by the reaction of an *N*-metalated aminoarsine with methyl chloride [40a].

[24] a) *O. J. Scherer, J. Schmidt, J. Wokulat,* and *M. Schmidt,* Z. Naturforsch. *20b*, 183 (1964); b) *C. H. Yoder* and *J. J. Zuckerman,* J. Amer. chem. Soc. *88*, 4831 (1966).

[25] Cf. *e.g. O. J. Scherer,* Organometallic Chem. Reviews, Part A *3*, 281 (1968).

[26] *O. J. Scherer* and *P. Hornig,* unpublished.

[27] a) *O. J. Scherer, P. Hornig,* and *M. Schmidt,* J. organometallic Chem. *6*, 259 (1966); b) *O. J. Scherer* and *M. Schmidt,* Angew. Chem. *76*, 787 (1964); Angew. Chem. internat. Edit. *3*, 702 (1964).

$$[(CH_3)_3C]_2As{-}NLi{-}Si(CH_3)_3 \xrightarrow[-LiCl]{CH_3Cl} [(CH_3)_3C]_2As(CH_3){=}N{-}Si(CH_3)_3$$

Nearly all compounds *(21)* are colorless liquids, whose sensitivity to oxygen and moisture decreases with increasing n and increases from the arsenic to the bismuth compounds. Like the tin derivative *(10c)*, the compounds with $n = 3$ melt around room temperature.

On comparison of the chemical shifts of the homologous series $(CH_3)_3Si{-}N(CH_3)El(CH_3)_2$, $[(CH_3)_3Si\text{-}N(CH_3)]_2ElCH_3$, and $[(CH_3)_3Si\text{-}N(CH_3)]_3El$, El = As to Bi, it is found that $\delta CH_3(Si)$ and $\delta CH_3(N)$ vary in the same direction as for corresponding compounds with El = IVa elements (Section 2.1).

$[(CH_3)_3Si{-}N(CH_3)]_nEl(CH_3)_{3-n}$ compounds with El = As to Bi, $n = 1-3$, like the comparable tin compounds *(10)*, show a shift of $\delta CH_3(Si)$ toward lower field strengths with increasing n; $\delta CH_3(N)$, on the other hand, is differently influenced (Table 4).

The spectra, like those of the IVa element compounds, can be interpreted by assuming a decrease in the (p → d)π-strengthening of the El–N bond from El = As to Bi.

Synthesis of compounds of the type *(21)* with aminophosphines instead of amines of group IVa elements leads surprisingly readily to compounds having this desired combination of IVa and Va elements, in which the thermal stability of the primary and secondary aminophosphines, compounds which have not been extensively studied, is increased by suitable ligands on the phosphorus atom, *e.g.* the $(CH_3)_3C$ group [28–31a].

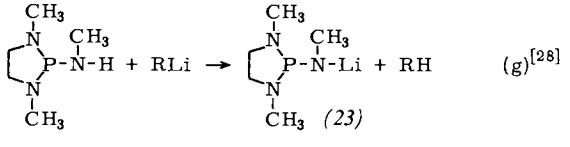
$$[(CH_3)_3C]_2P{-}NH{-}Sn(CH_3)_3 \ (26c) \xrightarrow{\Delta} \begin{cases} \rightarrow 1/2\ [(CH_3)_3C]_2P{-}N[Sn(CH_3)_3]_2 + 1/2\ [(CH_3)_3C]_2P{-}NH_2 & (i) \\ \rightarrow [(CH_3)_3C]_2P(H){=}N{-}Sn(CH_3)_3\ (27) & \\ \rightarrow [(CH_3)_3C]_2P[Sn(CH_3)_3]{=}NH\ (28) & (j) \end{cases}$$

It should be mentioned that the tin derivative (26c) unlike most stannylamines with NH bonds [12a], does not undergo dismutation at high temperatures [eq. (i)].

A type of "Michaelis-Arbuzov rearrangement" into one of the two possible iminophosphoranes *(27)* or *(28)* [eq. (j)] is not observed even when *(26c)* is heated at 150 °C for 20 hours.

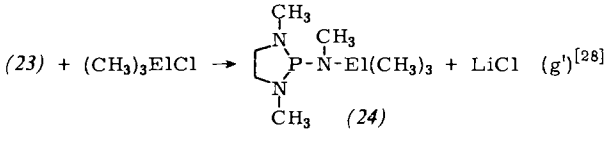
Table 4. Physical properties and ^1H–NMR data (in Hz) of the compounds *(21)* (in CCl_4, TMS as internal standard).

	Compound	M.p. (°C)	B.p. (°C/torr)	δ CH_3(Si)	δ CH_3(N)	δ CH_3(El)
(21a)	$(CH_3)_3SiN(CH_3)As(CH_3)_2$	−50	44–46/11	−3.5	−153.0	−59.5
(21b)	$[(CH_3)_3SiN(CH_3)]_2AsCH_3$		55–59/0.1	−5.5	−159.5	−66.5
(21c)	$[(CH_3)_3SiN(CH_3)]_3As$	11–13	67–70/0.1	−6.5	−153.5	
(21d)	$(CH_3)_3SiN(CH_3)Sb(CH_3)_2$		44–46/1	−3.0	−162.0	−48.5
(21e)	$[(CH_3)_3SiN(CH_3)]_2SbCH_3$		59–61/0.1	−5.0	−168.0	−52.5
(21f)	$[(CH_3)_3SiN(CH_3)]_3Sb$	9–11	78–79/0.1	−6.5	−161.5	
(21g)	$(CH_3)_3SiN(CH_3)Bi(CH_3)_2$		31–32/0.1	0.0	−200.0	−70.0
(21h)	$[(CH_3)_3SiN(CH_3)]_2BiCH_3$		70–71/0.1	−3.0	−213.0	−70.0
(21i)	$[(CH_3)_3SiN(CH_3)]_3Bi$	27–29	90–92/0.1	−4.5	−213.0	



(g) [28]

R = CH_3, n-C_4H_9



(g') [28]

El = Si *(24a)*, Ge *(24b)*, Sn *(24c)*

$$[(CH_3)_3C]_2P{-}NR{-}H + n\text{-}C_4H_9Li \rightarrow [(CH_3)_3C]_2P{-}NR{-}Li + n\text{-}C_4H_{10} \quad (h)$$
(25)

$$(25) + (CH_3)_3ElCl \rightarrow [(CH_3)_3C]_2P{-}NR{-}El(CH_3)_3 + LiCl \quad (h')$$
(26)

R = H; El = Si *(26a)*, Ge *(26b)*, Sn *(26c)*, Pb *(26d)* [29,30]
R = CH_3; El = Si *(26e)* [30]

$$(CH_3)_3C{-}P(NH_2)_2 + 2\ (CH_3)_3SiCl \ (29) \xrightarrow[-2\ (C_2H_5)_3N{\cdot}HCl]{2\ (C_2H_5)_3N} (CH_3)_3C{-}P[NH{-}Si(CH_3)_3]_2 \quad (k)$$
(30)

The first known low molecular weight diaminophosphine is *(29)* [31a, 32], which can be silylated with chlorotrimethylsilane in the presence of an auxiliary base [eq. (k)].

The new compounds of the type *(24)* exhibit interesting relations in their ^1H–NMR spectra, and can be used for a wide variety of chemical reactions [28, 30].

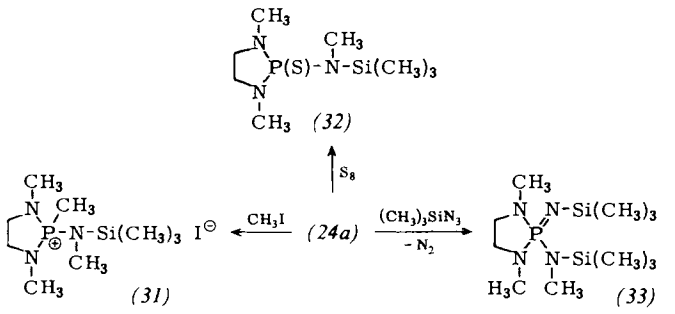
[28] *O. J. Scherer* and *J. Wokulat*, Z. anorg. allg. Chem. *361*, 296 (1968).

[29] *O. J. Scherer* and *G. Schieder*, Angew. Chem. *80*, 83 (1968); Angew. Chem. internat. Edit. *7*, 75 (1968).

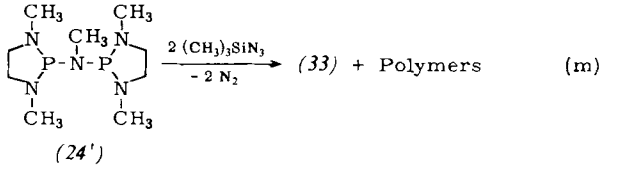
[30] *O. J. Scherer* and *G. Schieder*, Chem. Ber. *101*, 4184 (1968).

[31] a) *O. J. Scherer* and *P. Klusmann*, Angew. Chem. *80*, 560 (1968); Angew. Chem. internat. Edit. *7*, 541 (1968); b) Cf. $(C_6H_5)_2P[NSi(CH_3)_3][NLiSi(CH_3)_3]$: *H. Schmidbaur, K. Schwirten*, and *H. H. Pickel*, Chem. Ber. *102*, 564 (1969); c) Cf. *H. Schmidbaur, W. Wolfsberger, K. Schwirten*, and *H. H. Pickel*, Progress in Coordination Chemistry XI. ICCC, Haifa 1968, Elsevier, New York 1968, p. 378.

[32] *O. J. Scherer* and *P. Klusmann*, Z. anorg. allg. Chem., in press.



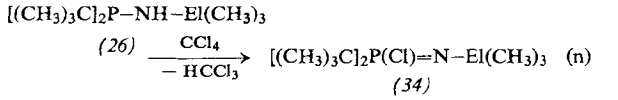
The aminoiminodiazaphospholidine derivative *(33)* is formed not only from *(24a)*, but also on reaction of *(24')* with two moles of trimethylsilyl azide [28].



(m)

On the other hand, if the two phosphorus atoms in *(24')* are separated by the -N(CH$_3$)-(CH$_2$)$_2$-N(CH$_3$)- group, the P–N bond is not broken [28].

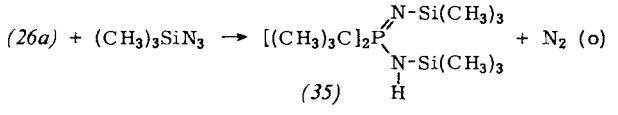
N-Organo(IVa)element-substituted aminophosphines *(26)* are almost quantitatively oxidized to *P*-chloroiminophosphoranes *(34)* by carbon tetrachloride [29,30]



(n)

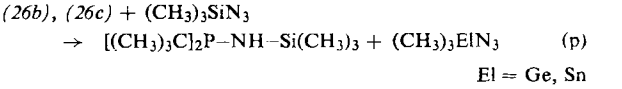
El = Si *(34a)*, Ge *(34b)*, Sn *(34c)*

Whereas oxidation with trimethylsilyl azide leads, in the case of the silicon compound *(26a)* [eq. (o)] [30], to the desired compound,



(o)

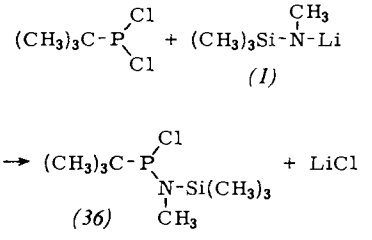
the reactions with *(26b)* and *(26c)* lead merely to cleavage [eq. (p)] of the Ge–N or Sn–N bond; this is a clear indication of the pseudohalogen character of trimethylsilyl azide [30].



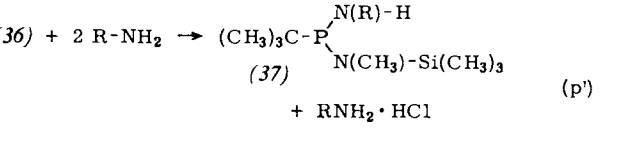
(p)

El = Ge, Sn

(1) On reaction of (CH$_3$)$_3$Si–N(CH$_3$)Li *(1)* with *tert*-butyldichlorophosphine instead of with methylphosphorus halides [26], it is even possible to displace the chlorine atoms successively [32].



(36) is an important starting material for the synthesis of diaminophosphines with different ligands on the amino groups [32].

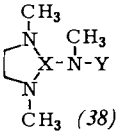


(p')

R = *e.g.* H *(37a)*, CH$_3$ *(37b)*

(37a) does not exist in the isomeric form expected from eq. (p'). The "more symmetrical" isomer (CH$_3$)$_3$CP[NHSi(CH$_3$)$_3$](NHCH$_3$) has been formed by an irreversible (CH$_3$)$_3$Si/H ligand exchange [32].

At this point we shall discuss the ^{1}H–NMR spectra of compounds that illustrate the influence of the hetero atom and of the oxidation state of the phosphorus on the P–N(CH$_3$) coupling constant. The models *(24)*, *(31)*–*(33)*, and *(38)* satisfy these requirements (Table 5).



X = P, P-CH$_3$, P=S, P=N-Si(CH$_3$)$_3$
Y = (CH$_3$)$_3$El, El = Si → Sn

Table 5. ^{1}H–NMR data (in Hz) for the compounds *(24)*, *(26)*, and *(31)*–*(34)* (in benzene, TMS as external standard).

Compound	δ CH$_3$(N$_R$) [c]	δ CH$_3$(N)	δ CH$_3$(El)	δ (CH$_3$)$_3$C(P)	$J_{^{31}PNCH_3(R)}$ [c]	$J_{^{31}PNCH_3}$	$J_{^{31}PNElCH_3}$	$J_{^{31}PCCH}$	Ref.
(24a)	−142.0 (d)	−128.0 (d)	+ 1.0 (d)		12.5	3.3	2.0		[28]
(24b)	−146.3 (d)	−136.7 (d)	−14.7 (d)		12.3	4.5	1.1		[28]
(24c)	−152.5 (d)	−148.7 (d)	−17.0 (d)		12.2	7.3	0.55		[28]
(31) [a]	−165.6 (d)	−180.0 (d)	−31.0 (s)		10.7	15.1	0		[28]
(32)	−120.5 (d)	−121.5 (d)	− 2.5 (s)		12.2	14.5			[28]
(33) [b]	−139.0 (d)	−129.0 (d)	+11.0 (d) }		9.8	14.3			[28]
			− 5.0 (s) }						
(26a)			+21.2 (d)	−28.5 (d)			0.6	11.0	[30]
(26b)			+12.0 (d)	−33.9 (d)			0.3	10.9	[30]
(26c)			+16.3 (s)	−36.2 (d)			0	10.7	[30]
(26d)			−29.3 (s)	−41.2 (d)			0	10.8	[30]
(34a)			+11.5 (d)	−47.2 (d)			0.5	17.3	[30]
(34b)			0.0 (s)	−49.0 (d)			0	17.0	[30]
(34c)			+ 5.5 (s)	−58.4 (d)			0	16.7	[30]

[a] δ CH$_3$(P)—144.5 (d), $J_{^{31}PCH}$ = 14.5 Hz (in CDCl$_3$); [b] $J_{^{31}P=NSiCH}$ = 0.35 Hz; $J_{^{117,119}Sn-C-H}$ and $J_{^{207}Pb-C-H}$ were not given; [c] R = −N(CH$_3$)−(CH$_2$)$_2$−N(CH$_3$)−; δ CH$_2$(R) possesses, with the exception of *(31)* [δ CH$_2$(R)—224.0 (d), $J_{^{31}PNCH_2(R)}$ = 8.8 Hz] a multiplet structure.

In *(38)*, the oxidation state of the phosphorus has little influence, and the ligand Y has practically none, on the coupling $J_{^{31}PNCH_3(R)}$ of the phosphorus with the protons of the ring CH_3N group. The coupling constant $J_{^{31}PNCH_3}$ of the phosphorus with the protons of the CH_3N bridge, on the other hand, shows a distinct dependence both on X and on Y. The constant increases from X = P^{III} to X = P^{V} [*e.g.* *(24a)* → *(32)*; 3.3 → 14.5 Hz]; $J_{^{31}PNCH_3(R)}$ remains practically unchanged (12.5 → 12.2 Hz). The influence of the hetero atom Y on the coupling constant $J_{^{31}PNCH_3}$ can be observed in the compounds *(24a)* → *(24c)*, since it increases from 3.3 to 7.3 Hz. In *(33)*, long-range coupling of the phosphorus is found only with the protons of the trimethylsilyl group bound to the imine nitrogen atom ($J_{^{31}P=NSiCH_3}$ = 0.35 Hz)[28].

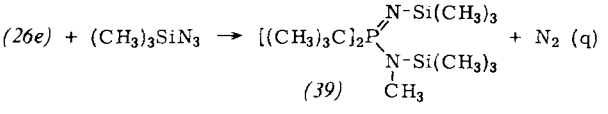
Whereas $J_{^{31}PCCH}$ for $[(CH_3)_3C]_2P-NH-El(CH_3)_3$ *(26a)–(26c)* is practically unaffected by the ligand El on the nitrogen atom, the long-range coupling $J_{^{31}PNElCH_3}$ decreases from 0.6 to 0 Hz [*(26a)–(26c)*]. As expected, $J_{^{31}PCCH}$ of the compounds *(26a)–(26c)* containing trivalent phosphorus increases on oxidation to the pentavalent phosphorus compounds *(34a)–(34c)*. The only sign of the influence of the hetero atom is a small linear decrease. $J_{^{31}PNElCH}$ is observed only for the silicon derivative *(34a)*.

Though the chemical shift varies with concentration when benzene is used as the solvent, $\delta CH_3(N)$ and $\delta CH_3(N_R)$ show the same tendency toward lower fields for El = Si → Sn as in corresponding IVa/IVa combinations.

2.2.1. *N,N'*-Bis(organoelement)-Substituted Aminoiminophosphoranes

Like the benzamidines *(16)*, the structurally related aminoiminophosphoranes *(39)* are suitable for the study of ligand migration processes.

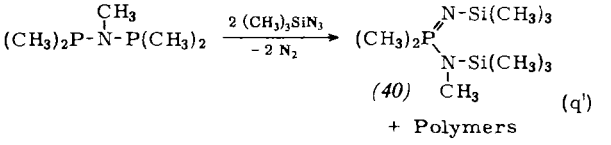
The first compound was obtained from triphenylsilyl azide and diphenylphosphine[33]. Other possible routes to these compounds are the oxidation of aminophosphines with silyl azides[28,30,31a] [eq. (q), cf. eq. (1), (m), (o)],



(26e) + $(CH_3)_3SiN_3$ → $[(CH_3)_3C]_2P(N\text{-}Si(CH_3)_3)(N(CH_3)\text{-}Si(CH_3)_3)$ + N_2 (q)

(39)

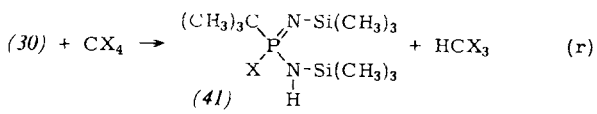
the cleavage of a P–N bond in diphosphinoamines[28, 34] [eq. (q'), cf. eq. (m)] with silyl azides,



$(CH_3)_2P(CH_3)N\text{-}P(CH_3)_2$ $\xrightarrow[-2\,N_2]{2\,(CH_3)_3SiN_3}$ $(CH_3)_2P(N\text{-}Si(CH_3)_3)(N(CH_3)\text{-}Si(CH_3)_3)$ + Polymers (q')

(40)

the reaction of *N,N'*-organoelement-substituted diaminophosphines with tetrahalogenomethanes[31a,32] [eq. (r), cf. eq. (n)], and the oxidation of stannylphosphines with phenyl azide[36].

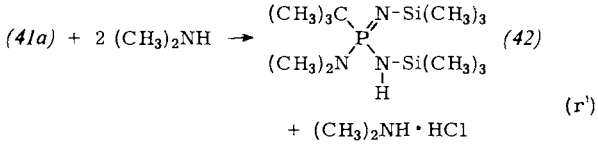


(30) + CX_4 → $(CH_3)_3C(N\text{-}Si(CH_3)_3)P(X)(N(H)\text{-}Si(CH_3)_3)$ + HCX_3 (r)

(41)

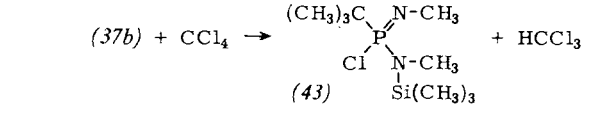
X = Cl *(41a)*, Br *(41b)*

(41a) contains a reactive P–Cl bond, as is shown by the reaction with dimethylamine[31a,32],



(41a) + 2 $(CH_3)_2NH$ → $(CH_3)_3C(N\text{-}Si(CH_3)_3)P(N(CH_3)_2)(N(H)\text{-}Si(CH_3)_3)$ *(42)* + $(CH_3)_2NH \cdot HCl$ (r')

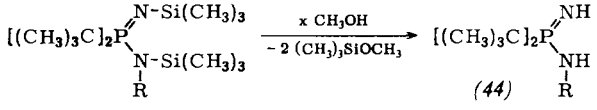
A number of other aminoiminophosphoranes *(43)* and *(46)* containing only one trimethyl(IVa)element group can be synthesized both in analogy with eq. (r) from *(37b)* and carbon tetrachloride[32]



(37b) + CCl_4 → $(CH_3)_3C(N\text{-}CH_3)P(Cl)(N(CH_3)\text{-}Si(CH_3)_3)$ + $HCCl_3$

(43)

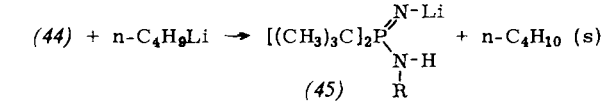
and by alcoholysis of *N,N'*-bis(trimethylsilyl)aminoiminophosphoranes, metalation with *n*-butyllithium, and reaction with *e.g.* chlorotrimethylsilane [eq. (s)][30,35].



$[(CH_3)_3C]_2P(N\text{-}Si(CH_3)_3)(N(R)\text{-}Si(CH_3)_3)$ $\xrightarrow[-2\,(CH_3)_3SiOCH_3]{x\,CH_3OH}$ $[(CH_3)_3C]_2P(NH)(N(H)R)$

(44)

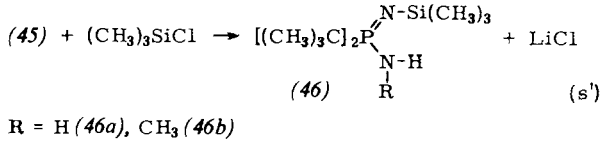
R = H *(44a)*, CH_3 *(44b)*



(44) + $n\text{-}C_4H_9Li$ → $[(CH_3)_3C]_2P(N\text{-}Li)(N(H)R)$ + $n\text{-}C_4H_{10}$ (s)

(45)

R = H *(45a)*, CH_3 *(45b)*



(45) + $(CH_3)_3SiCl$ → $[(CH_3)_3C]_2P(N\text{-}Si(CH_3)_3)(N(H)R)$ + LiCl (s')

(46)

R = H *(46a)*, CH_3 *(46b)*

The tautomeric form with the trimethylsilyl group on the amine nitrogen atom can be definitely ruled out for *(46)* on the basis of IR and ^1H–NMR studies[35].

The trimethylstannyl ligand can be introduced instead of trimethylsilyl in compounds of the type *(43)* by means of the multistep synthesis shown in scheme 2[32].

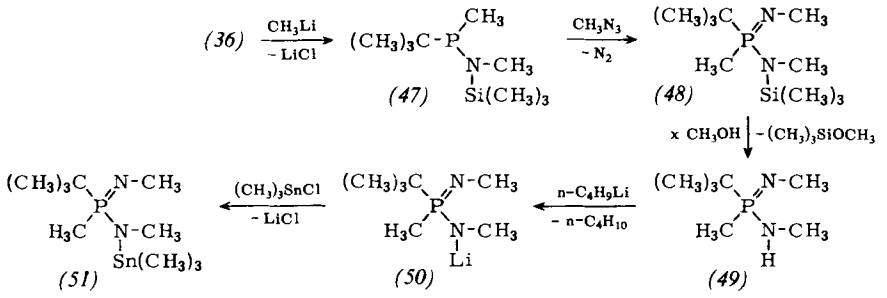
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[33] *K. L. Paciorek* and *R. H. Kratzer*, J. org. Chemistry *31*, 2426 (1966).

[34] *J. Wokulat*, Dissertation, Universität Marburg 1967.

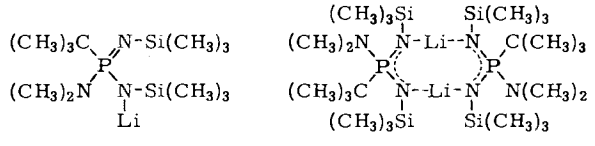
[35] *O. J. Scherer* and *G. Schieder*, J. organometallic Chem. *19*, 315 (1969).

[36] *H. Schumann* and *A. Roth*, J. organometallic Chem. *11*, 125 (1968).



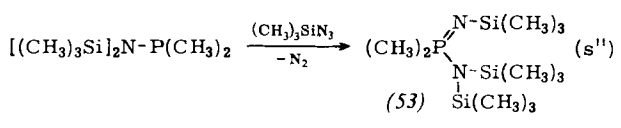
Scheme 2.

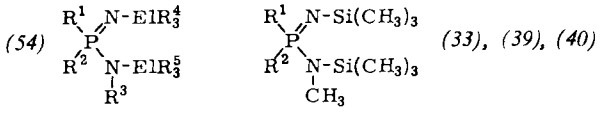
Attempted reactions of the metalation products of *(35)* and *(42)* with chlorotrimethylsilane have been unsuccessful evidently on steric grounds[31a,32]. The amide *(52)* is dimeric in benzene, as is shown by cryoscopic molecular weight determinations. Its ^{1}H–NMR spectrum contains only one sharp signal for the "differently bound" trimethylsilyl ligands (in various solvents and at high dilutions). These facts are best explained by the structure *(52a)* for the molecule in solution[31a,31b,32].



(52) *(52a)*

However, reaction of impure bis(trimethylsilyl)aminodimethylphosphine[37] [prepared from $[(CH_3)_3Si]_2NNa$ and $(CH_3)_2PCl$; see also section 3.2] with trimethylsilyl azide gives the first triply silylated aminoiminophosphorane *(53)*[31a,32].





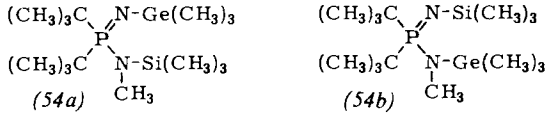
On the basis of the general formula *(54)*, we find a number of important questions in connection with reversible and irreversible migration processes:

1. How do the ligands R^1, R^2, and R^3 influence the ability of the R^4_3El and R^5_3El groups to migrate?

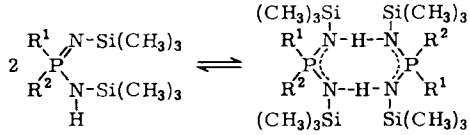
2. What part is played here by the ligands R^4 and R^5, and what part by the hetero atom El?

3. What happens if the R^4_3El group and R^3 are replaced by CH_3?

Compounds of the type *(33)*, *(39)*, and *(40)*, unlike benzamidine *(16a)*, do not exhibit migration of the trimethylsilyl groups (even at high temperatures) in any of the four examples studied $R^1 = R^2 = -N(CH_3)-(CH_2)_2-N(CH_3)-$ *(33)*[28]; $R^1 = R^2 = (CH_3)_3C$ *(39)*[30]; $R^1 = R^2 = CH_3$ *(40)*[34], and $R^1 = R^2 = C_6H_5$[8b]. In compounds containing different hetero atoms, the two isomeric forms [*(54a)* and *(54b)* in this case] are stable even at 150 °C[35].

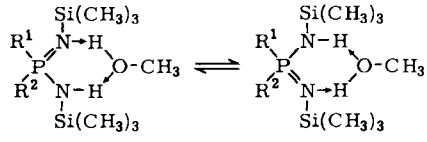


If the CH_3 group in the bis-silylated compounds *(33)*, *(39)*, and *(40)* is replaced by a proton, *(35)* is obtained with $R^1 = R^2 = (CH_3)_3C$[30], and *(42)* with $R^1 = (CH_3)_3C$, $R^2 = (CH_3)_2N$[31a,32]. A reversible intermolecular proton exchange can be detected in both compounds



(35), (42)

The NMR spectra in both cases contain one signal for the "differently bound" trimethylsilyl groups at high concentrations in benzene, and two trimethylsilyl signals at lower concentrations[30,31a,32]. Coalescence of the two signals can be observed by the addition of catalytic quantities of methanol [but not traces of amine, *e.g.* $(CH_3)_2NH$].



If tetrahydrofuran is used as the solvent for *(35)*[30], and acetone for *(42)*[32] (tetrahydrofuran gives no splitting in this case) instead of benzene, the spectrum both in concentrated and in dilute solution contains two $(CH_3)_3Si$ signals, which do not merge even on heating or an addition of small quantities of methanol. This supports the assumption that the formation of hydrogen bonds (detectable by IR spectroscopy[30]) with the solvent[38] takes precedence over the intermolecular proton exchange in this case.

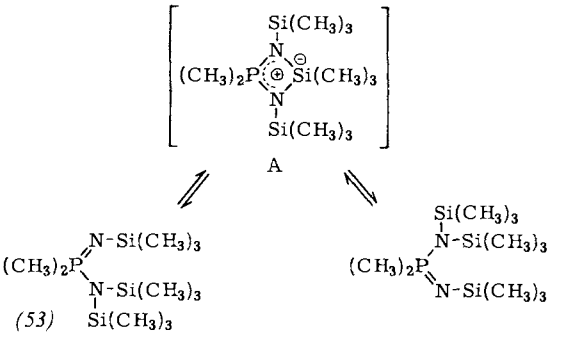
The proton exchange also stops when the $(CH_3)_2N$ group in *(42)* is replaced by the halogen atoms Cl *(41a)* and Br *(41b)*. Since the IR spectrum contains no evidence of hydrogen bonding to the halogen[32],

[37] *O. J. Scherer*, unpublished.

[38] Cf. *e.g. H. Suhr*: Anwendung der kernmagnetischen Resonanz in der organischen Chemie. Springer, Berlin 1965, p. 111 ff.

this difference in the behavior of *(41a)* and *(41b)* on the one hand and *(35)* and *(42)* on the other can perhaps be attributed to inductive effects.

A reversible intramolecular 1,3-trimethylsilyl migration occurs when the proton is replaced by the $(CH_3)_3Si$ ligand [31a, 31c, 32]. This migration, which has a low activation energy, can be "frozen in" at about −20 °C.



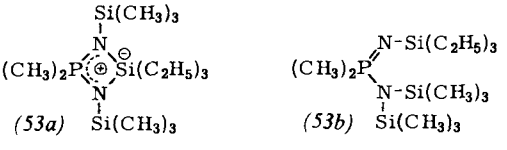
A

(53)

The replacement of a $(CH_3)_3Si$ group on the amine nitrogen atom by the $(C_2H_5)_3Si$ group in *(53)* leads to a compound *(53a)* [8b] that shows no splitting of the $(CH_3)_3Si$ signal in the NMR spectrum even at −55 °C and at high dilution. This observation is open to several interpretations:

1. The reversible intramolecular migration proceeds too rapidly even at −55 °C.

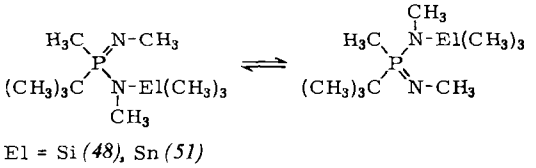
2. The substance is in the form of an "inner" symmetrical complex with pentacoordinated silicon (corresponds to transition state A).



(53a) *(53b)*

3. Both trimethylsilyl groups are bound to the amino nitrogen atom (this assumption is supported by the P=N band in the IR spectrum), and give no 1,3 migration in this isomeric form *(53b)*.

The driving force for the formation of *(53b)* may be the preference for the formation of sterically "balanced" molecules [cf. compound *(37a)*]. If the model compounds mentioned are modified in such a way that only one trimethyl(IVa)element ligand is now bound to the amine nitrogen atom [32], *(48)* exhibits a reversible intramolecular 1,3 migration of the $(CH_3)_3El$ ligand, which stops at −55 °C and can be readily detected by the splitting of the CH_3N doublet (NMR) into two doublets [32]. $\delta CH_3(N)$ for *(51)* consists of only one doublet down to −55 °C, even at high dilution. The absence of $J_{^{117},^{119}Sn-N-C-H}$ coupling (which would be expected for a pentacoordinated Sn atom with a trigonal bipyramidal arrangement, even with fast pseudorotation) indicates that even at this temperature the system is "stereochemically nonrigid".



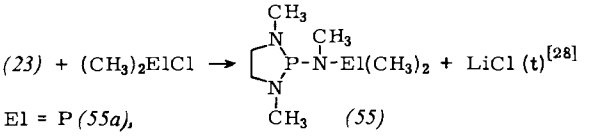
El = Si *(48)*, Sn *(51)*

All the results support the hypothesis that reversible intramolecular $(CH_3)_3M$ ligand migration in organo-(IVa)element-substituted aminoiminophosphoranes appears to be favored whenever, instead of a new isomeric form [*e.g.* *(53b)* or $R^1R^2P(=NCH_3)(N[Si(CH_3)_3]_2)$ for the compounds *(33)*, *(39)*, and *(40)*], an identical molecule [as a transition state, a molecule with identical *N* ligands (*e.g.* A)] can be postulated as an intermediate.

2.3. Va/Va Elements

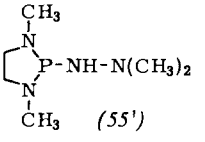
Compounds containing the atomic grouping $R_2P-NR^1-ElR^2_2$ (El = As → Bi) are at present known only in the form of aminophosphinoarsines $(CF_3)_2P-NR-As(CF_3)_2$, R=H, CH_3 [39].

Novel compounds of this type can be prepared by reaction of the lithium *N*-phosphinoamides *(23)* and *(25)* mentioned in equations (g) and (h) with dimethyl-(Va)element halides or 2-chloro-1,3-dimethyl-1,3,2-diazaarsenolane [27b] eq. (t') (cf. Table 6).

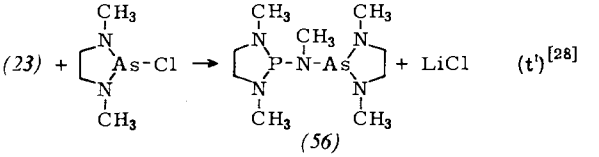


(23) + $(CH_3)_2ElCl$ → *(55)* + LiCl (t) [28]

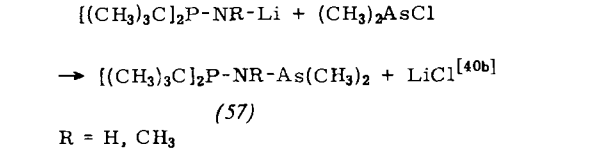
El = P *(55a)*,
As *(55b)*, Sb *(55c)*



(55')



(23) + → *(56)* + LiCl (t') [28]



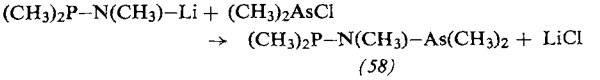
$[(CH_3)_3C]_2P-NR-Li + (CH_3)_2AsCl$

→ $[(CH_3)_3C]_2P-NR-As(CH_3)_2$ + LiCl [40b]

(57)

R = H, CH_3

The parent compound from which these alkyl-substituted products are derived, *i.e. As,As*-dimethyl-(*N*-dimethylphosphino-*N*-methylamino)arsine *(58)*, can also be prepared in this way [34].



(58)

[39] *J. Singh* and *A. B. Burg*, J. Amer. chem. Soc. *88*, 718 (1966).

[40] a) *O. J. Scherer* and *W. M. Janssen*, J. organometallic Chem. *16*, P 69 (1969); b) *ibid.*, in press.

Table 6. ^{1}H–NMR data (in Hz) for the compounds *(55)* and *(58)* (in benzene, TMS as external standard).

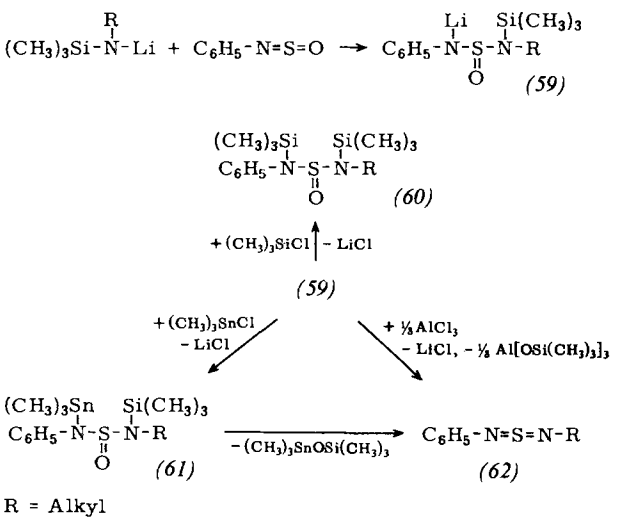
Compound	δ $CH_3(N_R)$	δ $CH_3(N)$	δ $CH_3(El)$	δ $CH_3(P)$	$J_{^{31}PNCH_3(R)}$ [a]	$J_{^{31}PNCH_3}$	$J_{^{31}PNElCH}$	$J_{^{31}PCH}$	Ref.
(55a)	−146.0 (d)	−138.0 (t)		−58.3 (d)	12.7	3.4	0	6.6	[28]
(55b)	−148.5 (d)	−148.3 (d)	−61.5 (d)		12.3	6.0	0.45		[28]
(55c)	−154.0 (d)	−163.0 (d)	−53.0 (d)		12.5	8.9	0.35		[28]
(58)		−154.0 (d)	−60.5 (d)	−60.3 (d)		6.3	0.70	6.25	[34]

[a] R = $-N(CH_3)-(CH_2)_2-N(CH_3)-$, δ CH_2(R) possesses multiplet structure in all cases.

Like the compounds *(24a)–(24c)*, the compounds *(55)* exhibit an increase in $J_{^{31}PNCH_3}$ from El = P to El = Sb (3.4–8.9 Hz), while $J_{^{31}PNCH_3(R)}$ remains practically unchanged. Unlike *(24a)*, the first member *(55a)* shows no long-range coupling $J_{^{31}PNElCH}$ (this is also true of the reference substance *(55')* [41]). The long-range coupling is however observed for the arsenic and antimony compounds *(55b)* and *(55c)* respectively. Comparison of the compounds *(55b)* and *(58)* reveals that the ligand on the phosphorus does not appreciably influence the coupling constants and chemical shifts of the $-N(CH_3)-As(CH_3)_2$ residue.

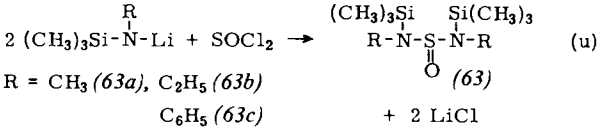
2.4. IVa/VIa Elements

Bis(organoelement)-substituted amines with this combination of elements are confined to the elements silicon and sulfur. Until recently these compounds were nearly always synthesized by heterolysis of *N*-silylated nitrogen compounds with sulfur halides [25]. We found that lithium *N*-alkyltrimethylsilylamides add smoothly to *N*-phenylthionylimide (*N*-sulfinylaniline) to give *(59)* [42].



R = Alkyl

Substitution of the 1:1 adducts *(59)* with chlorotrimethylsilane gives *N,N'*-disilylated sulfinyldiamides *(60)*, which split off hexamethyldisiloxane at temperatures above 100 °C. The resulting sulfur *N*-alkyl-*N'*-aryldiimides *(62)* can be isolated in this way in a fairly pure state. The pure compounds are however obtained when *(59)* is allowed to react with chlorotrimethylstannane or aluminum chloride instead of with chlorotrimethylsilane. Since the decomposition of *(61)* into *(62)* is accompanied by almost exclusive formation of trimethylsiloxytrimethylstannane, this must be taken as evidence of an intramolecular decomposition. *N,N'*-Dimethyl-*N,N'*-bis(trimethylsilyl)-sulfinyldiamide *(63a)*, which can be synthesized in accordance with eq. (u),

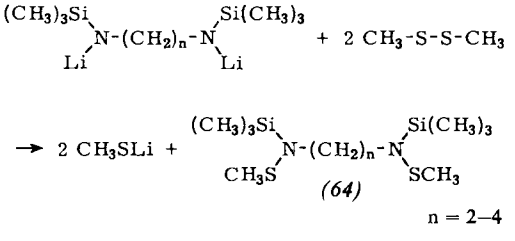


(u)

forms colorless crystals immediately after distillation; on storage in a stoppered flask at room temperature, these crystals slowly decompose into hexamethyldisiloxane and sulfur *N,N'*-dimethyldiimide [42b].

^{1}H–NMR spectroscopic measurements show that *(63a)* has decomposed to an extent of about 40 % after three days, and about 80 % after three weeks. Further enrichment of the thermally very unstable $CH_3N{=}S{=}NCH_3$ [43] is impossible at room temperature. Attempts to prepare the ethyl and phenyl derivatives *(63b)* and *(63c)* in accordance with eq. (u) showed that both suffer partial decomposition (detectable by NMR spectroscopy) during the reaction. Sulfur *N,N'*-diphenyldiimide is obtained by this method in a yield of 40 %.

Organo(IVa/VIa)element-substituted amines can also be obtained by nucleophilic cleavage of sulfur-sulfur bonds (for detailed discussion cf. Section 3.3), as is shown by the reaction of dimethyldisulfane with metalated *N,N'*-bis(trimethylsilyl)alkylenediamines [44].



n = 2–4

Selective hydrolysis or alcoholysis of the Si–N bond to form the silicon-free aminosulfanes $CH_3S-NH-(CH_2)_n-NH-SCH_3$ cannot be achieved with *(64)* (the compounds are recovered unchanged). More vigorous reaction conditions (*e.g.* acid or alkaline hydrolysis) lead at higher acid or base concentrations to simultaneous cleavage of the S–N bond. This may be regarded as evidence of the unusual stability of this class of substances toward hydrolysis.

[41] *O. J. Scherer* and *J. Wokulat*, Z. Naturforsch. *22b*, 474 (1967).

[42] a) *O. J. Scherer* and *P. Hornig*, Angew. Chem. *78*, 776 (1966); Angew. Chem. internat. Edit. *5*, 729 (1966); b) *P. Hornig*, Dissertation, Universität Würzburg 1968.

[43] *B. Cohen* and *A. G. MacDiarmid*, J. chem. Soc. (London) *A 1966*, 1780.

[44] *O. J. Scherer* and *J. Wokulat*, Z. anorg. allg. Chem. *357*, 92 (1968).

3. Tris(organoelement)-Substituted Amines with Two Different Hetero Atoms

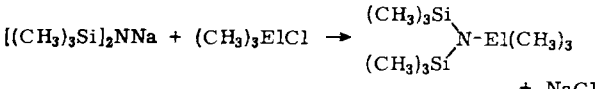
3.1. IVa/IVa Elements

Tris(organoelement)-substituted amines can be derived from the ammonia molecule in the same way as bis(organoelement)-substituted amines.



X,Y = organoelement ligand

An excellent starting material for the synthesis of bis(trimethylsilyl)trimethyl(IVa)element-substituted amines *(65)* [45] is sodium bis(trimethylsilyl)amide, which was synthesized by *Wannagat* [46] (Table 7).



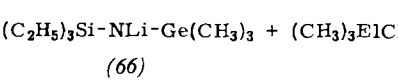
El = Ge *(65b)*, Sn *(65c)*, Pb *(65d)* *(65)*

Table 7. Physical properties and spectra of the compounds *(65)* (in CCl_4, TMS as internal standard).

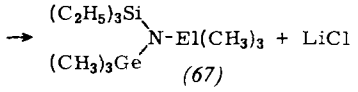
Compound	B.p.(°C/torr)	M.p.(°C)	δ CH_3(Si)	$J_{^{13}CH(Si)}$ (Hz)	ν_{as} SiN(Si) (cm^{-1})	Ref.
(65a) [a]	78—80/13	67—69	— 10.7	118.0	916	[50]
(65b)	54—56/1	29—32	— 7.2	118.0	931	[45b]
(65c) [b]	58—59/1	20—22	— 5.0	118.0	950	[45b]
(65d) [c]	85—87/3		0	118.0	970	[45b]

[a] El = Si. [b] $J_{117,\,119SnCH}$ = 54.0/56.5. [c] $J_{^{207}PbCH}$ = 67.0.

(65c) is also formed from bis(trimethylsilyl)amine and *N,N*-diethyltrimethylstannylamine [47]. Alkoxy derivatives are also known in the germanium series [48]. Lithium *N*-triethylsilyl-*N*-trimethylgermylamide *(66)* [14] has proved valuable as a starting material for the synthesis of the compounds *(67)* with a new IVa/IVa element combination [8b].



(66)



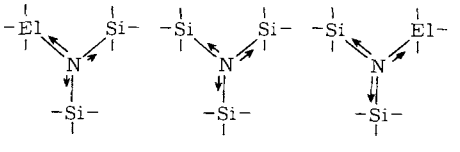
(67)

El = Si, Ge

$[(CH_3)_3Sn]_2NSi(CH_3)_3$ can be obtained both from lithium bis(trimethylstannyl)amide [12d] and chlorotrimethylsilane [though the product always also contains *(65c)*] and by substitution of impure sodium trimethylsilylamide with chlorotrimethylstannane [49].

The compounds *(65)* differ very markedly in their behavior toward protonic solvents. *(65b)*, like *(65a)*, El = Si, is surprisingly resistant to moisture. This behavior, which is unusual for alkylgermanium-nitrogen compounds, is probably due to steric factors. *(65c)* and *(65d)* react immediately with water at the Sn–N and Pb–N bonds respectively.

The tris(organoelement)-substituted amines are suitable for the study of the relative inductive effects of the IVa elements (cf. also [51]). This effect can either



El = Ge → Pb

weaken (–I effect, A) or strengthen (+I effect, C) the Si–N bonds, which are strengthened in the symmetrically substituted derivative (B) by equal sharing of the formally "lone" pair of electrons on the nitrogen atom. IR (increase in the frequency of the antisymmetric SiN(Si) stretching vibration for El = Si → Pb) and ^{1}H-NMR spectra (shift of δCH_3(Si) to higher field strengths for El = Si → Pb; $J_{^{13}CH(Si)}$ remains constant), as can be seen from Table 7, indicate strengthening of the Si–N bond by the incorporation of the hetero atom El, *i.e.* a + I effect (C):

$(CH_3)_3Pb > (CH_3)_3Sn > (CH_3)_3Ge > (CH_3)_3Si$

As in the case of the bis(organoelement)-substituted amines with different hetero atoms, these observations can be taken as evidence that (p → d)π strengthening of the El–N bond is of minor importance for the higher homologs of silicon [52]. Two other classes of compounds, *i.e.* the heterosiloxanes, which were studied by *Schmidbaur* [53] and the trimethyl(IVa)-element azides, which were investigated by *Thayer* and *West* [54], exhibit the same relations.

[45] a) *O. J. Scherer* and *M. Schmidt*, Angew. Chem. *75*, 642 (1963); Angew. Chem. internat. Edit. *2*, 161 (1963); b) J. organometallic Chem. *1*, 490 (1964).

[46] *U. Wannagat* and *H. Niederprüm*, Chem. Ber. *94*, 1540 (1961).

[47] *J. Lorberth* and *M. R. Kula*, Chem. Ber. *98*, 520 (1965).

[48] *A. Köster-Pflugmacher* and *E. Termin*, Naturwissenschaften *51*, 554 (1964).

[49] *O. J. Scherer* and *M. Schmidt*, Sci. Commun. Internat. Sympos. on Organosilicon Chemistry, Prague 1965, p. 315.

[50] Cf. *e.g. J. Goubeau* and *J. Jiménez-Barberá*, Z. anorg. allg. Chem. *303*, 217 (1960).

[51] a) Cf. *e.g. T. N. Srivastava* and *M. Onyschuk*, Canad. J. Chem. *41*, 1244 (1963); b) *R. W. Bott, C. Eaborn, K. C. Pande*, and *T. W. Swaddle*, J. chem. Soc. (London) *1962*, 1217.

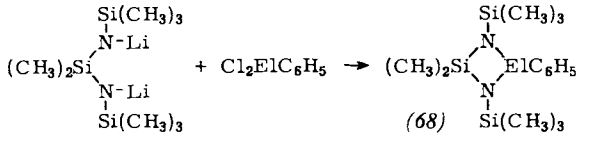
[52] Cf. *e.g. E. W. Randall* and *J. J. Zuckerman*, J. Amer. chem. Soc. *90*, 3167 (1968).

[53] *H. Schmidbaur*, Angew. Chem. *77*, 206 (1965); Angew. Chem. internat. Edit. *4*, 201 (1965).

[54] *J. S. Thayer* and *R. West*, Inorg. Chem. *3*, 889 (1964).

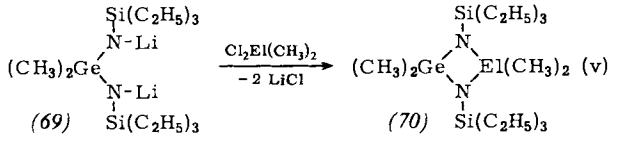
3.1.1. Heterocycles

Cyclic amines of this type with two different hetero atoms were described by *Fink* [55] in the form of the four-membered heterocycles *(68)*.

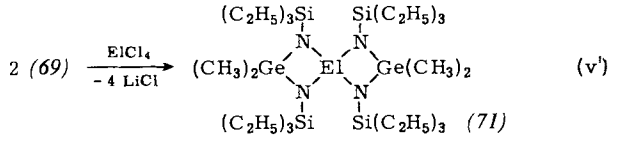


El = B *(68a)*, P *(68b)*

Starting with metalated bis(*N*-triethylsilylamino)dimethylgermane *(69)* [14], it is possible to synthesize not only the derivatives *(70)* [*e.g.*(v)] but also spiranes *(71)* [eq. (v')] [8b].



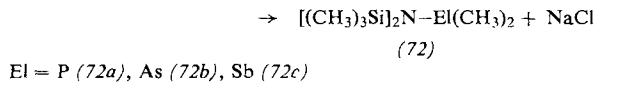
El = Si *(70a)*, Ge *(70b)*



El = Si *(71a)*, Ge *(71b)*

3.2. IVa/Va Elements

Attempts to obtain definite *N*-silylated phosphorus-nitrogen compounds by reaction of PCl_3 [56] or variously substituted phosphorus chlorides with sodium bis(trimethylsilyl)amide have been successful only in the case of chlorodiphenylphosphine [57]. Whereas bis(trimethylsilyl)aminodimethylphosphine *(72a)* [31a,32] cannot be obtained in the pure state (detectable by NMR spectroscopy) in accordance with,

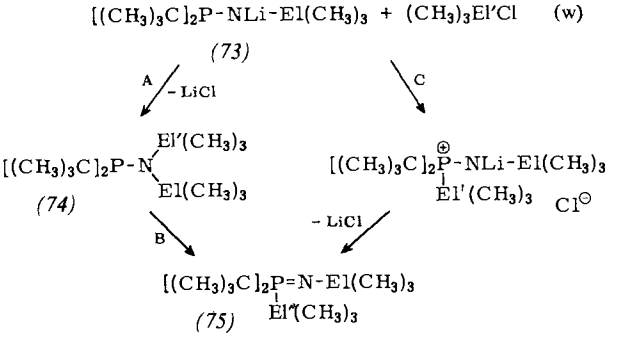


El = P *(72a)*, As *(72b)*, Sb *(72c)*

the analogous reactions with chlorodimethylarsine [58] and chlorodimethylstibine [1] present no difficulties. In view of the incompleteness of the class of substances *(72)*, we shall not discuss their ^1H–NMR spectra in detail [δCH_3(Si) is slightly displaced toward higher field strengths from *(72b)* to *(72c)*; −10.0 → −8.5 Hz]. *(72a)*, unlike *(72b)*, gives the triply silylated amino-iminophosphorane *(53)* on oxidation with trimethylsilyl azide [eq. (s')]. Unlike bis(trimethylsilyl)-amine [58], *(72b)* does not react with excess chlorodimethylarsine to give tris(dimethylarsino)amine $[(CH_3)_2As]_3N$.

3.2.1. *N,P*-Bis(organoelement)-Substituted Iminophosphoranes

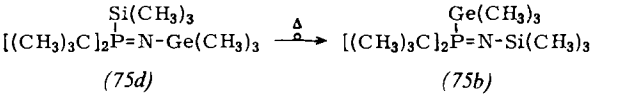
Attempts to prepare compounds of the type *(72)* by the reverse route, *i.e.* by substitution of *N*-silylated lithium *N*-phosphinoamides *(73)* in accordance with eq. (w) led us to the first *N,P*-bis(organo(IVa)element)-substituted iminophosphoranes *(75)* [29,30], but gave no amines *(74)*.



El = El' = Si *(75a)*; El = Si, El' = Ge *(75b)*;
El = Si, El' = Sn *(75c)*; El = Ge, El' = Si *(75d)*;
El = El' = Ge *(75e)*; El = Ge, El' = Sn *(75f)*.

The fact that *(75b)* is obtained from $[(CH_3)_3C]_2P$–NLi–$Si(CH_3)_3$ and chlorotrimethylgermane, and *(75d)* from $[(CH_3)_3C]_2P$–NLi–$Ge(CH_3)_3$ and chlorotrimethylsilane shows that the reaction is actually an addition (path C) and not a substitution (path A). If *(74)* were the intermediate, the end product should be the same in both cases, *i.e.* *(75)*.

As was found by *Schmitz-Du Mont* and *Jansen* [59], on the other hand, substitution occurs on reaction of $(C_6H_5)_2P$–NK–$Si(CH_3)_3$ with chlorotrimethylsilane. *(75d)* rearranges irreversibly into the isomer *(75b)* when heated at 120–130 °C for several hours; so far as we know, this is the first example of isomerism of an iminophosphorane.



It is not yet known whether this rearrangement proceeds intermolecularly or intramolecularly [*(74)* would presumably occur as an intermediate in the latter case]. The stronger tendency of silicon, as compared with its heavier homologs, to form (p → d)π bond components may be the driving force of this ligand exchange. Another decisive factor may be the more favorable energy balance resulting from the conversion

[55] *W. Fink*, Angew. Chem. *78*, 803 (1966); Angew. Chem. internat. Edit. *5*, 760 (1966).

[56] *U. Wannagat*, Angew. Chem. *75*, 173 (1963); Angew. Chem. internat. Edit. *2*, 161 (1963).

[57] *H. Nöth* and *L. Meinel*, Z. anorg. allg. Chem. *349*, 225 (1967).

[58] *O. J. Scherer* and *M. Schmidt*, Angew. Chem. *76*, 144 (1964); Angew. Chem. internat. Edit. *3*, 137 (1964).

[59] *O. Schmitz-Du Mont* and *W. Jansen*, Angew. Chem. *80*, 399 (1968); Angew. Chem. internat. Edit. *7*, 382 (1968).

of Ge–N and Si–P bonds into Si–N and Ge–P bonds.

All the iminophosphoranes *(75)* are sublimable solids, and their sensitivity to moisture decreases in the following order:

(75f) ⩾ *(75e)* > *(75d)* > *(75c)* ⩾ *(75b)* > *(75a)*

The increased reactivity of the El′–P as compared with the El–N bond is clearly shown in the alcoholysis [eq. (x)] and in the reaction with carbon tetrachloride [eq. (x′)], which leads in quantitative yield to the *P*-chloroiminophosphorane *(34a)* prepared earlier in accordance with eq. (n).

$$[(CH_3)_3C]_2\overset{Si(CH_3)_3}{\overset{|}{P}}{=}N{-}Si(CH_3)_3 \quad (75a)$$

$$\xrightarrow[-(CH_3)_3SiOCH_3]{CH_3OH} [(CH_3)_3C]_2\overset{H}{\overset{|}{P}}{=}N{-}Si(CH_3)_3 \quad (76) \quad (x)$$

$$[(CH_3)_3C]_2\overset{C}{\overset{|}{P}}{-}NH{-}Si(CH_3)_3 \quad (26a)$$

$$(75a) \xrightarrow[-(CH_3)_3SiCCl_3]{CCl_4} [(CH_3)_3C]_2P(Cl){=}N{-}Si(CH_3)_3 \quad (34a) \quad (x')$$

The alcoholysis of *(75a)* suggests that iminophosphoranes of the type *(76)*, or at least these model substances, are unstable and rearrange into the thermodynamically more stable isomeric aminophosphine (NH → PH tautomerism has so far been observed only in cyclotriphosphazenes [60]).

3.3. IVa/VIa Elements

Sulfur-sulfur bonds can be broken both electrophilically [61] and nucleophilically [61,62].

Sodium bis(trimethylsilyl)amide not only reacts with chlorosulfanes [63], S_8 [64], and dithiocyanogen [65] to form *N*-silylated aminosulfanes having the composition

$$[(CH_3)_3Si]_2N{-}S_n{-}N[Si(CH_3)_3]_2 \qquad n = 1 \rightarrow 4$$

but also readily cleaves a wide range of disulfane derivatives [eq. (y)] [44,66].

This cleavage of disulfanes confirms the observation that the ease of nucleophilic cleavage of sulfur-sulfur

$$[(CH_3)_3Si]_2NNa + R{-}S{-}S{-}R \rightarrow [(CH_3)_3Si]_2N{-}S{-}R + RSNa \quad (y)$$

(77)

R = CH_3 *(77a)*, C_2H_5 *(77b)*, *n*-C_4H_9 *(77c)*, C_6H_5 *(77d)*, $C_2H_5OC(O)$ *(77e)*, $C_6H_5C(O)$ *(77f)*, *i*-$C_3H_7OC(S)$ *(77g)*, $(CH_3)_2NC(S)$ *(77h)*, $(C_6H_5CH_2)_2NC(S)$ *(77i)*, $(C_2H_5O)_2P(S)$ *(77j)*.

bonds increases as the substituent R becomes more strongly electron-attracting [44]. If the cleavage of dialkyldisulfanes (very few anions $A^{\ominus}$ cleave dimethyl- or diethyldisulfane) is taken as a measure of the nucleophilic strength of $A^{\ominus} = N[Si(CH_3)_3]_2^{\ominus}$, it can be seen that sodium bis(trimethylsilyl)amide is one of the strongest nucleophilic agents. If the disulfane derivative in eq. (y) is replaced by dimethyldiselenane, the reaction yields bis(trimethylsilyl)aminomethylselenane *(78)* [44].

$$[(CH_3)_3Si]_2N{-}Se{-}CH_3 \quad (78)$$

Comparison of the ^1H–NMR and IR spectra of *(78)* with those of the analogous sulfur compound *(77a)* shows that the replacement of sulfur by selenium leads to slight changes in $\delta CH_3(Si)$ and $\nu_{as}SiN(Si)$, the chemical shift being displaced to higher field strengths [*(77a)* –10.7, *(78)* –9.2 Hz], and the antisymmetric SiN(Si) stretching vibration to higher wave numbers [*(77a)* 935, *(78)* 940 cm^{-1}]. These observations are in good agreement with the results obtained for tris(organo(IVa/IVa)element)-substituted amines. However, the differences are more pronounced than for the latter (cf. Section 3.1).

A distinct weakening of the "thiophilic character" in alkali metal silylamides can be achieved by introduction of electron-attracting substitutents on the silicon atom. $[(i\text{-}C_3H_7O)_3Si]_2NNa$ cleaves only the sulfur-sulfur bond of the particularly reactive diethyl dithiodiformate [44].

$$[C_2H_5OC(O)S]_2 + [(i\text{-}C_3H_7O)_3Si]_2NNa \rightarrow [(i\text{-}C_3H_7O)_3Si]_2N{-}S{-}C(O){-}O{-}C_2H_5 + C_2H_5OC(O)SNa$$

(79)

Many of the *N*-silylated aminosulfanes are surprisingly insensitive to water. Their chemical behavior toward thionyl chloride is interesting. In most cases cleavage of the Si–N and not of the S–N bond occurs, even under very mild conditions [67].

$$[(CH_3)_3Si]_2N{-}S{-}R \xrightarrow[-2\,(CH_3)_3SiCl]{SOCl_2} R{-}S{-}N{=}S{=}O \quad (80)$$

R = CH_3 *(80a)*, C_2H_5 *(80b)*, $CH_2{=}CH{-}CH_2$ *(80c)*, C_6H_5 *(80d)*, $C_6H_5C(O)$ *(80e)*, $C_2H_5OC(O)$ *(80f)*, *i*-$C_3H_7OC(S)$ *(80g)*.

This provided the first preparative route to the *N*-alkylsulfenylthionylimides, as well as to many other derivatives of this class of compounds [67,68].

[60] *A. Schmidpeter* and *J. Ebeling*, Angew. Chem. *80*, 197 (1968); Angew. Chem. internat. Edit. *7*, 209 (1968).

[61] *E.g. A. J. Parker* and *N. Kharasch*, Chem. Reviews *59*, 583 (1959).

[62] *E.g. M. Schmidt*, Österr. Chemiker-Ztg. *64*, 236 (1963).

[63] *U. Wannagat* and *H. Kuckertz*, Angew. Chem. *74*, 117 (1962); Angew. Chem. internat. Edit. *1*, 113 (1962).

[64] *O. J. Scherer* and *M. Schmidt*, Naturwissenschaften *50*, 302 (1963).

[65] *O.J. Scherer* and *M. Schmidt*, Z. Naturforsch. *18b*, 415 (1963).

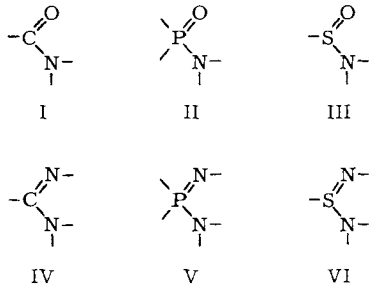
[66] *O. J. Scherer* and *M. Schmidt*, Angew. Chem. *75*, 139 (1963); Angew. Chem. internat. Edit. *2*, 98 (1963).

[67] a) *O. J. Scherer* and *R. Schmitt*, Chem. Ber. *101*, 3302 (1968); b) IIe Symposium international sur la Chimie des Composés organiques du Silicium, Bordeaux 1968, p. 165.

[68] *O. J. Scherer* and *R. Schmitt*, unpublished.

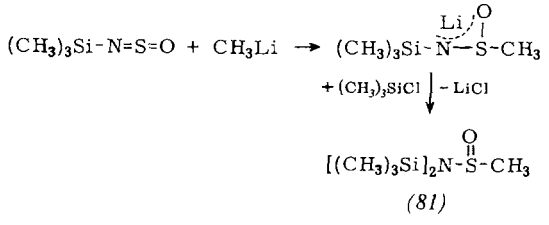
3.4. Ligand Migration Processes in *N*-silylated Sulfinamides and Aminosulfimines

Fluxional organometallic molecules (particularly transition element compounds) have recently been intensively studied [69]. Whereas amides I [70], thioamides [71], ureas [72], and amidines (skeleton IV) are used to study the 1,3 migration of $(CH_3)_3El$ ligands attached to nitrogen for elements of group IVa, aminophosphine oxides II [73] and aminoiminophosphoranes V for elements of group Va, *N*-silylated sulfinamides III and aminosulfimines VI should be suitable for this purpose in the case of group VIa (Scheme 3).



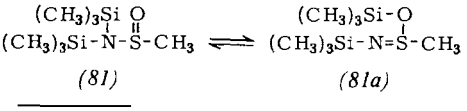
Scheme 3. The free valences on the N represent $(CH_3)_3El$ ligands.

Methyllithium adds to the double bond system of *N*-sulfinyltrimethylsilylamine. The 1:1 adduct reacts further with chlorotrimethylsilane to give the bis-silylated sulfinamide *(81)* [74].



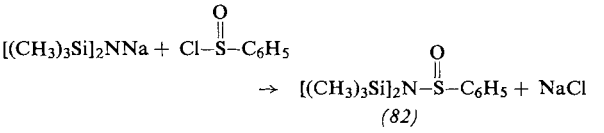
(81)

The ^1H–NMR spectrum of *(81)* (in CCl_4 solution and undiluted at 35 °C contains three $(CH_3)_3Si$ and two CH_3S signals. Whereas coalescence of the silyl and sulfenyl signals occurs at about 100 °C, the spectrum resumes its original form when the specimen is cooled to 35 °C again. This shows that *(81)* is in equilibrium with its imine tautomer *(81a)* at 35 °C [about 60 % of *(81)* and 40 % of *(81a)*], this equilibrium being displaced even more in favor of the amine form *(81)* on further cooling to −50 °C.



(81) *(81a)*

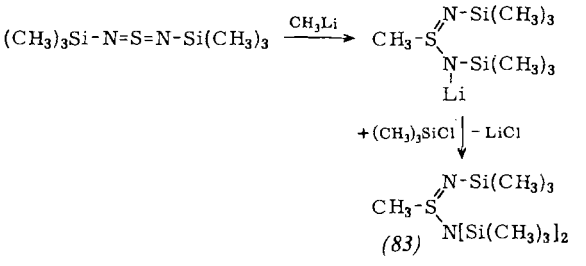
If the CH_3 group on the sulfur atom is replaced by C_6H_5, no amine-imine tautomerization is observed between about −50 and 100 °C.



(82)

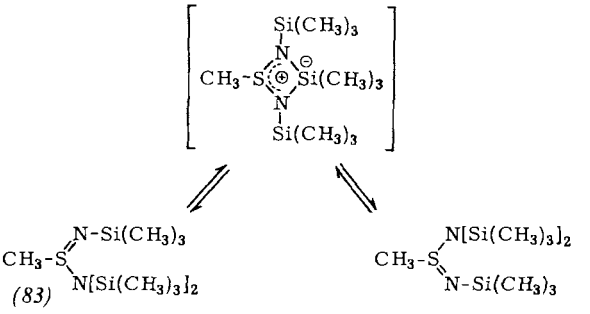
The difference in the behavior of *(81)* and *(82)* is probably due to an increase in the electron density on the oxygen atom as a result of the inductive effect of the methyl group.

1,2-Addition of methyllithium is also possible in the case of sulfur bis(trimethylsilyl)diimide [75].



(83)

N,N',N''-Tris(trimethylsilyl)-*S*-methylaminosulfimine *(83)*, like the analogous aminoiminophosphoranes, exhibits dynamic properties.



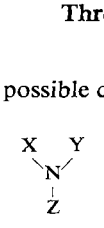
(83)

The ^1H–NMR spectrum contains one $(CH_3)_3Si$ signal at 35 °C, even at high dilution, two at about −50 °C, and three at about −80 °C.

It may be concluded from these observations that the reversible intramolecular $(CH_3)_3Si$ ligand migration indicated in the formulas stops at about −50 °C [75]. The additional splitting of the signal due to the amine-bound $(CH_3)_3Si$ groups at about −80 °C can be interpreted as resulting from hindered rotation about the S–N bond.

4. Tris(organoelement)-Substituted Amines with Three Different Hetero Atoms

The number of possible combinations for the formula



X, Y, Z = organoelement ligand

[69] For example, *F. A. Cotton*, Accounts chem. Res. *1*, 257 (1968).

[70] a) *J. Pump* and *E. G. Rochow*, Chem. Ber. *97*, 627 (1964); b) *L. Birkofer* and *A. Ritter*, Angew. Chem. *77*, 414 (1965); Angew. Chem. internat. Edit. *4*, 417 (1965); c) *J. F. Klebe* and *J. B. Bush jr.*, Sci. Commun. internat. Sympos. on Organosilicon Chemistry. Prague 1965, p. 328.

[71] *K. Itoh*, *K. Matsuzaki*, and *Y. Ishii*, J. chem. Soc. (London) *C 1968*, 2709.

[72] a) *J. F. Klebe*, *J. B. Bush jr.*, and *J. E. Lyons*, J. Amer. chem. Soc. *86*, 4400 (1964); b) *I. Matsuda*, *K. Itoh*, and *Y. Ishii*, J. chem. Soc. (London) *C 1969*, 701.

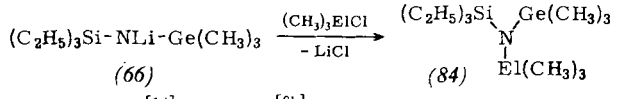
[73] *M. Meyer zur Heyde*, Tetrahedron Letters *1969*, 1425.

[74] *O. J. Scherer* and *R. Schmitt*, Tetrahedron Letters *1968*, 6235.

[75] *O. J. Scherer* and *R. Schmitt*, J. organometallic Chem. *16*, P 11 (1969).

which would appear to be large "on paper", is limited in practice, since only one synthetic route has so far led to the desired result. The starting material is a primary elemento-organic amine that has no great tendency toward condensation and whose element-nitrogen bond is not unstable toward organolithium compounds.

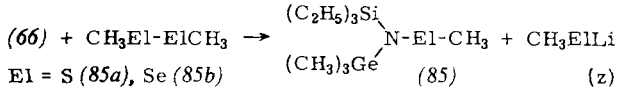
These conditions are satisfied by *N*-triethylsilylamine and aminodi-*tert*-butylphosphine derivatives with elements of the second short period. The choice of the second ligand is also limited, since the element-nitrogen bond in this compound also must resist cleavage during the metalation. In tris(organoelement)-substituted amines with three different homologs from one group of the periodic system, only an element from the first long period is possible.



El = Sn *(84a)*[14], Pb *(84b)*[8b]

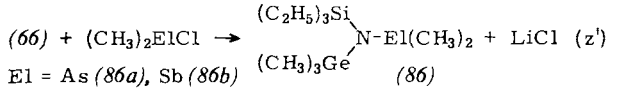
(84a) and *(84b)* are the first stable ammonia derivatives with three different homologs of carbon [8a, 8b, 14].

The introduction of the third ligand is practically free from any restrictions, as is shown by the following reactions [eq. (z), (z'), and (z'')]:



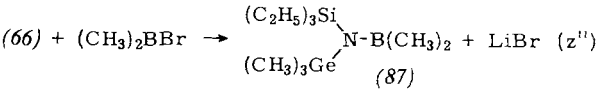
El = S *(85a)*, Se *(85b)*

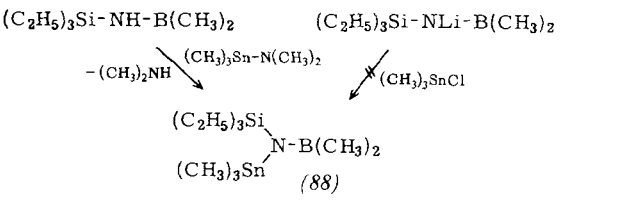
Like sodium bis(trimethylsilyl)amide, *(66)* also cleaves chalcogen-chalcogen bonds [8b] [eq. (z)]. The reaction of this compound with dimethyl(Va)element-halogen compounds presents difficulties only in the case of chlorodimethylphosphine [8b].



El = As *(86a)*, Sb *(86b)*

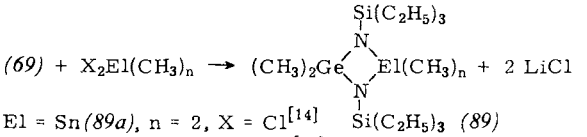
In addition to tris(organoelement)-substituted amines with IVa/VIa and IVa/Va combinations, IVa/IIIa combinations are also possible [8b].



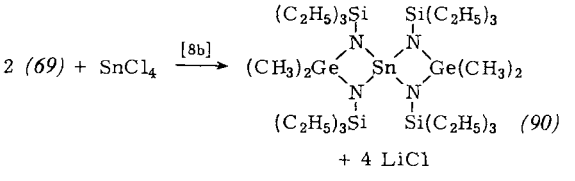


It should be noted that in the case of *(88)*, the desired result cannot be obtained by double decomposition [76], but only by transamination.

The variety of possibilities offered by this interesting field of elemento-organic nitrogen compounds with different hetero atoms is finally illustrated by the syntheses of two heterocycles [8b].



El = Sn *(89a)*, n = 2, X = Cl [14]
El = B *(89b)*, n = 1, X = Br [8b]



Special thanks are due to Dipl.-Chem. D. Biller, Dr. P. Hornig, W. M. Janssen, P. Klusmann, Dipl.-Chem. G. Schieder, Dr. J. Schmidt, Dipl.-Chem. R. Schmitt, and Dr. J. Wokulat for their valuable cooperation, to Professor Max Schmidt for his kind encouragement, and to the Deutsche Forschungsgemeinschaft and the Verband der Chemischen Industrie for their financial support.

Received: October 15, 1968 [A 724 IE]
German version: Angew. Chem. *81*, 871 (1969)
Translated by Express Translation Servive (London)

[76] Cf. *H. Nöth* and *H. Vahrenkamp*, J. organometallic Chem. *16*, 357 (1969).

[77] For example *W. McFarlane*, Quart. Reviews *23*, 187 (1969).

Reductive Cleavage of Bonds by Complexes of Zerovalent Transition Metals

By *H. Schott* and *G. Wilke*[*]

We have observed that in nickel(0) complexes — hereafter symbolized as [Ni⁰] — the nickel atoms render possible the ready cleavage of certain bonds. For example, ethylenebis(triphenylphosphine)nickel and benzoyl peroxide react spontaneously in benzene solution according to the following equation:

$$[Ni^0] + C_6H_5{-}C(=O){-}O{-}O{-}C(=O){-}C_6H_5 \rightarrow Ni^{II}(C_6H_5CO_2)_2$$

Dialkyl peroxides, *e.g.* di-*tert*-butyl peroxide or ascaridol, likewise undergo reaction with cleavage of the O—O bond.

$$[Ni^0] + R{-}O{-}O{-}R \rightarrow Ni^{II}(OR)_2$$

A simple, pure nickel alkoxide has been prepared for the first time in this way from di-*tert*-butyl peroxide and bis(cycloocta-1,5-diene)nickel. (The compounds prepared by reaction of nickel halides with alkali metal alkoxide are always contaminated with basic products[1].)

The blue di-*tert*-butoxynickel *(1)* is completely insoluble in the commonly used solvents. It decomposes at about 100 °C with separation of nickel, as has also been observed in the case of nickel-aluminum ethoxide[2]. 75 % of the *tert*-butoxy groups give rise to *tert*-butanol, the remainder decomposing into compounds having a lower number of carbon atoms — *inter alia*, butane, butene, propane, propene, acetone, methane, and CO_2. If compound *(1)* is decomposed in the presence of suitable electron donors, complexes containing zerovalent nickel are again formed, *e.g.*

$$\underset{(1)}{Ni[OC(CH_3)_3]_2} + 4\,P(OC_6H_5)_3 \xrightarrow{120\,^\circ C} Ni^0[P(OC_6H_5)_3]_4\,(80\%) + \text{decomposition products}$$

If the reaction is carried out under similar conditions and in the presence of butadiene, catalysts are obtained which facilitate the formation of cycloocta-1,5-diene or cyclododeca-1,5,9-triene.

The reaction of nickel(0) complexes with organic disulfides, *e.g.* dibenzyl disulfide or di-β-naphthyl disulfide, proceeds in analogous fashion to the O—O cleavage described above:

$$[Ni^0] + R{-}S{-}S{-}R \rightarrow Ni(SR)_2$$

Possibly, the synthesis of bis(trityl)nickel[3] previously reported by us also involves such a bond cleavage; however, one must take into consideration in this case that the trityl radical already in solution can react with the nickel(0).

$$[Ni^0] + (C_6H_5)_3C{-}C(C_6H_5)_3 \rightarrow Ni[C(C_6H_5)_3]_2$$

In the reductive cleavage described, the various Ni⁰ compounds exhibit widely differing reactivities. While O—O cleavage is possible with all known Ni⁰ compounds — including $Ni(CO)_4$ — only complexes containing olefinic ligands — *e.g.* cycloocta-1,5-diene — are suitable for the preparation of bis(trityl)nickel. Further examples involving bond cleavage by nickel(0) are the formation of π-allylnickel bromide from tetracarbonylnickel and allyl bromide (cleavage of a C—Br bond) reported by *Fischer* and *Bürger*[4] and the preparation of a nickel(I) phosphide from a nickel(0) complex and triphenylphosphine (cleavage of a P—C bond) *via* a non-isolable phenylnickel diphenyl phosphide as described by *Herrmann*[5].

Other transition metal(0) complexes also react with di-*tert*-butyl peroxide. *Hagihara* and *Yamazaki*[6] have prepared tetra-*tert*-butoxychromium from di-*tert*-butyl peroxide and dibenzenechromium. We have found that both $Fe(CO)_5$ and $Co_2(CO)_8$ react with di-*tert*-butyl peroxide — to give tri-*tert*-butoxyiron and tri-*tert*-butoxycobalt respectively.

Representative procedure:

Di-*tert*-butyl peroxide (8 ml) in toluene (120 ml) is allowed to react with an ethylene-saturated solution of ethylenebis(triphenylphosphine)nickel in toluene (250 ml) for 5 h at 110 °C. The reaction mixture is then filtered, and the residue is washed with toluene and ether and finally dried. Yield: 2.3 g (87 %) of $Ni[OC(CH_3)_3]_2$. The filtrate contains 7 g (98 %) of triphenylphosphine oxide.

Received: October 24, 1966 [Z 79 IE]
German version: Angew. Chem. *81*, 896 (1969)
Publication delayed at authors' request

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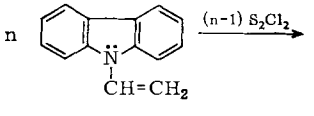
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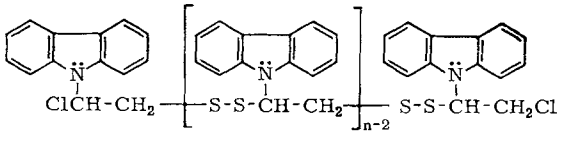
A New Reaction of *N*-Vinylcarbazole with Disulfur Dichloride

By *J. Pielichowski*[*]

Disulfur dichloride is known to react with olefins to give bis(β-chloroalkyl) sulfide and sulfur[1,2]. On reaction of *N*-vinylcarbazole with disulfur dichloride hardly any sulfur separates but gaseous chlorine is evolved.

In this case the disulfur dichloride causes polycondensation to a polymer having a molecular weight of about 1300 (ebullioscopic). The polymer contains two atoms of sulfur per molecule of *N*-vinylcarbazole and only little chlorine (about 2 %) probably in the end groups. The course of the reaction depends primarily on the concentration of the two reagents.





The structure of the polymer follows from its IR spectrum after polarographic reduction (solvent: dimethylformamide) of the disulfide groups to sulfide groups (νS—S = 400—500 cm^{-1} [3]). The other absorption bands confirm the presence of carbazole and ethyl groups (values: 720, 750, and 2880 cm^{-1}).

Procedure

N-Vinylcarbazole (5 g) is dissolved in CCl_4 (100 ml); S_2Cl_2 (3 g) is passed into the solution, which is then allowed to stand for 12 h. An olive-green polymer (8 g) is obtained which is boiled for 1 h with a 10% aqueous solution of Na_2SO_3. After filtration, the residue is washed and dried to give a brown powder (yield 7.5 g, m.p. 190—220 °C, solubility in dioxane: 1 g/100 ml, in toluene: 0.5 g/100 ml).

Received: July 31, 1969; revised: September 1, 1969 [Z 81 IE]
German version: Angew. Chem. *81*, 896 (1969)

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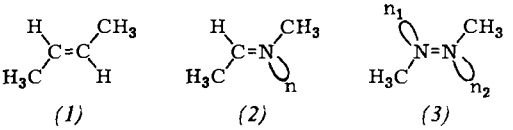
The Interaction between the Lone Pairs in Azomethane[1]

By *E. Haselbach, J. A. Hashmall, E. Heilbronner*, and *V. Hornung* [*]

The extent of the interaction between the lone pairs n_1 and n_2 of the *trans* azo group in aromatic and aliphatic azo compounds has long been a subject of debate. On the basis of electronic spectra and theoretical studies, values between 0 and 7 eV have been derived [2] for the splitting of the levels of the two linear combinations

$$n_+ = \frac{1}{\sqrt{2}}(n_1 + n_2),\ (A_g);\quad n_- = \frac{1}{\sqrt{2}}(n_1 - n_2),\ (B_u)$$

We now wish to report on the result obtained by photoelectron spectroscopy [3] on *trans*-azomethane *(3)* [4]. The photoelectron spectra of *trans*-2-butene *(1)* and of *trans-N*-ethylidenemethylamine *(2)* were taken as a basis for comparison.



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

The π-ionization potential, π-IP, (all values refer to the relevant band maxima; vertical ionization) is shifted toward higher values on successive replacement of C atoms by N atoms: π-IP *(1)* = 9.11 eV; π-IP *(2)* = 10.66 eV; π-IP *(3)* = 11.84 eV. In the case of *(1)* and *(3)*, the corresponding band shows a marked vibrational fine structure with a splitting of 0.17 and 0.15 eV, respectively. (Characteristic stretching frequencies of the un-ionized double bonds in the ground state: *(1)* C=C : 0.21 eV [5]; *(3)* N=N : 0.17 eV [6].) The σ-ionization potentials also shift toward higher values along the series *(1)*, *(2)*, *(3)*, the envelope of the σ bands essentially retaining its form.

The band occurring at 9.49 eV in the spectrum of *(2)* therefore has to be assigned to the ionization of one of the lone pair electrons in the orbital n.

In the spectrum of *(3)*, the first band lies at 8.98 eV, *i.e.* at a lower value than in the spectrum of *(2)*. This is indicative of a strong splitting of the orbitals n_+ and n_-, the relevant band being assigned — on the basis of theoretical calculations — to ionization from n_+ : n_+-IP = 8.98 eV. The band corresponding to ionization from the energetically lower orbital n_- is found at 12.3 eV. It partly overlaps with the π-band at 11.84 eV; the potential for the n_- ionization can therefore only be given to within 0.2 eV: n_--IP = 12.3 ± 0.2 eV. These values give

$$\Delta = n_-\text{-IP} - n_+\text{-IP} = 3.3 \pm 0.2\ \text{eV}$$

for the desired splitting.

Semi-empirical SCF—MO calculations by the MINDO/1 technique [7] show qualitative agreement with the experimental results, as regards both the assignment of the bands and the magnitude of the observed shifts and splittings. In particular, a splitting of Δ (calculated) = 2.2 eV is predicted for *(3)*; it is relatively insensitive to changes of the angle C—N=N in the range 110 to 130 °.

Received: August 25, 1969 [Z 83 IE]
German version: Angew. Chem. *81*, 897 (1969)

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Formation of a Silylene Complex by Base-Catalyzed Decomposition of Hexachlorodisilane

By *D. Kummer* and *H. Köster* [*]

A yellowish white stable 1 : 1 adduct [1,2] is formed on reacting hexachlorodisilane with 2,2′-bipyridine (bipy) in pentane, whereas in tetrahydrofuran (THF) the reaction mixture rapidly turns green, even at 25 °C. On investigating this reaction (with Si_2Cl_6 and bipy in a molar ratio of 1 : 3) we have now been able to isolate $SiCl_2 \cdot 2$ bipy *(1)* and thus gain the first direct proof of a base-catalyzed disproportionation of Si_2Cl_6 proceeding *via* an $SiCl_2$ intermediate (cf. [3]).

$$Si_2Cl_6 + 3\ \text{bipy} \xrightarrow[25\,^\circ C]{\text{THF}} \underset{(1)}{SiCl_2 \cdot 2\ \text{bipy}} + \underset{(2)}{SiCl_4 \cdot \text{bipy}}$$

Both reaction products are formed quantitatively and separate out as a green precipitate. At other molar ratios of Si_2Cl_6 and bipy (1 : 1 to 1 : 3), 1 mole of *(2)* is always formed per mole of Si_2Cl_6 since *(2)* is much less soluble than *(1)*, *e.g.*:

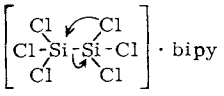
$$Si_2Cl_6 + 2\ \text{bipy} \rightarrow SiCl_4 \cdot \text{bipy} + \frac{1}{2}\ SiCl_2 \cdot 2\,\text{bipy} + \frac{1}{2n}(SiCl_2)_n$$

$$Si_2Cl_6 + \text{bipy} \rightarrow SiCl_4 \cdot \text{bipy} + \frac{1}{n}(SiCl_2)_n$$

In the latter case the precipitate is almost colorless. The compound formally represented as $(SiCl_2)_n$ has not been investigated. Compound *(1)* is slightly soluble in benzene [4] and can be separated from the practically insoluble *(2)* by extrac-

tion. The composition of both substances has been confirmed by analysis and by X-ray powder diagrams. The debyeogram of *(1)* is identical with that of the $SiCl_2 \cdot 2$ bipy prepared according to *Herzog*[4] from $SiCl_4 \cdot$ bipy and $Li_2 \cdot$ bipy.

According to our investigations, compound *(1)* is formed by way of an α-elimination.



During the rearrangement an intermediate can be detected which, according to ^1H–NMR spectra, corresponds to the product of slow decomposition of $(Cl_2CH_3Si)_2 \cdot$ bipy in its structural features[1]; the disproportionation reactions of Si_2Cl_6 and of $(Cl_2CH_3Si)_2$ are, therefore, of the same type. Since previously reported results on the disproportionation of $[CH_3O(CH_3)_2Si]_2$[3] indicated a different reaction route, further investigations will have to be carried out in order to ascertain to what extent the reaction path found by us is valid in other base-catalyzed disproportionations of disilane.

Dichlorosilylene-bis(2,2′-bipyridine) (1)

Si_2Cl_6 (3.60 g, 13.4 mmoles) is condensed under reduced pressure into a solution of bipy (6.26 g, 40.2 mmoles) in THF (100 ml). After warming to 25 °C, the almost colorless reaction mixture (solution and white precipitate) turns dark green within a few minutes. After 6 hours' standing the solution is filtered by suction and the dark green residue is extracted with benzene (100 ml) at 30 °C until the extraction liquid is colorless (in this case 25 days). The extraction is accelerated if carried out at 40—50 °C. 4.2 g of *(1)* was isolated from the concentrated extract and a further 0.8 g from the original reaction solution; thus a total yield of 5.0 g (90%) of *(1)* was obtained. 4.7 g of a pale green colored extraction residue remained (calc. for *(2)* 4.37 g). Since the products are extremely sensitive to moisture and oxygen all operations were carried out in an all-glass apparatus fitted with break-seals.

Debyeogram ($Cu_{K\alpha}$): 6.00 vs, 7.25 m, 7.80 s, 860 w, 9.05 m, 9.70 m, 11.20 s, 11.60 m, 12.30 s, 12.85 w, 13.75 s, 14.40 vw, 15.00 s, 16.00 s, 17.30 vw, 18.10 w, 18.20 w, 19.00 vw, 19.70 m, 20.60 vw, 21.10 w, 22.30 m, 22.80 m, 23.30 w, 25.20 w, 26.00 vw, 28.10 vw, 28.80 w, 29.5 vw, 30.5 vw, 33.4 w.

Received: August 28, 1969 [Z 84 IE]
German version: Angew. Chem. *81*, 897 (1969)

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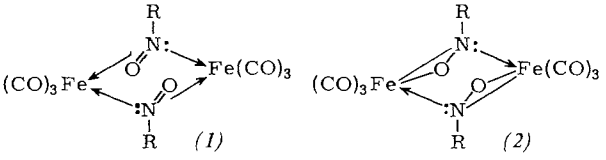
The Crystal Structure of Bis(tricarbonyl-2-methyl-3-chloronitrosobenzeneiron)

By *M. J. Barrow* and *O. S. Mills*[*]

A series of tricarbonylnitrosobenzeneiron complexes[1] results from the γ or UV irradiation of nitrobenzenes in the presence of pentacarbonyliron. Colligative properties suggested that both monomeric and dimeric forms exist dependent on the particular nitrobenzene precursor. The authors were unable, on the basis of the IR and UV spectroscopic data, to establish unequivocally the molecular structure and later Mössbauer studies[2] have shown that if the complexes are dimeric, then both iron atoms must have identical environments. Most of the complexes precipitate as fine powders from which it is difficult or impossible to obtain crystals large enough for single-crystal X-ray analysis and we have examined the only compound which, as far as we know[3], has yielded suitable crystals, *i.e.* that formed from 2-methyl-3-chloronitrobenzene.

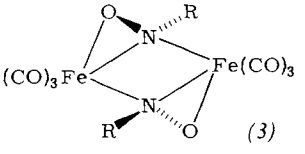
This complex $(C_{10}H_6ClFeNO_4)_n$, mol. wt. = $n \times 295.5$, crystallizes in the monoclinic space group $P2_1/c$ (No. 14, C_{2h}^5) with $a = 18.26$, $b = 7.25$, $c = 8.71$ Å, $\beta = 90.85°$, $V = 1151$ Å^3, $d_{calc} = 1.71$ gcm^{-3} ($Z = 4$ or 2 for $n = 1,2$ respectively). The structure, solved by conventional Fourier methods (1008 reflections, present $R = 0.11$), establishes that this complex is a dimer. The space group requires that the dimer be centrosymmetric, in accord with the Mössbauer observations. The mass spectrum, taken at 70 eV, showed a peak at the *m/e* for the parent monomeric ion with low intensity peaks at values up to 50% greater and suggests that the dimeric molecules are probably easily dissociated.

The structure (cf. formula *(3)*) contains two novel features. The tricarbonyliron units are bridged by the two nitrosobenzene groups but only the nitrogen atoms are bonded to



(1) *(2)*

R = 2-CH_3-3-Cl-C_6H_3



(3)

both iron atoms. The central Fe—N—Fe—N ring is hence strictly planar and has edges of length 2.00 (3) Å, a value close to those found in other nitrogen-bridged bis(tricarbonyliron) complexes, 1.96—2.02 Å[4–8]. The NO group is placed unsymmetrically between the iron atoms. The oxygen atom is 1.91 Å from one iron yet is more than 2.7 Å away from the second iron. The former distance is less than that found in bis(μ-phenyloxycarbenetricarbonyliron)[9] 1.97, triacetylacetonatoiron[10] 1.99, and tris(*N*-nitrosophenylhydroxylamine)iron[11] 2.00 Å in which the bonds have some covalent character. The Fe—O and Fe—N distances can be discussed in terms of structures *(1)* and *(2)* written with either two sigma bonds or with interaction through the π-electrons of the NO group to the metal. The N—O distance, at present 1.39 Å, is one of the largest values yet recorded and favors representation *(2)*.

Hitherto, all carbon- or nitrogen-bridged iron complexes have shown metal-metal distances which can be interpreted in terms of Fe—Fe bonds and the question has been raised as to whether or not these Fe—Fe bonding distances are inevitable consequences of the presence of the bridging atoms, *i.e.* is the Fe—Fe distance determined by the requirement of the angle subtended at the bridge atom *or* is it the involvement of a metal-metal bond, with some optimum separation, which determines the angle subtended? Nitrogen-bridged compounds have been associated with the shortest distances reported between zerovalent iron atoms, 2.37—2.43 Å[4–8]. The present value, 3.13 Å, proves conclusively that these shorter separations cannot exclusively be due to the presence

of the bridge nitrogen atoms. We interpret the distance in this example as involving a null bond and indeed no bond need be invoked to account for the diamagnetism. The situation can be compared to that in bis(diaryldiazomethane)tris-(tricarbonyliron) in which a non-bonded separation of 3.06 Å is reported [12]. The angle subtended at the nitrogen atom by the iron atoms is 100°, some 25—30° larger than those found in complexes which involve metal-metal bonds.

Received: August 19, 1969 [Z 87 IE]
German version: Angew. Chem. *81*, 898 (1969)

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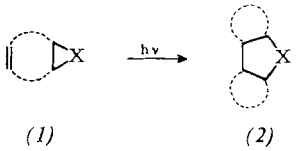
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5-Acetyl-1,2,3,4,5-pentamethylbicyclo[2.1.0]-pentene

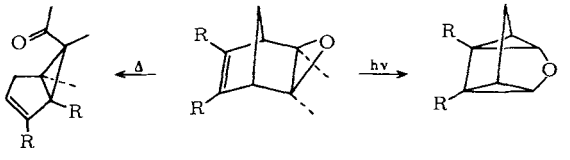
By *M. Klaus, H. Prinzbach,* and *H. Achenbach* [*]

We have attempted to imitate the ethylene/cyclopropane → cyclopentane photoisomerization, realized several times for *(1)* → *(2)* when X = CR_2 [1], with the analogous ethylene/oxirane substrates, *i.e. (1)* → *(2)* where X = O.



(1) *(2)*

As a first example we recently described the conversion *(4)* → *(5)* [2].

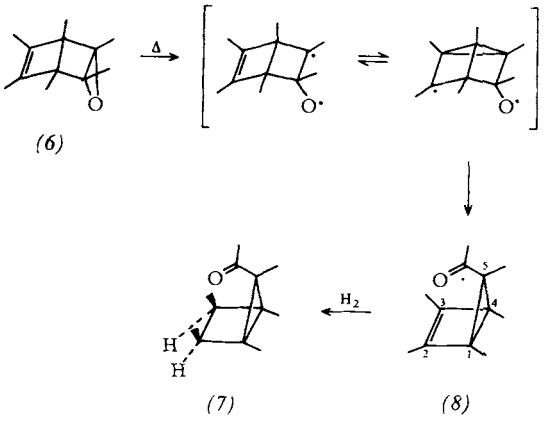


(3) *(4)* *(5)*

Attempts to convert the epoxide *(6)* [4] of hexamethyl(Dewar benzene) [5] — which probably exists in the *endo*-form [3] — into hexamethyloxaquadricyclane [6] have so far been without success [7]; however, we found that pyrolysis of *(6)* led to the very stable bicyclo[2.1.0]pentene derivative *(8)*, as expected in view of the conversion of *(4)* into *(3)* [8].

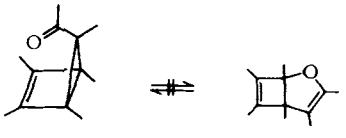
When *(6)* was heated (190 °C, 9 h) in a well-cleaned Teflon vessel, a mixture of products (*ca.* 90%) was isolated by distillation and this could be separated by fractional distillation followed by column chromatography (silica gel, cyclohexane/ethyl acetate 8 : 2) into hexamethylbenzene (5%), 5-acetylpentamethylcyclopentadiene (the product of acid-catalyzed isomerization [3,4]) (3—7%), 2,3,4,5,6,6-hexamethyl-2,4-cyclohexadienone (69%) [9], and *(8)* (16%).

The bicyclic product *(8)* is stable up to at least 210 °C [10]. In the presence of Pd/C it absorbs 1 mole of hydrogen selectively, to give *(7)*. Isomerization to 5-acetylpentamethylcyclopentadiene [4] is not effected by passing HCl into a CCl_4 solution of *(8)* or by addition of acetic or sulfuric acid.



(6) *(7)* *(8)*

The structures of *(7)* and *(8)* were confirmed in particular by the spectroscopic data. Molecular ions that appeared with medium intensity in the mass spectrum of *(8)* occurred only very weakly in that of *(7)*; with both compounds elimination of C-2 and C-3 led to a very intense peak at *m/e* = 124 (weak metastable peaks at *m/e* = 85 and 85.5, respectively); the species corresponding to this peak can pass by loss of a methyl



(8) *(9)*

	^{1}H-NMR in C_6D_6 [a]	UV in C_2H_5OH	IR [d] (cm^{-1})	*m/e* (I_{rel})
(7)	7.84	$\varepsilon_{220} \approx 5500$	2960	180 (2)
b.p. 68—70	(2H, br. m)		2920	
°C/11 torr	8.31		2870	151 (6)
	(3H, q) [b]		1696	
	8.54		1459	137 (6)
	(3H, q) [b]		1448	
	8.70		1374	124 (100)
	(3H, s)		1230	
	8.94		920	109 (29)
	(3H, d) [c]			
	9.02			43 (90)
	(3H, s)			
	9.10			
	(3H, d) [c]			
(8)	8.32	$\varepsilon_{220} \approx 2400$	2958	178 (58)
b.p. 68—71	(3H, q) [b]	227 (1800, sh)	2920	136 (67)
°C/11 torr	8.45		2860	135 (65)
m.p. 13 °C	(3H, q) [b]	$\varepsilon_{290} \approx 26$	1686	124 (92)
	8.50 (6H, s)		1435	109 (63)
	8.68 (3H, s)		1370	43 (100)
	9.02 (3H, s)		1075	
			978	
			880	

[a] τ values, TMS as internal standard. [b] Coupling constants *ca.* 1 Hz. [c] Coupling constants 6.8 Hz. [d] Pure, liquid.

radical into the fragment ion m/e = 109 (acetyldimethylcyclopropenyl cation) (metastable signal at m/e = 96).

The C=O stretching bands at 1686 and 1696 for *(8)* and *(7)*, respectively, are typical of cyclopropyl ketones [11]. The NMR spectrum of *(7)* suggests that the two quartets observed for *(8)* are to be assigned to the methyl groups on C-1 and C-4. The asymmetry due to hindered rotation around C-5/C=O is no longer effective for the methyl protons on C-2 and C-3 [12]. There is no indication of an equilibrium *(8)* $\rightleftarrows$ *(9)* between 30 and 120 °C [13].

The *endo*-orientation is assigned to the acetyl group only for mechanistic reasons, but the *exo*-hydrogenation of *(8)* to give *(7)* is made probable by an earlier example [14].

Received: July 14, 1969 [Z 66 IE]
German version: Angew. Chem. *81*, 899 (1969)

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7,9-Di-*tert*-butylsesquifulvalene: Its Synthesis and Cycloadditions [**] [1]

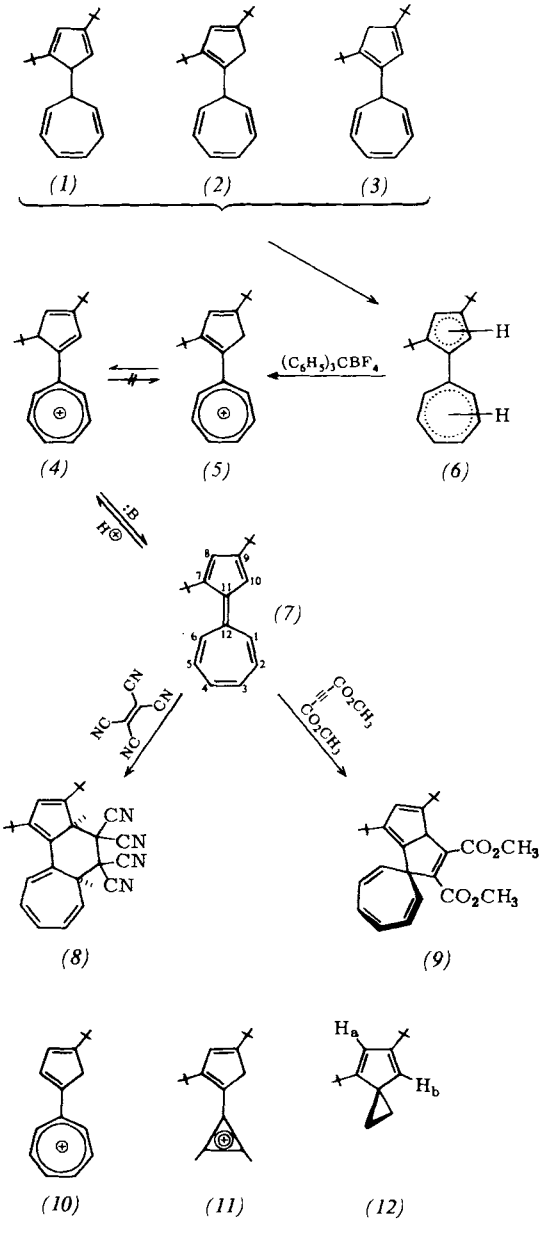
By *H. Prinzbach* and *H. Knöfel* [*]

We have prepared 7,9-di-*tert*-butylsesquifulvalene *(7)*, which, unlike other sesquifulvalene derivatives [2], undergoes [12 + 2] cycloaddition.

Treatment of lithium 1,3-di-*tert*-butylcyclopentadienide [3] (0.1 mole in 200 ml of anhydrous ether at −50 °C) with tropylium bromide (0.1 mole) precipitates a mixture of the dihydrosesquifulvalenes *(1)*, *(2)*, and *(3)* (b.p. 104–109 °C/10^{-3} torr; 70–75%) [4]. When heated at 165 °C for 30 min *(1)*–*(3)* isomerize to the complex mixture *(6)* which is formed by several sigmatropic H shifts in the five- [5] and the six-membered ring [6]. As expected, hydride elimination from *(6)* by trityl tetrafluoroborate [7] (0.8 equivalent of trityl salt in CH_2Cl_2 at 0–5 °C) to give the cyclopentadienyltropylium salts *(4)* and *(5)* is very rapid; the non-planar π-system *(5)* rearranges slowly to *(4)*. This compound *(4)* can be isolated as red needles, m.p. 165 °C, by precipitation from ether and can be purified by prolonged extraction with ether. We have been able to prepare the conjugate acids *(10)* and *(11)* analogously [8].

Adding a CH_2Cl_2 solution of *(4)* to a vigorously stirred mixture of trimethylamine with benzene or with CCl_4 at 0–5 °C liberates the base *(7)*; repeated concentration to at most a 10^{-3} M solution and renewed addition of benzene or CCl_4, followed by filtration through an Al_2O_3 column (basic, IV) leads to solutions of pure *(7)* in these solvents. If light and air are excluded, *(7)* is stable in *ca.* 10^{-2} M solution at 0 °C for several days, and also for a short time (NMR) in 10^{-1} M solution. As expected [2], protonation gives *(4)* preferentially.

When benzene solutions of *(7)* and tetracyanoethylene are mixed, the deep red solution at once fades to yellow. The 1 : 1 adduct *(8)* is precipitated from benzene/CCl_4 as pale yellow needles, m.p. 104–106 °C. However, *(7)* and dimethyl acetylenedicarboxylate in boiling benzene (4 h) give a yellow 1 : 1 adduct *(9)*.



Compound	UV λ_{max} (nm, ε)	NMR (τ) [a]
(4)	[b] 497 (22000) 308 (2400) 284 (6600) 234 (21350)	[d] 0.7–1.5 (H^1–H^6, M); 2.20 (H^{10}, dD); 3.03 (H^8, dD); 6.00 (H^7, dD); 8.70 (9 BuH, S) [e]; 8.95 (9 BuH, S)
(5)		[d] 0.7–1.5 (H^1–H^6, M); 3.20 (H^8, S); 6.20 (2 H^{10}, S); 8.62 (9 BuH, S); 8.70 (9 BuH, S)
(7)	[b] 376 (10500 ± 1000)	[f] 2.9–3.4 (H^1, H^6, M); 3.7–4.15 (H^2–H^5, M); 3.85 (H^8 D, J = 2.3); 4.11 (H^{10}, D, J = 2.3); 8.68 (9 BuH, S); 8.87 (9 BuH, S)
(8)	[b] 330	[g] 2.99–3.16 (H^4, H^5, M); 3.25 (H^8, D, J = 1.0); 3.31–3.69 (H^3, H^6, M); 4.32 (H^2, dD. J = 9.0 and 7.0); 6.14 (H^{10}, D, J = 1.0); 7.74, (H^1, dD, J = 7.0 and approx. 1); 8.56 (9 BuH, broad S); 9.01 (9 BuH, S)
(9)	[c] 334 (S, 1300) 280 (7900) 232 (21950)	[f] 3.70–4.25 (H^1–H^6, M); 3.77 (H^8, D, J = 1.6); 5.52 (H^{10}, D, J = 1.6); 6.28 (6 Ester- H, S); 8.77 (9 BuH, broad S); 8.95 (9 BuH, S)
(10)	[b] 500 283, 230	
(11)		[d] 3.00 (1 H, S); 6.14, (2 H, S); 7.13 (6 H, S); 8.48 (9 H, S); 8.65 (9 H, S)

[a] TMS as internal standard, coupling constants in Hz. To aid comparisons, the numbering of *(7)* is retained for all the compounds.
[b] In CH_2Cl_2. [c] In ethanol. [d] In CF_3COOH.
[e] BuH = *tert*-Butyl-H. [f] In CCl_4. [g] In $CDCl_3$.

The new compounds (Table) have been characterized by elemental analysis, spectroscopic data, and differing reactions.

Useful comparative data for the UV and NMR results for the sesquifulvalene *(7)* and the conjugate acid *(4)* were available from previous experiments[2,9]. The hypsochromic shift of the longest-wavelength maximum of *(7)* relative to that in unsubstituted sesquifulvalene (λ_{max} = 391 nm in isooctane) is preliminarily interpreted as due to the increased departure from planarity. Very considerable localization of the double bonds in *(7)* is indicated, by, *inter alia*, the size of the coupling constants $J^{8,10}$ (2.3 Hz) [cf. *(12)* τ = 3.80 (H^a, D); 4.81 (H^b, D); J^{ab} = 2.2 Hz (in CCl_4)][8].

The apparently very long wavelength of the first UV maximum of *(4)* is also well fortified by analogies [cf. *(10)*][8,10]. The *cis*-configuration in the [12 + 2] adduct *(8)* is postulated on the basis of the Woodward-Hoffmann rules. There are also several analogies for the quite different direction of addition of dimethyl acetylenedicarboxylate that gives *(9)*[11]. We are testing on 8-*tert*-butylsesquifulvalene the hypothesis that the ester, like tetracyanoethylene, first attacks as an electrophile at C-10 and then closes the ring with C-12, and not with C-1, so as to avoid steric compression between H-6 and the neighboring *tert*-butyl group.

Received: August 11, 1969 [Z 88a IE]
German version: Angew. Chem. *81*, 900 (1969)

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

[1] Cyclic Cross-conjugated π-Systems, Part 19. – Part 18: *H. Prinzbach* and *E. Woischnik*, Helv. chim. Acta, in press.

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10,11-Dicyanopentaphenafulvalene[**][1]

By *H. Prinzbach* and *E. Woischnik*[*]

Attempts to extend the series of "mixed" fulvalenes (calicene, sesquifulvalene, fidecence[2]) to combinations containing the phenalene cation or anion have long remained without success[3]. Only a few "phenafulvalenes" stabilized by powerful acceptor groups[4] or dimethylamino-substituted vinylogs[5] have been obtained pure and characterized.

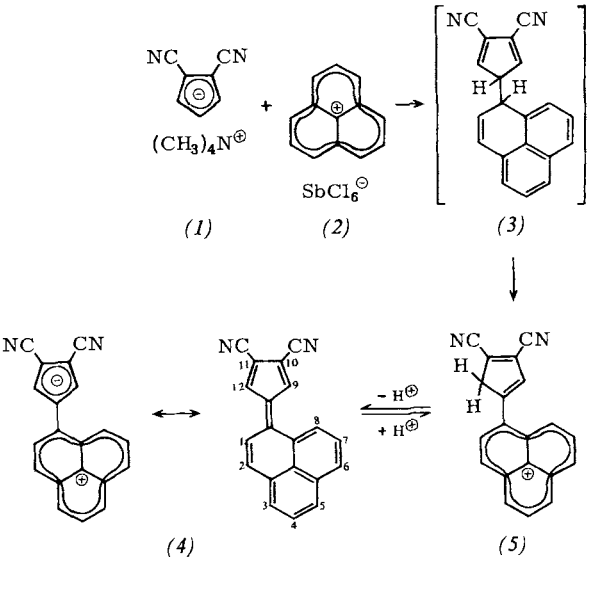
In the dicyano compound *(4)* we have prepared a stable, comparatively simple derivative with the $6\pi + 12\pi$ system[6].

Treatment of the dicyanocyclopentadienyl salt *(1)*[7] with the phenalenium salt *(2)*[8] yields the dihydro product *(3)*, but this reacts so rapidly with *(2)* to give *(5)* or with loss of $HSbCl_6$ to give *(4)* that no attempt was made to isolate the intermediate stages *(3)* and *(5)*. Because *(4)* is so reactive and especially because it decomposes readily in contact with various chromatographic carrier materials, reaction conditions were chosen which made it unnecessary to separate or purify the product because it could be separated directly from the reaction medium in a pure state. In the absence of air, pure crystalline *(4)* can be kept for some days without decomposition.

In agreement with the low basicity of 14,14-dicyanophenafulvene[4] the equilibrium *(4)*⇄*(5)* in CF_3COOH (*ca.* 5% solution) lies largely towards *(4)* (H/D exchange in CF_3COOD at positions 9 and 12 requires several days); however, *(4)* is protonated in 80% sulfuric acid almost wholly to the orange conjugate acid *(5)* which, nevertheless, is not very stable in this medium; *(4)* is largely regenerated by adding water rapidly[9].

The structures *(4)* and *(5)* are proved by the results of elemental analysis and the spectroscopic data[10].

(4), *m/e* = 278 (M^+). IR (KBr), ν = 2205, 1609, 1558, 1508, 1489, 1474, 1312, 1205, 928, 767 cm^{-1}. UV, λ_{max} (CH_3CN) =



587 nm (ε = 23400), 394 (sh, 4500), 368 (5100), 348 (sh, 4700), 300 (sh, 12600), 287 (13800), 270 (12000).

The first band displays strong positive solvatochromism: 555 nm (C_6H_{12}), 560 (CCl_4), 569 (C_6H_6), 579 ($CHCl_3$), 585 (CH_2Cl_2), 585 (C_2H_5OH), 587 (CH_3CN), 596 (CF_3COOH).

NMR (220 MHz, CF_3COOH), τ = 1.67 (1, D, J = 8.1 Hz; H^8), 1.78 (1, D, $J \approx$ 8 Hz; H^6), 1.82 (1, D, $J \approx$ 7 Hz, H^5), 2.01 (1, D, J = 7.2 Hz; H^3), 2.10–2.35 (2, M; H^7, H^4), 2.22 (1, D, J = 9.5 Hz; H^2), 2.41 (1, D, J = 9.5 Hz; H^1), 2.94 (2, S; H^9, H^{12}).

(5), UV, λ_{max} (80% H_2SO_4) = 528 nm (sh, ε = 7900), 458 (16100), 401 (16300), 327 (8300), 314 (8100), 226 (27200).

NMR (60 MHz, 80% H_2SO_4), τ = 0.95–1.35 (5, D + T), 1.80–2.20 (3, D + T), 3.15 (1, S), 5.85 (2, br. S).

The signals at τ = 3.15 and 5.85 disappear in 80% D_2SO_4/D_2O; presumably the proton adds at both positions H-9 and H-12 of *(4)*.

Insufficient solubility prevented exact determination of the dipole moment of *(4)*. As judged from the chemical shifts of the protons that are not influenced by anisotropic effects, the electron density at the carrier carbon atoms of the phenalene skeleton is always less than in phenalenone and comparable with conditions in 14,14-dicyanophenafulvene.

10,11-Dicyanopentaphenafulvalene (4):

A CH_2Cl_2 solution of *(1)* (760 mg, 4 mmoles; in 100 ml) is added dropwise to a slurry of finely powdered *(2)* (4.0 g, 8 mmoles) in CH_2Cl_2 (80 ml) at 0 °C during *ca.* 30 min with stringent exclusion of oxygen and moisture. The solution changes rapidly from red to deep violet; it is stirred for 4 h at 30 °C, then the $(CH_3)_4NSbCl_6$ is filtered off under N_2, and the filtrate is concentrated to a quarter of its volume. On storage, 10,11-dicyanopentaphenafulvalene *(4)* separates as bluish-black crystals with a reddish surface sheen; they are almost pure and melt at 255–258 °C (yield 380–400 mg, 34–36%).

Received: August 11, 1969 [Z 88b IE]
German version: Angew. Chem. *81*, 901 (1969)

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[1] Cyclic Cross-conjugated π-Systems, Part 20. – Part 19: *H. Prinzbach* and *H. Knöfel*, Angew. Chem. *81*, 900 (1969); Angew. Chem. internat. Edit. *8*, 881 (1969).

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[8] *H. Prinzbach*, *V. Freudenberger*, and *U. Scheidegger*, Helv. Chim. Acta *50*, 1087 (1967).

[9] The same behavior has been observed with dicyanodiphenylcalicenes by *H. Prinzbach* and *E. Woischnik*, Helv. chim. Acta, in press.

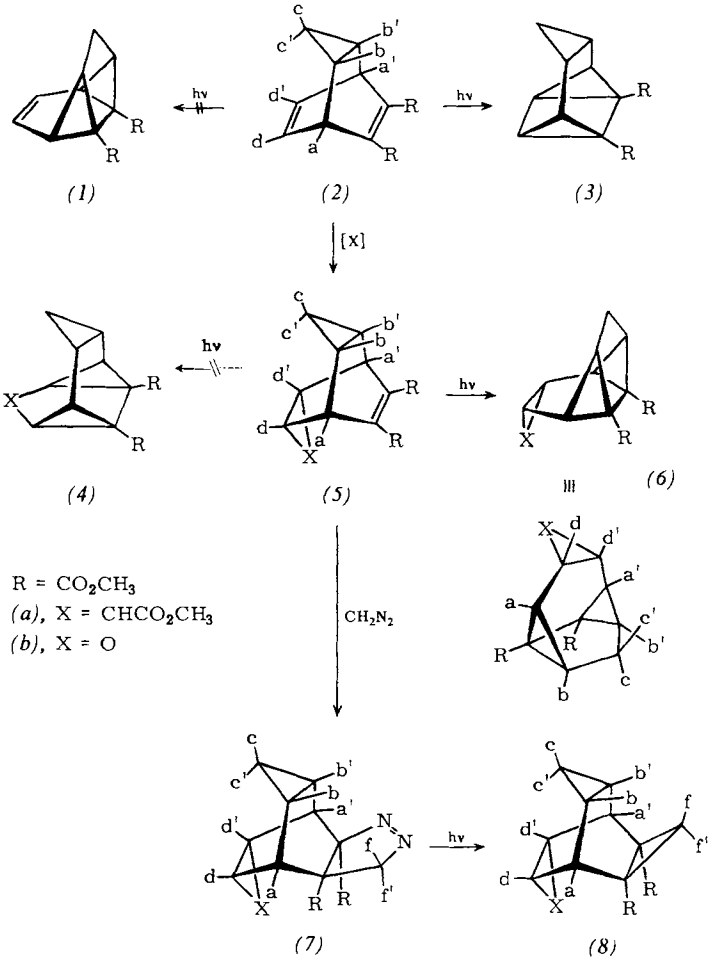
[10] Additional information is provided by the ESR spectrum of the anion radical obtained from *(4)* by potassium in 1,2-dimethoxyethane (*H. Prinzbach*, *E. Woischnik*, and *K. Volkamer*, unpublished work).

Photochemical [2π + 2σ] Cycloadditions in Tetracyclo[3.3.2.0^{2,4}.0^{6,8}]decene Systems[**][1]

By *H. Prinzbach*, *M. Klaus*, and *W. Mayer*[*]

We recently showed that photochemical [2π + 2π] cycloaddition can occur also in the bicyclo[2.2.2]octadiene skeleton and that in monohomobarrelene *(2)* this [2π + 2π] addition *(2)*→*(3)* leaves no opportunity for the [2π + 2σ] addition *(2)*→*(1)* to occur[2].

We have now realized such [2π + 2σ] additions in the two tetracyclenes *(5a)* and *(5b)* obtained[3] from *(2)*. On direct irradiation, *(5a)* and *(5b)* isomerize to the "trishomobenzene" derivatives *(6a)* and *(6b)*, respectively, the reaction being very smooth (86–96% yield) and probably occurring through the excited singlet state[4]. There was no convincing evidence of competitive formation of *(4a)* or *(4b)*[5]. This selective cycloaddition between the excited maleic chromophore and the *exo*-three-membered ring[6] underlines the importance, noted earlier, of stereoelectronic factors in such [2π + 2σ] additions.



The structures were proved by elemental analyses and spectral data (Table). For comparison we synthesized the 1-pyrazolines *(7a)*, m.p. 183.5–184.5 °C, and *(7b)*, m.p. 177 to 178 °C, and also the novel "trishomobarrelenes" *(8a)*, m.p. 93–94.5 °C, and *(8b)*, m.p. 173.5–174.5 °C[7].

The *endo*-position[8] of X in *(5)* is expected because of the directing influence of the cyclopropane ring in *(2)*, but it could not be proved by $J^{a,d}$ because of the approximately equal interplanar angles a–C–C–d^{exo} and a–C–C–d^{endo}; however, the considerable paramagnetic shift of δH^e on transition from *(5a)* to *(7a)* or *(8a)* (τ = 9.06, 7.98, and 8.15, respectively) is in favor of placing H^e[9] above the C=C plane in *(5a)*.

Compound M.p. (°C)	UV [a] (nm; ε)	NMR (τ); J (Hz) [b]								CO_2CH_3	Molecular ion at m/e[c]
		H^a	$H^{a'}$	H^b	$H^{b'}$	H^c	$H^{c'}$	H^d	$H^{d'}$	H^e	
(5a) 89–89.5	sh 239 (3100)	6.59 (M) [d] $\Sigma J_{a,b} + J_{a,b'} = 3.5$ $\Sigma J_{a,d} + J_{a,d'} = 4.0$		8.78 (bM) $J_{b,c} = 7.3$ $J_{b,c'} = 3.5$		9.22 (bM) $J_{c,c'} = 6.1$ $J_{c,b} = 7.3$	8.21 (M) $J_{c',c} = 6.1$ $J_{c',b} = 3.5$	8.58 (M) $J_{d,e} = 2.9$		9.06 (T) $J_{e,d} = 2.9$	6.29 (S, 6) 6.46 (S, 3)	
(6a) 117–117.5	$\varepsilon_{220} = 550$	8.08 [e] $J_{a,b} = 8.5$		7.60 (M) $J_{b,a} = 8.5$ $J_{b,c} \approx 7$		7.71 (M) $J_{c,c'} = 13.5$ $J_{c,b} \approx 7$	8.27 (D) $J_{c,c'} = 13.5$	8.17 (M) $J_{d,e} = 3.7$ $J_{d,a} \approx 1.3$		8.42 (T) $J_{e,d} = 3.7$	6.27 (S, 3) 6.30 (S, 6)	306
(5b) 87–88	sh 233 (3600)	6.50 (M) [d]		8.74 (M) $J_{b,c} = 7.5$ $J_{b,c'} = 3.5$		9.33 (M) $J_{c,b} = 7.5$ $J_{c,c'} = 6$	8.43 (M) $J_{c',c} = 6$ $J_{c',b} = 3.5$	7.02 (M)			6.30 (S)	
(6b) 103–104	$\varepsilon_{220} = 410$	7.96 [e] $J_{a,b} = 8.5$		7.50 (M) $J_{b,a} = 8.5$ $J_{b,c} \approx 7$		7.62 (M) $J_{c,c'} = 14.5$ $J_{b,c} \approx 7$	8.23 (D) $J_{c',c} = 14.5$	6.59 (M)			6.31 (S)	250

[a] In C_2H_5OH. [b] Measured at 100 MHz [*(5)*] and 220 MHz [*(6)*]. We thank Drs. *W. Brügel* and *H. Friebolin* for the 220 MHz spectra. [c] We thank Dr. *H. Moll* for the mass spectra. [d] In CCl_4. [e] In $CDCl_3$.

The *endo*-position of the epoxide ring in *(5b)* is rendered probable by absence of long-distance coupling $J^{b,d}$ (the H^d signal becomes a sharp singlet on decoupling of $H^{a,a'}$; the $H^{d,d'}$ multiplet suffers no change at all on irradiation of $H^{b,b'}$).

The direction of cycloaddition of *(5)* to give *(6)* follows from, *inter alia*, the changes of $J^{c,c'}$ and $J^{d,e}$; the $J^{c,c'}$ value [6.1 Hz in *(5a)*, 6.0 Hz in *(5b)*], which is typical for geminal cyclopropane coupling, increases to the values 13.5 Hz in *(6a)* and 14.5 Hz in *(6b)* [10] which are reasonable for geminal cyclopentane protons, whilst $J^{d,e}$ retains the values normal for *trans*-vicinal cyclopropane protons [2.9 Hz in *(5a)*, 3.7 Hz in *(6a)*].

$J^{a,b}$ $J^{b,c}$, and $J^{c,c'}$ for the photoproducts *(6)* agree well with the coupling constants evaluated for the related tetracyclo[3.3.0.$0^{2,4}$.$0^{6,8}$]octane skeleton [11].

The attachment of the pyrazoline ring shown in *(7)* and consequently the similar orientation of all the three-membered rings in *(8)* are based on the criteria that were determinative for addition of X to *(2)*.

Received: August 11, 1969 [Z 88c IE]
German version: Angew. Chem. *81*, 902 (1969)

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

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[3] Cu-catalyzed reaction of methyl diazoacetate with *(2)* (ratio *ca.* 1 : 2) at 125 °C, followed by distillation and recrystallization, gives *(5a)* in non-optimal yield of *ca.* 50%. With a nine-fold excess of 40% peracetic acid in CH_2Cl_2 at 40 °C for 11 h, *(2)* gives *ca.* 80% of *(5b)*.

[4] Varying the oxygen content of the solution does not affect the rate or product of the reaction; preliminary findings indicate that sensitization by acetone or benzophenone does not lead to *(6)*.

[5] Total reaction is achieved in 4–5 hours' irradiation of a solution of *(5a)* (1 g) or *(5b)* (1.2 g) in CH_3CN (280 ml) at –30 °C with Vycor-filtered light from a Hanau-Q 81 mercury high-pressure lamp. In the case of *(5a)*, 1% of a second component *(24)* could be detected by gas chromatography alongside 99% of *(6a)*.

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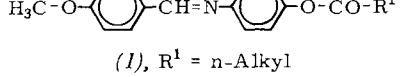
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A Liquid-crystalline (Nematic) Phase with a Particularly Low Solidification Point

By *H. Kelker* and *B. Scheurle* [*]

We have prepared a chemically homogeneous, stable, nematogenic substance that is still liquid at room temperature: *N*-(*p*-methoxybenzylidene)-*p*-*n*-butylaniline *(2k)*. This melts at 20 °C to a mobile, turbid, pale yellowish liquid with all the properties of a nematic phase; its clarification point is approximately 41 °C. Comparison with homologous and isomeric compounds [1] enables its transition temperatures and other physical properties to be discussed in relation to constitution. The optical and electrooptical properties that characterize some higher-melting liquid-crystalline substances are also observed with *(2k)*.

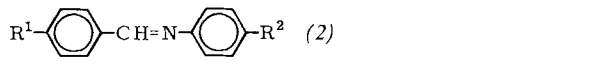
Our investigations started from the finding that in the azomethine series *(1)* there is a very obvious melting-point minimum at the butyric ester (R^1 = *n*-propyl) [2]. The melting



(1), R^1 = n-Alkyl

point of the butyrate is 50 °C and the clarification point 112 °C. According to *Weygand* alkyl chains are all to be regarded as "wing groups"; examples are *n*-alkyldiphenylpyridazines and *p*-butylbenzoic acid.

Comparison of compounds containing an azoxy, azo, or azomethine group shows that the homologous azomethines have the lowest clarification point. There are, however, no general rules for melting-point series, least of all for the initial members of homologous series. We synthesized azomethines of series *(2)* by the known method, condensation of an aromatic aldehyde with an alkylaniline. [*(2a)* [3] and *(2b)* [4] are known.] From the series of solidification and clarification points it could not be deduced with certainty that the butyl



(2)

	R^1	R^2	M.p. (°C)	Transition point (°C), behavior
(a)	CH_3O	H	60–63 [3]	isotropic
(b)	CH_3O	CH_3	92–93 [4]	38 (monotr. nemat.)
(c)	CH_3O	C_2H_5	57	28 (monotr. nemat.)
(d)	CH_3O	n-C_3H_7	42	57 (enantiotr. nemat.)
(e)	C_2H_5O	CH_3	94	80 (monotr. nemat.)
(f)	C_2H_5O	C_2H_5	67	70 (enantiotr. nemat.)
(g)	C_2H_5O	n-C_3H_7	76	97 (enantiotr. nemat.)
(h)	CH_3	CH_3	92–93	isotropic
(i)	C_2H_5	CH_3	49	isotropic
(j)	n-$C_9H_{19}O$	n-C_3H_7	51	74/84 (smectic I/II)
(k)	CH_3O	n-C_4H_9	20	41 (enantiotr. nemat.)
(l)	C_2H_5O	n-C_4H_9	36	80 (enantiotr. nemat.)
(m)	CH_3	C_4H_9O	80	71 (monotr. nemat.)

derivatives *(2k)* and *(2l)* would have the desired properties [**].

Compounds *(2k)* and *(2l)* were prepared by condensing *p*-methoxy- and *p*-ethoxy-benzaldehyde with *p*-*n*-butylaniline. After the usual working up procedure, *(2l)* was recrystallized several times from ethanol; *(2k)* was obtained in about 80% yield by distillation in a high vacuum. *Gabler* [5], who briefly mentions this type of compound, prepared only members with longer alkoxy chains R^1 (C_8 and C_9) and $R^2 < C_4H_9$, and these also showed as few peculiarities as did the Schiff base *(2m)* which is isomeric with *(2k)*.

Since *(2k)* is readily accessible, physical properties can be studied for this compound which would be hard to study without special apparatus (thermostat) for higher-melting compounds. For instance, we were able to demonstrate the "dynamic scattering" effect [6] for *(2k)*, the phenomenon that forward scattering of incident light is increased in an electric field; this effect is utilized industrially for display of numbers, *etc.* By use of *(2k)* it is also possible to demonstrate strain figures on plastics or glass at room temperature. Here we are clearly dealing with "epitaxy" effects such as have been utilized in the manufacture of polarization films [7].

(2k) can also be used as solvent for *Saupe*'s technique of NMR spectroscopy [8] (direct spin-spin coupling in the nematic phase).

Finally it was of interest to prepare cholesteric mixed phases containing *(2k)* and to study their possible use in thermotopography [9,10]. It is known that nematic phases become cholesteric on addition of optically active cholesteric substances. Use of *(2k)* had the result that the typical cholesteric reflection color appeared but that this was not shifted towards the violet on increase in temperature as is characteristic of many mixtures and for mixtures of various proportions. In mixtures of *(2k)* with cholesteryl benzoate, methyl carbonate, nonanoate, or oleate, a cholesteric phase is formed on cooling below the clarification point; this shows a reflection color which depends on the composition but which remains almost unchanged over a wide temperature range. The color shifts slightly towards the violet before it vanishes at 0 °C. These experiments were carried out on cover slips with the reverse side blackened and placed on a Kofler hot stage.

The mixtures behave like binary mixtures when $\beta > \beta_0$ [9]. [β_0 is the composition of a binary cholesteric mixture at which the relation between reflection color and temperature changes sign.] Above β_0 the wavelength of the reflected light shifts to red with increase in temperature, and to blue with decrease in temperature. Whereas the mixtures of *(2k)* and cholesteryl oleate are stable for weeks, the three other esters rapidly crystallize out.

Received: August 15, 1969; revised: October 1, 1969 [Z 91 IE]
German version: Angew. Chem. *81*, 903 (1969)

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[**] *Note added in proof*: The next higher homolog, *N*-(*p*-methoxybenzylidene)-*p*-*n*-pentylaniline, melts at 38 °C to a nematic phase whilst the clarification point is 58 °C.

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Polyethylene Glycol for Fractionation and Crystallization of L-Asparaginase

By *O. Wagner*, *K. Bauer*, *E. Irion*, *E. Rauenbusch*, *W. Kaufmann*, and *A. Arens* [*]

Clinical trials of the antilymphoma effects of L-asparaginase (EC 3.5.1.1.) of type II from *E. coli* [1] required large amounts of high-purity preparations of the enzyme. After acetone treatment of the cells the intracellular enzyme can be extracted with water and precipitated with acetone. The crude asparaginase thus obtained contains 12–18 units/mg of protein [2]. We have found that an exceptionally selective fractionation leading to highly pure preparations that crystallize spontaneously may be accomplished by use of a 50% aqueous solution of polyethylene glycol (average molecular weight 1550) [3].

Precipitation of the asparaginase from aqueous solutions at low salt concentrations with polyethylene glycol is largely independent of pH. The fractionation can be refined by addition of urea (3 moles/l) and by precipitation in the region of the isoelectric point (I.P.) at pH = 5 (see Table 1).

Table 1. Fractionation of L-asparaginase (asparaginase A) from *E. coli* ATCC 9637; 3000 l culture broth. A 10% enzyme solution was used for each of the fractionations 1–3.

	Polyethylene glycol (%)	Yield (g)	Spec. activity (units/mg protein)	Total activity (units)	Yield (%)
Crude enzyme	–	380	17	4960000	100
1. pH = 8.5 3 mole/l urea	17–33	81	63	4210000	85
2. pH = 5.1	8–12	22.8	137	2780000	56
3. pH = 5.1	3.8–7.0	6.7	248	1530000	31

Asparaginase preparations containing more than 180 units/mg can be crystallized by careful precipitation with polyethylene glycol at the I.P. Well-formed crystals (needles) can be grown particularly readily by precipitation with a mixture of polyethylene glycol (50 g) (average molecular weight 6000), water (25 ml), and methanol (25 ml). The crystalline asparaginase obtained in this manner has a specific activity of 280 units/mg of protein [4] which cannot be increased by further recrystallization.

The L-asparaginase from strain 9637 and strain 11303 differ in their migration rates on electrophoresis. Crystalline L-

asparaginase (asparaginase B) from strain ATCC 11303 is equally well obtainable by slight variations of the fractionation limits (see Table 1). The L-asparaginases obtained by this technique[5] from the crude asparaginases of the two strains of bacteria are identical with those purified by column chromatographic procedures.

Received: September 15, 1969 [Z 94 IE]
German version: Angew. Chem. 81, 904 (1969)

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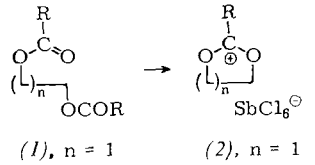
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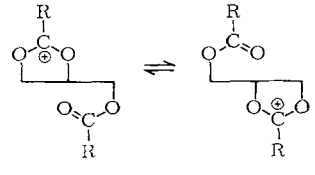
Valence Isomerism in Acyloxonium Cations of 1,2,3-Triols. Simple Synthesis of Acyloxonium Salts[1]

By *H. Paulsen* and *H. Behre*[*]

We have found that reaction of 1,2- or 1,3-diol esters *(1)* and *(3)* with $SbCl_5$ in CH_2Cl_2 serves as a simple, general method for the preparation of acyloxonium salts[2,3] of types *(2)* and *(4)*. The reaction obviously proceeds by way of neighboring group participation and loss of a carboxylate ion, since only the *trans* form of diesters of cyclic diols undergoes reaction; thus, we have prepared acetoxonium salts from the acetates of *trans*-1,2-cyclopentanediol (56%); *trans*-1,2-cyclohexanediol (25%); *trans*-1,3-cyclopentanediol (40%); *trans*-1,3-cyclohexanediol (59%). These salts crystallize out at different rates, varying from a few minutes at room temperature to 24 hours at 40 °C, depending on the neighboring group activity and stereochemistry of the compound in question. The following compounds *(2)* and *(4)* (arranged according to decreasing reactivity) have been prepared from *(1)* and *(3)*: Compound *(2)*, R = CH_3 (55%, 5 min. at 20 °C), C_2H_5 (55%, 5 min. at 20 °C), *tert*-butyl (60%, 5 min. at 20 °C), C_6H_5 (65%, 1 h at 20 °C), *p*-$C_6H_4CH_3$ (56%, 24 h at 40 °C), *p*-$C_6H_4OCH_3$ (70%, 48 h at 40 °C); compound *(4)*, R = CH_3 (48%, 3 h at 40 °C), C_6H_5 (51%, 5 h at 40 °C), *p*-$C_6H_4CH_3$ (67%, 12 h at 40 °C), *p*-$C_6H_4OCH_3$ (69%, 48 h at 40 °C). In each case the fastest reactions are those involving the acetyl and pivaloyl compounds.

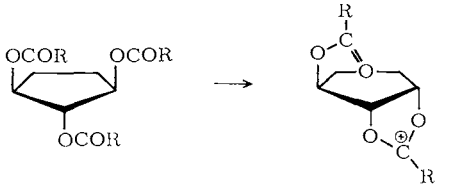


(1), n = 1 *(2)*, n = 1
(3), n = 2 *(4)*, n = 2

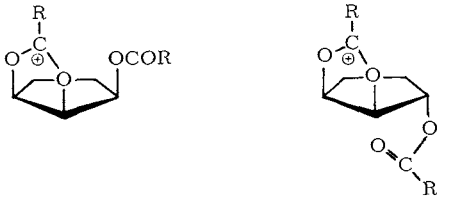


(5a), R = CH_3 *(6a)*, R = CH_3
(5b), R = $(CH_3)_3C$ *(6b)*, R = $(CH_3)_3C$

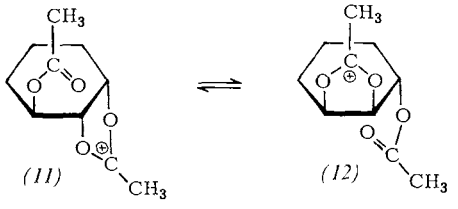
Esters of cyclic triols form acyloxonium salts if, like *(7)*, they contain *trans*-diol groups — a salt of *(5a)* is formed from glycerol triacetate. The cation *(5a)* is interesting since it can undergo rearrangement *via* a *trans* opening reaction into the cation *(6a)*, which is identical in structure with *(5a)*. The



(7a), R = CH_3 *(8a)*, R = CH_3
(7b), R = $(CH_3)_3C$ *(8b)*, R = $(CH_3)_3C$



(9a), R = CH_3 *(10a)*, R = CH_3
(9b), R = $(CH_3)_3C$ *(10b)*, R = $(CH_3)_3C$



(11) *(12)*

NMR spectrum of *(5a)* in CD_3NO_2 at room temperature contains a sharp acetoxonium methyl signal (τ = 6.95) at low field strength and a normal acetyl methyl signal (τ = 7.84). On increasing the temperature both signals become broader and finally coalesce at 105 °C. Referred to the NMR timescale a rapid reversible rearrangement *(5a)* ⇌ *(6a)* takes place. The rearrangement can be observed still better in the case of the pivaloxonium ion *(5b)* since the frequency difference of both *tert*-butyl signals is smaller and the coalescence temperature (87 °C) consequently lower, so that fewer decomposition reactions interfere with the investigation. The rearrangement *(5)* ⇌ *(6)* can be considered as valence isomerism of a cation. (The $\Delta G^{\ddagger}$ values determined for this rearrangement are given in Table 1.)

Esters of (1,3/2)-cyclopentanetriol *(7)* can react with $SbCl_5$ to give the acyloxonium cation *(8)* or *(9)*. The triacetate *(7a)* yields *(8a)* only. *(8a)* exhibits a rapid valence isomerization *(8a)* ⇌ *(10a)* at higher temperatures (see Table 1). The tri-

Table 1. $\Delta G^{\ddagger}$ values determined by NMR spectroscopy for the rearrangement of acyloxonium cations. T_c = coalescence temperature; solvent: CD_3NO_2.

	Signal	T_c (°K)	$\Delta\nu$ (Hz)	$\Delta G^{\ddagger}$ (kcal/mole)
(5a) ⇌ *(6a)*	CH_3	≈378	53.5	18.7
(5b) ⇌ *(6b)*	$(CH_3)_3C$	360	21.8	18.4
(8a) ⇌ *(10a)*	CH_3	365	54.0	18.0
(8b) ⇌ *(10b)*	$(CH_3)_3C$	348	22.3	17.8
(11) ⇌ *(12)*	CH_3	≈368	43.0	18.4

pivalate, on the other hand, affords *(8b)* (43%) and *(9b)* (57%). The ion *(8b)* exhibits a rapid rearrangement *(8b)* ⇌ *(10b)* (see Table 1) whereas the ion *(9b)* does not. The salt *(9b)*, from which (1,2,3/0)-cyclopentanetriol is easily accessible, can be obtained by crystallization from a mixture of the hexachloroantimonates of *(8b)* and *(9b)*. The cation *(11)* also exhibits a rapid valence isomerization *(11)* ⇌ *(12)* (see Table 1). *(11)* is best prepared as the tetrafluoroborate by removal of hydride from 3-*O*-acetyl-1,2-*O*-ethylidene-(1,2/3)-cyclohexanetriol with $(C_6H_5)_3C^{\oplus}BF_4^{\ominus}$.

4-Acetoxymethyl-2-methyl-1,3-dioxolan-2-ylium hexachloroantimonate (5a)

$SbCl_5$ (4.5 ml) is dissolved in CH_2Cl_2 (5 ml) and then added dropwise with stirring at −10 °C to a solution of glycerol triacetate (7.7 g) in anhydrous CH_2Cl_2 (7 ml). After 24 h at room temperature the acetoxonium salt *(5a)* crystallizes (yield 50%, m.p. 145—148 °C).

Received: August 29, 1969 [Z 98a IE]
German version: Angew. Chem. *81*, 905 (1969)

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Cyclorearrangement of 3,4,5-Tri-*O*-acetyl-(1,2,4/3,5)-cyclopentanepentol-1,2-*O*-acetoxonium Tetrafluoroborate

By *H. Paulsen* and *H. Behre* [*]

In acyloxonium salts of 1,2,3-triols a rapid valence isomerism takes place between the two possible dioxolanylium cations [1]. The $\Delta G^{\neq}$ value of this rearrangement is lower in the case of (1,2/3)-cyclopentanetriol derivatives than it is in the case of glycerol or (1,2/3)-cyclohexanetriol compounds, since the neighboring group reaction [2] in the cyclopentane ring is apparently sterically favored. As was to be expected, we have found that a total valence isomerization takes place in the cyclopentanepentol system.

Penta-*O*-acetyl-(1,2,4/3,5)-cyclopentanepentol reacts heterogeneously with $SbCl_5$. We therefore prepared 3,4,5-tri-*O*-acetyl-1,2-*O*-ethylidene-(1,2,4/3,5)-cyclopentanepentol *(1)* by reaction of the free pentol [3] with acetaldehyde diethylacetal and subsequent acetylation. [*(1)* consists of 65% of the *exo* form (m.p. 120 °C) and 35% of the *endo* form (m.p. 110 °C)]. The acetal *(1)* reacts with $(C_6H_5)_3C^{\oplus}BF_4^{\ominus}$ in CH_3CN with loss of hydride [4] to give the $BF_4^{\ominus}$ salt of *(2)*. By successive neighboring group reactions the cation *(2)* can be converted into a second cation that is structurally identical with *(2)*. The prerequisites for a neighboring group reaction are fulfilled at each stage of the conversion. After ten conversion steps the starting material is re-formed.

The NMR spectrum of the acetoxonium salt *(2)* in CD_3CN at room temperature contains an acetoxonium methyl signal at low field strength with $\tau = 7.13$ (3H) and two signals due to normal methyl groups at $\tau = 7.90$ (6H) and $\tau = 7.95$ (3H). At 80 °C all signals are considerably broadened, thus indicating that at this temperature the rearrangement is rapid according to the NMR time scale. Careful integration of the changed methyl signals shows that all the acetyl methyl groups participate in the process; this can be considered as proof that the substance undergoes rearrangement in the manner mentioned. The exact coalescence temperature cannot be determined since *(2)* rapidly decomposes at temperatures above 80 °C. The value of $\Delta G^{\neq}$ can be estimated as being approximately 18 kcal/mole by extrapolation and comparison with the heating curves of the acetoxonium salts of 1,2,3-triols.

We have also examined whether "jumping" takes place during the cyclic rearrangement, *i.e.* whether a C-atom can be "jumped over" *via* 1,3-neighboring group reaction. If this were the case then other isomers of cyclopentanepentol would have to be formed. GLC analysis of the hydrolyzed reaction mixture showed that other isomeric cyclopentanepentols [5] are formed in amounts of 3%.

Received: August 29, 1969 [Z 98b IE]
German version: Angew. Chem. *81*, 906 (1969)

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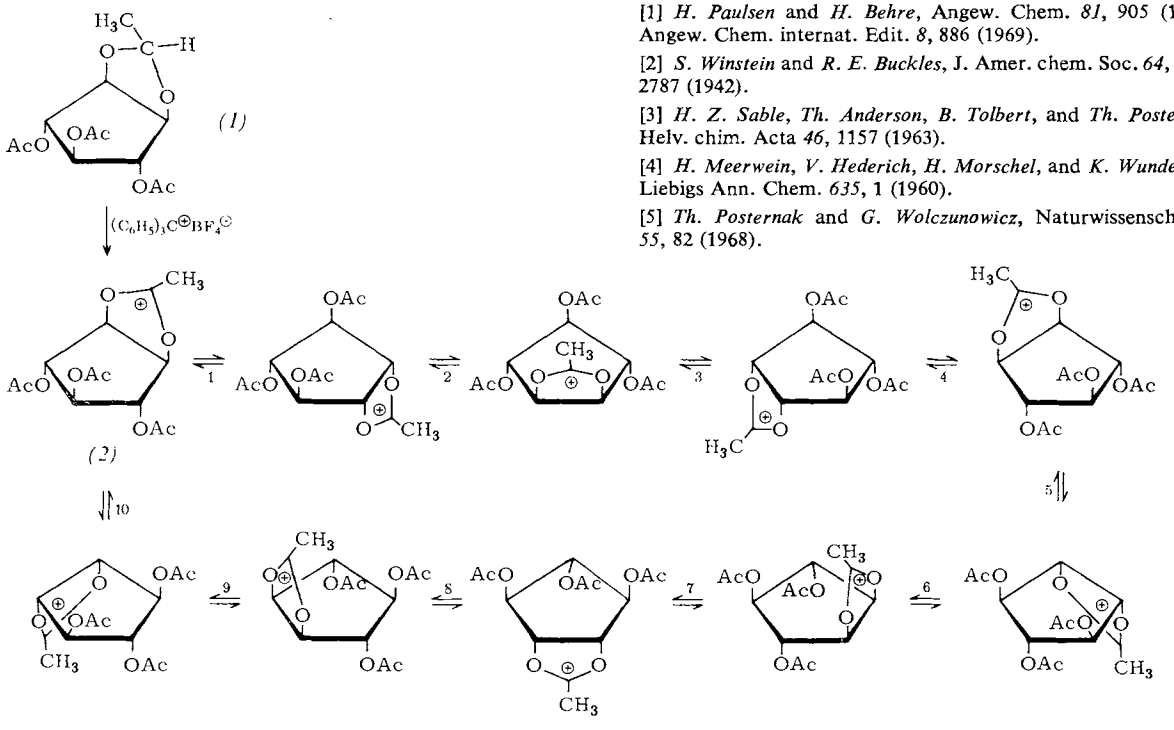
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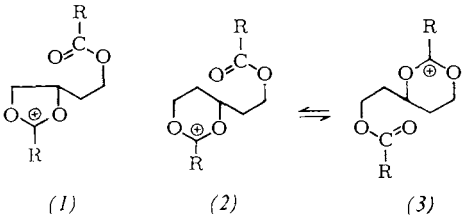
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Cyclorearrangement of Di-*O*-pivaloylpentaerythritol-*O*-pivaloxonium Hexachloroantimonate

By *H. Paulsen, H. Meyborg,* and *H. Behre*[*]

1,2-Diol esters react faster with $SbCl_5$ to give an acyloxonium salt containing a five-membered ring than do 1,3-diol esters to give such a salt having a six-membered ring. The reaction of 1,2,4-butanetriol esters with $SbCl_5$ permits direct comparison of the stabilities of dioxolanylium and dioxanylium salts and shows that the five-membered ring is the more stable since a salt of *(1)* is formed preferentially (90%).



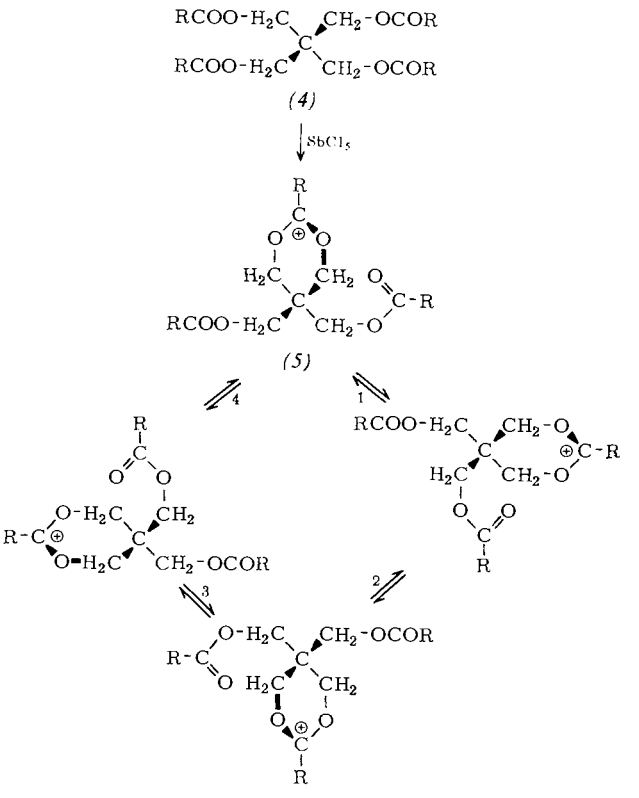
(1) *(2)* *(3)*

R = $(CH_3)_3C$

Valence isomerization should, however, occur in the case of acyloxonium salts of 1,3,5-triols. Since the above findings indicate that this conversion should have a higher $\Delta G^{\ddagger}$ value than in the case of 1,2,3-triols[1] we have directed our attention to the more readily investigatable pivalic esters. On heating with $SbCl_5$ in CH_2Cl_2 (20 h), 1,3,5-pentanetriol tripivalate affords the salt of *(2)* in 61% yield. At room temperature, the NMR spectrum of *(2)* in CD_3CN contains two sharp *tert*-butyl signals, that at lower field (τ = 8.64) being assigned to the group attached to the dioxanylium ring and the other (τ = 8.81) to the normal pivaloyl group. Coalescence of the two signals occurs at 110 °C (solvent $C_6H_5NO_2$), apparently due to a fast reversible 1,3-neighboring group reaction *(2)* ⇌ *(3)*. The $\Delta G^{\ddagger}$ value of 19.3 kcal/mole is 0.9–1.0 kcal/mole higher than the value found for the valence isomerization of the glycerolpivaloxonium salt[1].

As with cyclopentanepentol[2], a system can also be found for the dioxanylium ion in which a cyclorearrangement with total valence isomerization is observed. Pentaerythritol tetrapivalate *(4)* affords the monopivaloxonium salt *(5)* (2-*tert*-butyl-5,5-bis(pivaloyloxymethyl)-1,3-dioxan-2-ylium hexachloroantimonate) in 35% yield on heating with one mol. equiv. of $SbCl_5$ in CH_2Cl_2. As shown in the reaction scheme, *(5)* can undergo a 1,3-neighboring group reaction to give an ion which is structurally identical with the starting ion. Four rearrangement steps suffice to regenerate the starting material. Rearrangement takes place in a spiral manner about the central tetrahedral carbon atom.

The NMR spectrum of the pivaloxonium salt *(5)* at room temperature in CD_3NO_2 shows a 9-proton signal (τ = 8.51)



R = $(CH_3)_3C$

for the *tert*-butyl group attached to the dioxanylium ring and an 18-proton signal (τ = 8.77) for the two pivaloyl groups. In addition, a downfield singlet (τ = 4.82, 4H) is observed for the methylene protons of the dioxanylium ring, and another singlet at τ = 5.72 for the remaining methylene protons. The signals due to the *tert*-butyl groups and those of the methylene groups coalesce when the solution is heated to 110 °C and 122 °C respectively. This observation can be regarded as proof that *(5)* does undergo rearrangement in the manner indicated above. The coalescence temperature of 110 °C ($\Delta\nu$ = 20.0 Hz) for the *tert*-butyl groups gives a value of $\Delta G^{\ddagger}$ = 19.3 kcal/mole for the rearrangements.

Received: August 29, 1969 [Z 98c IE]
German version: Angew. Chem. *81*, 907 (1969)

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General Meeting of the Gesellschaft Deutscher Chemiker 1969

This year's General Meeting was held at Hamburg (Germany) from 15th to 20th September. A selection of abstracts of the lectures and discussions that took place on this occasion is given below. Only work that has not yet been published or presented for publication is included. The abstracts are listed in the alphabetical order of authors' names.

From the lectures:

Effective Charge and Specific Energy Loss of Fission Fragments in Metal Absorbers

By *H. Albrecht* (lecturer) and *H. Münzel*[*]

It is important for users of heavy-ion accelerators to know the energy loss and the effective charge of heavy ions as a function of their energy and mass. To obtain experimental data for the range 100—150 atomic weight units, dE/dx measurements were carried out for fission fragments in thin aluminum, silver, and gold foils. The fission source was a ^{252}Cf preparation. Both the mass and the energy of the fission products could be determined by the use of two semiconductor counters with 180° geometry. The specific energy loss was then calculated by comparison of measurements with and without absorbers.

An attempt was also made to determine the effective charge of the fragments and to obtain information about recharging processes in the absorber material by measurement of the deflection of the fission products in a magnetic field of 10000 oersted with the aid of position-sensitive detectors.

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Influence of Foreign Atoms on the Formation and Structure of Boron Modifications and Boron-Rich Borides

By *E. Amberger* (lecturer) and *K. Ploog*[*]

On pyrolysis of very pure boron halides (BCl_3, BBr_3) on hot (900—1300 °C) substrate surfaces (Ta, SiC, BN) in an atmosphere of hydrogen, we obtained monocrystalline α-rhombohedral and II-tetragonal boron and also microcrystalline β-rhombohedral boron and compact vitreous deposits of amorphous boron in a reproducible synthesis. We are now engaged in the determination of the as yet unknown, very complicated structure of II-tetragonal boron (space group $P4_122$; $a = 10.12$; $c = 14.14$ Å; $d = 2.36$ g/cm³), which has now been obtained for the first time in the monocrystalline state, though it has been known in the microcrystalline form since 1959.

If small quantities of foreign gases (*e.g.* CH_4, $CHBr_3$, CI_4, N_2) are introduced under conditions that would otherwise lead exclusively to the formation of II-tetragonal boron, the well known I-tetragonal boron structure is formed instead. The foreign atoms C and N are incorporated into the lattice. The I-tetragonal structure [theoretical formula of "I-tetragonal boron": $(B_{12})_4B_2$] has been found in the following boron-rich borides, which have now been synthesized for the first time: $(B_{12})_4B_2C_2$, $(B_{12})_4B_2C$, and $(B_{12})_4B_2N_2$.

In media containing no foreign atoms, I-tetragonal boron is never formed at 900 to 1300 °C. It is therefore very doubtful whether it is in fact possible to prepare pure "I-tetragonal boron, $(B_{12})_4B_2$". In any case, the addition of foreign gases to the boron halide-hydrogen mixture is a simple and reliable method for the reproducible synthesis of the I-tetragonal lattice.

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NMR Spectroscopic Investigation of the Complex Formation in the Extraction of Uranium and Plutonium with Organophosphorus Compounds

By *R. v. Ammon*[*]

The nuclear fuels uranium and plutonium are often purified by solvent extraction with organophosphorus compounds. Some of the complexing equilibria involved have been studied by NMR spectroscopy. The types of nuclei that are suitable for this purpose are those situated close to the coordination center, *i.e.* the phosphoryl group of the organophosphorus compound. Thus they are the α-CH_2 protons of the alkyl group, the hydrogen bond proton, and the phosphorus atom. The extracting agents are tri-*n*-butyl phosphate (TBP) and tri-*n*-octylphosphine oxide (TOPO) in an inert diluent. HNO_3 and H_2O are extracted as well as uranyl nitrate and plutonium(IV) nitrate.

HNO_3. The ^1H resonance confirms the presence of the compound TBP·HNO_3 or TOPO·HNO_3. The ^{31}P resonance, together with the ^1H resonance, also indicates the nature of the bonding of a second molecule of HNO_3 to the 1:1 adduct; with TBP it is bound by hydrogen bonds to the nitrate oxygen atoms, while with the more basic TOPO, both HNO_3 molecules are bound to the phosphoryl group.

Uranyl nitrate [$UO_2(NO_3)_2$]. NMR shifts of ligand nuclei in uranyl complexes are mainly determined by the magnetic anisotropy of the uranyl group. Therefore the pronounced shift of the signal due to the rapidly exchanging HNO_3 and H_2O protons to lower field shows that when the uranium content in the organic phase is low, water is coordinated directly to the uranyl group, probably in the complexes TBP·$UO_2(NO_3)_2$·H_2O and TOPO·$UO_2(NO_3)_2$·H_2O. The complexes $UO_2(NO_3)_2$·2 TBP and $UO_2(NO_3)_2$·2 TOPO are formed only at higher uranium concentrations.

Pu(IV) nitrate [$Pu(NO_3)_4$]. Because of its paramagnetism, Pu^{IV} causes a pseudo-contact shift of the α-CH_2 protons to a higher field strength. From the sign of this shift it can be qualitatively concluded that the principal axis of symmetry of the complex $Pu(NO_3)_4$·2 TBP cannot pass through the plane formed by the central atom and the TBP ligands, but that there must be a twofold rotation axis normal to this plane.

NMR spectroscopy is thus found to be a valuable aid in the investigation of complex formation reactions of this type, even when the central atoms of the complexes are paramagnetic.

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Studies on the Course of a Chloramine Oxidation of Hydroxyproline

By *W. Arneth*[*]

There are two principal methods for the determination of hydroxyproline, which differ basically only in the substance used to oxidize the hydroxyproline to a chromogen that can be converted into a dye with *p*-dimethylaminobenzaldehyde. Dilute hydrogen peroxide is used in one case, and buffered chloramine solution in the other. Whereas the course of the peroxide oxidation of hydroxyproline is known, nothing is known as yet about the processes that take place during a chloramine oxidation.

The two reactions appear to be different. In the peroxide method, the excess of oxidizing agent must be removed *completely* by heating before dye formation. In the chloramine method, on the other hand, it appears from the procedure that this can be achieved by acidification of the reaction mixture. We have found, however, that even after acidification the chloramine is still almost completely unchanged, and so cannot interfere with the determination. The conditions in a chloramine oxidation cannot, therefore, be the same as those prevailing during a peroxide oxidation. This is confirmed by the observation that on oxidation with peroxide, even a few μg of hydroxyproline yields steam-volatile products that give a color with *p*-dimethylaminobenzaldehyde whereas about one hundred times as much hydroxyproline is required to obtain the same result in a chloramine oxidation.

A similar situation is found in the detection of pyrrole, the end product of the peroxide oxidation, with mercury(II) chloride solution. When hydroxyproline is oxidized with peroxide, a few μg are sufficient to give a milky turbidity on steam distillation into $HgCl_2$ solution, whereas more than twenty times as much hydroxyproline is required in a chloramine oxidation. After the oxidation with chloramine, some oxidation products can be detected by thin layer chromatography, but none of these is identical with the pyrrolecarboxylic acid that can be readily isolated from the reaction solution after a peroxide oxidation.

It can be concluded from the results obtained so far that the chloramine oxidation of hydroxyproline proceeds differently from the peroxide oxidation.

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Radiochemical Investigations on High-Energy Nuclear Reactions of Tantalum

By *B. Neidhart, R. U. Trabitzsch,* and *K. Bächmann* (lecturer)[*]

Tantalum was bombarded with high-energy protons (19 GeV and 580 MeV), and the cross-sections (σ) and ranges (*R*) of lanthanides, Rb, Sr, Y, and Zr were determined by radiochemical methods. Mass yield curves were constructed from the cross sections. At 580 MeV the σ values of products with mass numbers of 82 to 88 are about 0.5 mb, whereas the cross sections in this mass range increase to about 6 mb at 19 GeV. In the lanthanide range, the σ values increase steeply from ≈0.4 to 70 mb with increasing mass number, whereas at 19 GeV the cross sections in this mass range remain approximately constant at ≈18 mb up to atomic mass numbers of 165, and increase only above this mass number.

The distribution of the Rb isotopes was studied in detail. Preferential formation of neutron-deficient products was observed. The isotopic distribution curve shows a maximum at mass number 83 for 580 MeV and at mass number 82.5 for 19 GeV.

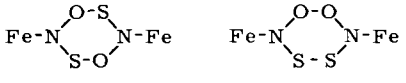
Comparison of the range of Rb isotopes at 580 MeV ($R \approx 8$ mg/cm²) and 19 GeV ($R \approx 3$ mg/cm²) shows that the ranges of neutron-deficient products are considerably lower than those of neutron-excess ones. The ranges of the lanthanides are smaller than those of rubidium isotopes and exhibit a much smaller dependence on energy.

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The Structure of the Reaction Product of $Fe[(CN)_5NO]^{2-}$ with S^{2-} Ions

By *E. J. Baran* (lecturer) and *A. Müller*[*]

Although the reaction of pentacyanonitrosylferrate(II) and sulfide ions ("Gmelin reaction") is generally known as an important reaction for the detection of sulfur, there is no definite proof of the structure of the red-violet reaction product, whose anion is nearly always formulated as the pentacyanomonothionitroferrate(II) ion $[Fe(CN)_5NOS]^{4-}$ *(1)*. We have carried out a spectroscopic investigation of the solid formed on reaction in methanol. The frequencies obtained by model calculations in which reasonable assumed force constants were used for *(1)* are not, however, compatible with the experimental vibrational spectrum. This spectrum suggests that the reaction product is probably a dimeric compound $Na_8[Fe(CN)_5NOS]_2 \cdot 4H_2O$ *(2)*.



(2a) *(2b)*

The question whether the grouping *(2a)* or *(2b)* is present cannot be definitely answered. Earlier kinetic measurements can also be reconciled with dimerization.

(2) is analytically pure and amorphous to X-rays. The IR spectrum contains the following principal absorption bands (in cm^{-1}): 3400 = ν (OH), 1620 = δ (HOH), 2050 = ν (CN), 672 and 655 = δ (CN), 435 = ν (FeC), 1140, 1005, 962 and 575 = ring vibrations (?). The presence of two or more non-equivalent iron atoms can be ruled out on the basis of the Mössbauer spectrum of the ^{57}Fe nuclei. As expected, the spectrum is similar to that of $Na_4[Fe(CN)_5NO_2]$ *(3)*. It follows that the π back-bonding strength $Fe \overset{\sigma}{\underset{\pi}{<}} L$ in *(2)* and *(3)* should be approximately equal.

The electronic spectrum of the solid contains a strong band at 580 nm, which is responsible for the characteristic color, and two weaker bands at 390 and 305 nm. Since the electronic spectrum of the aqueous solution is not identical with that of the solid, it is possible that a different species exists in solution.

On reaction of $[Fe(CN)_5NO]^{2-}$ with other compounds containing sulfur (*e.g.* thioacetamide and thiourea), color reactions very similar to the Gmelin reaction are observed. Spectroscopic investigation of the solid reaction products showed however that no related compounds are formed.

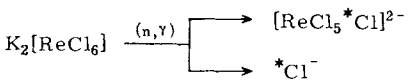
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Ligand Recoil in Hexahalo Complexes of Re^{IV} and Rh^{III} and the Production of Practically Carrier-Free ^{36}Cl

By *R. Bell* (lecturer) and *G. Stöcklin*[*]

The chemical consequences of (n,γ)- and (n,2n)-processes on the halogen ligands of crystalline complexes of the type $K_2[ReX_6]$ (X = F, Cl, Br, I) and $K_3[RhCl_6]$, respectively,

have been investigated. The resulting radiohalogen appears mainly in two products, *i.e.* as labeled parent compound (retention) and as free halide (yield), *e.g.*:



The radiohalide yield is independent of the type of nuclear process, *i.e.* of recoil energy and range. However, it shows a distinct dependence on the nature of the ligand. From the fluoro to the iodo complex, the yield decreases in the order of the Re–X bond energies (F^-: 17.5 %; Cl^-: 15.6 %; Br^-: 12.2 %; I^-: <2 %). It is smaller for the less stable hexachlororhodate than for the corresponding rhenium complex.

Thermal annealing, which was investigated at 80, 120, 160, and 200 °C, leads to a decrease in the halide fraction and to temperature-dependent plateau values. The observed reformation of the labeled parent complex can be explained by a halogen isotope exchange in the solid state (see abstract by *Rössler* and *Upadhyay* in this collection).

With respect to the enrichment of ^{36}Cl ($T_{1/2}$ = 3.1×10^5 a), which is difficult to obtain in high specific activities, the dose dependence of the chloride yield was investigated in the $K_2[ReCl_6]$-system. The yields of $^{38}Cl^-$ and $^{36}Cl^-$ remained constant over a wide range of radiation dose (10^{13} to 10^{20} n/cm^2). Practically carrier-free ^{36}Cl activities in the mCi range can thus be obtained.

Information about the reactions of recoil halogen atoms in the solid and the retention processes was obtained by intermolecular competition experiments using $K_2[ReCl_6]/K_2[ReBr_6]$ mixed crystals (1:1). In the case of the Br recoil component, it could be shown by electrophoretic separation of the chlorobromo complexes that the radiobromine (apart from that in the form of bromide) occurs practically only in the monosubstituted parent compounds, *i.e.* as labeled hexabromo complex and as monobromopentachloro complex ($^*Br^-$: 12 %; $[ReBr_5{}^*Br]^{2-}$: 50 %; $[ReCl_5{}^*Br]^{2-}$: 30 %; other complexes with mixed ligands: each < 2 %).

These results again confirm that the environment of the recoil atom after the nuclear process is not a molten zone in the sense of the "hot spot" model, as has already been shown for the recoil of the Re central atom[1]. Furthermore, it becomes obvious that the reactions of the recoil halogens in the solid are simple ligand exchange reactions involving substantially intact complexes.

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[1] *H. Müller*, J. inorg. nuclear Chem. *27*, 1745 (1965); for a review see *H. Müller*, Angew. Chem. *79*, 128 (1967); Angew. Chem. internat. Edit. *6*, 133 (1967).

Breakdown of Sugars during the Ripening of Camembert: Enzymatic Determination of D-Lactose, D-Glucose, and D-Galactose

By *G. Berner*[*]

During the ripening and storage of cheese products, many compounds undergo transformations as a result of metabolic processes. We used enzymatic sugar determinations to follow the breakdown of D-lactose, D-glucose, and D-galactose in samples of Camembert over a period of 30 days after the salt-bath treatment. D-Lactose was hydrolyzed with β-galactosidase, and the resulting D-glucose was determined. After 30 days, D-lactose and D-galactose can no longer be detected, whereas the D-glucose content increases steadily during storage.

The rates of breakdown of the sugars in the interior and in the outside layer of Camembert are different. The accuracy of the enzymatic analyses was tested by the admixture technique.

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The High-Temperature Ammonolysis of UF_4

By *H. J. Berthold* (lecturer) and *H. G. Hein*[*]

The reaction of UF_4 in a stream of NH_3 begins at 890–900 °C with reduction to UF_3 by the hydrogen present. If the gas stream contains sufficient NH_3 for ammonolysis to occur, the UF_3 is then converted *via* crystalline $U(NH_2)F_2$ into higher uranium nitride $UN_{1.90}$.

The vacuum degradation of $U(NH_2)F_2$ in a mass spectrometer between 600 and 900 °C results in elimination of hydrogen fluoride to give U(NH)F, which loses further HF to give UN when pumping is continued for about half an hour.

The ease of elimination of hydrogen fluoride and the detection of the existence of crystalline U(NH)F suggest that the ammonolysis of $U(NH_2)F_2$ also proceeds mainly *via* the intermediate U(NH)F. The UN formed by elimination of HF from U(NH)F is thermodynamically unstable at 900 °C in the presence of nitrogen, and changes immediately into higher uranium nitride $UN_{1.90}$. It cannot therefore be isolated as an intermediate in the ammonolysis.

$U(NH_2)F_2$ crystallizes in the orthorhombic system (Z = 2) with the lattice constants a = 3.89 Å, b = 4.02 Å, and c = 5.70 Å (all values ± 0.01 Å).

The diffraction diagram of U(NH)F indicates a face centered cubic structure (CaF_2 type) with a = 5.532 ± 0.003 Å.

The $UN_{1.90}$ formed as the final product in the ammonolysis of UF_4 or UF_3 at 900 °C is the highest stable uranium nitride known at present. It has a cubic primitive lattice with a = 10.605 ± 0.001 Å and its structure may be described as a defect CaF_2 structure with ordered nitrogen vacancies. The nitride fits in with the known nitrides UN, α-UN_x ($1.5\leq x<1.8$), β-UN_x ($1.33<x\leq1.47$), and the unstable UN_2 (CaF_2 type, a = 5.414 Å), which was first observed by us in other investigations, as a new "γ phase". According to our previous results, the range of existence of γ-UN_x is given by $1.8\leq x\leq1.9$.

Nitrides of the γ phase with compositions $UN_{1.80-1.86}$ are formed on nitriding of uranium metal or uranium nitrides with NH_3 between 500 and 1000 °C.

Unlike the ordered γ-$UN_{1.90}$, however, these nitrides have disordered structures, and of the superstructure lines of the cubic primitive γ phase, only the two strongest lines 12.2.0 and 12.2.2 are generally just visible in their diffraction diagrams. The nitrides are frequently described in the literature as having a CaF_2 structure.

$UN_{1.90}$ can be readily degraded under vacuum at 1000 °C to UN, which can be used as a nuclear fuel for fast breeder reactors.

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Carrier-Free Separation of ^{131}Cs from Irradiated Barium Salts by Countercurrent Electrolysis

By *B. A. Bilal*[*]

On neutron activation of barium, the nuclide ^{131}Ba is formed from the isotope ^{130}Ba by (n, γ) reaction. ^{131}Ba is unstable, and disintegrates by electron capture with a half-life of 12 d into ^{131}Cs, which also changes by electron capture, with a half-life of 9.7 d, into ^{131}Xe.

If an aqueous solution of an irradiated barium salt (barium acetate) is subjected to countercurrent electrolytic separation[1,2], the submicro quantity (order of magnitude 10^{-13} mole) of ^{131}Cs formed by the radioactive decay can be continuously isolated without a carrier.

The relative difference in the mobilities of the components Cs and Ba is 22 % in very dilute solutions. This value, which increases with increasing concentration, allows a fast and complete separation of the Cs/Ba mixture.

The separation chamber[3] consists of two parallel vertical cooling plates held a constant distance apart (1—2 mm) and firmly cemented to the lower edges and the two sides. Depressions at corresponding points form the electrode compartments and the reservoir compartment. Nylon gauze diaphragms are gripped in the facing grooves.

By suitable choice of the current strength and the flow rate of the countercurrent electrolyte (2 M acetic acid), it is possible to obtain a steady state with the desired concentration of the mixture (cf. [1] which was at first regarded as homogeneous. The components now separate, until they finally occupy adjacent zones. Since the quantity of ^{131}Cs to be separated is extremely small, the Cs zone at all the possible concentrations would be so vanishingly small that it would be practically impossible to separate the Cs from the Ba. A third component (in this case NH_4 ions) whose mobility is intermediate between those of Cs and of Ba is therefore added to the mixture. The NH_4 ions form a zone adjacent to the Ba zone. The more mobile Cs ions penetrate through the ammonium zone and accumulate in the cathode compartment. In order to remove the ammonium acetate it is sublimed off under vacuum at 160 °C after the solution has been evaporated to dryness.

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[1] *K. Wagener*, HMI B 44. The report may be requested from the library of the Hahn-Meitner-Institut. (HMI-reports are listed under Series AB of the "Zentralstelle Atomkernenergie beim Gmelin-Institut") and are abstracted in the Nuclear Science Abstracts of the USAEC.

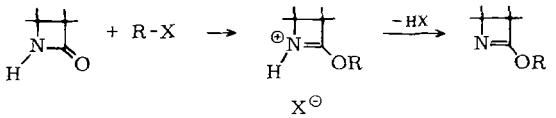
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[3] *B. A. Bilal*, Dissertation, Technische Universität Berlin 1966.

Preparation and Properties of β-Lactim Ethers

By *D. Bormann*[*]

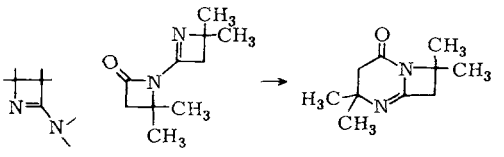
The alkylation of β-lactams (azetidin-2-ones) *(1)* in the absence of bases leads to 2-alkoxyazetinium salts *(2)*, which are converted by deprotonation into β-lactim ethers (2-alkoxyazetines) *(3)*.



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

β-Lactim ethers are organic bases, the reactivities of which differ with their degree of substitution. As azaenol ethers, they contain two reactive centers, *i.e.* the nitrogen and the C atom 2. Reaction with acylating agents gives *N*-acyl adducts, some of which change into *N*-acylazetidin-2-ones.

Nucleophiles react with the C atom 2 of β-lactim ethers, though the reaction is slower than with the larger-ring lactim ethers (γ-butyrolactim ether or ε-caprolactim ether). Thus the reaction of *(3)* with strongly nucleophilic amines leads to elimination of alcohol and formation of 2-aminoazetines *(4)*.



(4) *(5)* *(6)*

Thermally stable β-lactams, such as β,β-dimethyl-β-lactam, react similarly. This compound condenses with β,β-dimethyl-β-lactim ether to form azetinylazetidinone *(5)*, which can be rearranged to the tetrahydropyrimidine derivative *(6)*.

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Radionuclides as a Source of Energy

By *H.-J. Born*[*]

The conversion of radiation energy from radionuclides is becoming increasingly important, particularly in maintenance-free sources of electric current, both for space travel and for terrestrial purposes.

In the conversion *via* thermal energy, which is the most important process at present, electric current is produced with the aid of thermocouples, thermionic diodes, or even a turbine or a piston machine. Photoelectric radionuclide batteries, on the other hand, convert the radiation first into light and then, with the aid of photoelectric cells, into electrical energy.

The choice of the conversion process and of the radionuclide depends on the power, life, stability, screening, space, and weight requirements and on the required purity of the nuclide.

The data of the nuclides may be regarded as criteria of their usefulness. Thus whereas about 2270 Ci of ^{147}Pm are required for one watt (thermal), only 30 Ci of ^{238}Pu are required for the same power. The power density, based on the radionuclide in question in the form of the usual compound with no foreign additives, but including the radiation of any radioactive daughter products, is, *e.g.*, about 2 W_{th}/cm^3 for the β-emitting ^{147}Pm, but 1530 W_{th}/cm^3 for the α-emitting ^{228}Th, which has a similar half-life, together with its numerous α-emitting daughter products. Impurities reduce this power density.

The availabilities of the nuclides vary considerably and are continuously changing with the steady development of nuclear technology. Despite the great abundance of β-emitting fission products, the α-emitters among the transuranium elements are taking the lead in this respect. This is partly because special separation stages for the isolation of transuranium elements can be incorporated at relatively low cost into the new concentration plants being planned.

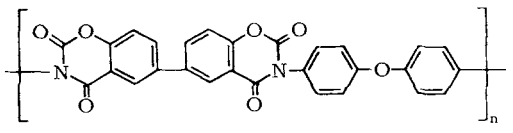
The use of preparations having very high specific powers in the form of alloys or mixed oxides and their observation will increase our knowledge of radiation damage and hence of the condensed phase in general.

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Polybenzoxazinediones, a Class of Heat-Resistant Polymers

By *L. Bottenbruch*[*]

Poly-1,3-benzoxazine-2,4-diones such as *(1)* can be prepared by several methods from *p,p'*-dihydroxybiphenyl-*m,m'*-dicarboxylic acids.



(I)

Reaction of esters of these acids with diamines yields highly polymeric polyamides, whose cyclization by reaction with carbonic acid derivatives such as phosgene or diesters of carbonic acid leads to the polybenzoxazinedione. The reaction of esters of these acids with diisocyanates gives polyurethanes, which cyclize when heated, with loss of the monohydroxy compound and formation of polybenzoxazinediones.

Quantitatively cyclized polymers of uniformly high molecular weight can be prepared surprisingly readily by reaction of diphenyl esters of dihydroxybiphenyldicarboxylic acids with diisocyanates in dimethyl sulfoxide with tertiary amines as catalysts. If a solution of equimolar quantities of the diester and the diisocyanate in dimethyl sulfoxide is heated to about 90 °C with the addition of a little tertiary amine, a fast reaction takes place, as can be seen from the rapid increase in the viscosity of the reaction solution. The polybenzoxazinedione is formed quantitatively with elimination of phenol, and can be precipitated from the solution.

Polybenzoxazinediones have been prepared *e.g.* with the following compounds as starting materials: hydroquinonedicarboxylic acid; resorcinoldicarboxylic acid; dihydroxybiphenyldicarboxylic acid; and methylenedisalicylic acid; as well as phenylene diisocyanate; biphenyl diisocyanate; naphthylene diisocyanate; diphenylmethane diisocyanate; diphenylpropane diisocyanate; and diphenyl ether diisocyanate.

Some polybenzoxazinediones dissolve in industrial solvents such as dimethylformamide, dimethylacetamide, *N*-methylpyrrolidone, and cresol, and can be made into films and fibers by conventional methods using solutions in these solvents.

Films of a polybenzoxazinedione prepared from dihydroxybiphenyldicarboxylic acid ester and diphenyl ether diisocyanate are characterized by high mechanical strength, high tear propagation resistance, and constant mechanical properties between −180 °C and +300 °C. The films also exhibit good long-term thermal stability. No embrittlement occurs within one year at 235 °C. At 275 °C, the elongation falls to 5 % after 6 weeks. The electrical properties are good, and, like the mechanical properties, they are constant over a wide temperature range. Fibers or films can be drawn at very high temperatures, and their mechanical strength is then many times that of the undrawn material. The films are stable towards concentrated acids, dilute bases, and most solvents, but they are unstable towards strong bases.

"Peraromatic" polybenzoxazinediones can be used as starting materials for heat-resistant films and fibers.

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Structural Chemistry of Ternary Sulfides Containing Alkali and Transition Metals

By *W. Bronger* [*]

Little is known as yet about ternary sulfides having the general composition $A_xM_yS_z$, where A = alkali metal and M = transition metal, in contrast with the corresponding oxides. The first detailed glimpses into this field have been provided by investigations carried out in recent years, which were concerned mainly with the structure of compounds containing 3d transition metals.

The 3d-element sulfides whose existence has been confirmed and which have been investigated in some detail are listed in the table. Sulfides containing heavier transition metals are known only for molybdenum [1a], palladium [1b], and platinum [1c].

Cr	Mn	Fe	Co	Ni	Cu
$NaCrS_2$					
$KCrS_2$	$K_2Mn_3S_4$	$KFeS_2$		$K_2Ni_3S_4$	KCu_4S_3
	$Rb_2Mn_3S_4$	$RbFeS_2$	$Rb_2Co_3S_4$	$Rb_2Ni_3S_4$	$RbCu_4S_3$
	$Cs_2Mn_3S_4$	$CsFeS_2$	$Cs_2Co_3S_4$	$Cs_2Ni_3S_4$	

The chromium(III) compounds listed have a structure in which the alkali metal and chromium atoms, which are arranged in alternating layers, are octahedrally surrounded by sulfur (α-$NaFeO_2$ type) [2]. The manganates(II) and cobaltates(II) [3] also have layer structures. In this case, sulfur tetrahedra surrounding transition metal atoms are joined by their edges. The structures of the alkali metal thioferrates(III) [4] are characterized by chain linkage of the iron atoms *via* edges of the surrounding sulfur tetrahedra. The arrangement of the alkali metal atoms in $CsFeS_2$ is responsible for a unique type of structure.

The structure of the alkali metal nickel sulfides is not yet known. However, their magnetic behavior, like that of the palladium compounds of the same type, point to planar coordination of Ni^{2+} and Pd^{2+} [1b]. The structure of $Cs_2Pd_3S_4$ [5] confirms this. The palladium atoms, again in a layer structure, are surrounded by sulfur rectangles joined up by their edges to give a two-dimensional arrangement. Finally, in the copper compounds listed in the table, the Cu atoms, which are situated inside sulfur tetrahedra, are incorporated into double layers [6].

In general it can be seen from the structures of these ternary sulfides that they are intermediate between the more alloy-like binary transition metal sulfides and the more salt-like complexes of the transition metals.

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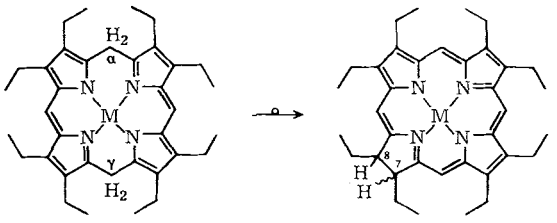
Influence of the Central Metal on the Hydrogenation of the Porphin System

By *J. W. Buchler* (lecturer) and *H. H. Schneehage* [*]

Whereas a magnesium-porphin complex is specifically hydrogenated *in vivo* to chlorophyllide a, this process has not yet been achieved *in vitro*. Following investigations by *Closs* [1], *Mauzerall* [1], and *Inhoffen* [1], we are studying the dependence of the "reductive protonation" (addition of electrons in an anhydrous medium followed by protonolysis) on the central metal M in metal octaethylporphins (P)M.

$$(P)M \xrightarrow{2e^{\ominus}} (P)M^{2\ominus} \underset{-2X^{\ominus}}{\overset{2HX}{\rightleftharpoons}} (PH_2)M \quad \circ\!\!\rightarrow (H_2P)M$$

We found (see Table 1) that the initial products are α,γ-dihydroporphins $(PH_2)M$, which do not rearrange with M = Mg, and in other cases, depending on the strength of the acid HX, rearrange slowly into chlorins $(H_2P)M$.



$(PH_2)M$ $(H_2P)M$

Table 1. Variation of M and HX.

$M^{n\oplus}$	HX	Result
$Mg^{2\oplus}$	CH_3OH	demetalation
$Zn^{2\oplus}$	CH_3OH	rearrangement
$Zn^{2\oplus}$	CH_3COOH	demetalation
$Al^{3\oplus}$ or $Sn^{4\oplus}$	CH_3OH	no rearrangement
$Al^{3\oplus}$ or $Sn^{4\oplus}$	HCl	rearrangement

The air-sensitive α,γ-dihydroporphins $(PH_2)M$ were characterized in the form of their methyl derivatives, which were obtained from (P)M by reductive methylation[1]. From the data in Table 1 and other observations we derive the working hypothesis that the rearrangement $(PH_2)M \rightarrow (H_2P)M$, and hence the formation of chlorins, proceeds best under conditions of partial demetalation of $(PH_2)M$. With magnesium as the central metal, this state might be reached under particularly mild conditions, and this could be one aspect of its importance in chlorophyll. For M = Zn, it was found that *cis*- and *trans*-octaethylchlorins[2] are formed in roughly equal quantities.

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Phthalocyanine and Perfluorophthalocyanine Complexes of Thorium, Protactinium, Uranium, and Neptunium

By *F. Lux, D. Brown, D. Dempf* (lecturer), *R. D. Fischer*, and *W. Hagenberg* [*]

Bis(phthalocyaninato)thorium(IV) ($ThPc_2$) and -uranium(IV) (UPc_2) have already been described[1]. On extension of the group of compounds to other actinides, $PaPc_2$ and $NpPc_2$ were first detected radiochemically;

$$^{232}ThPc_2(n,\gamma)\,^{233}ThPc_2 \xrightarrow[t_{1/2}=22.1\ min]{\beta^-} {}^{233}PaPc_2;\ \beta^-,\ t_{1/2} = 27.4\ d$$

$$^{238}UPc_2(n,\gamma)\,^{239}UPc_2 \xrightarrow[t_{1/2}=23.5\ min]{\beta^-} {}^{239}NpPc_2;\ \beta^-,\ t_{1/2} = 2.35\ d$$

The existence of the protactinium and neptunium compounds is shown by the observation that the specific activities of ^{233}Pa and ^{239}Np remain constant in the sublimates obtained on repeated resublimation of the irradiated $ThPc_2$ and UPc_2.

Another proof for the existence of $NpPc_2$: Uranium tetraiodide was prepared from neutron-irradiated, and hence ^{239}Np-containing, uranium metal, and was used as starting material for the preparation of UPc_2[1]; the ^{239}Np behaves in practically the same way as uranium.

Weighable quantities of bis(phthalocyaninato)protactinium(IV) ($PaPc_2$) were prepared in the same way as the thorium and uranium compounds from PaI_4 and phthalodinitrile. PaI_5 may also be used as a starting material. This is surprising since Pa^V can otherwise be converted into Pa^{IV} only with very strong reducing agents. $PaPc_2$, like $ThPc_2$ and UPc_2, can be sublimed without decomposing and is stable in air, whereas protactinium(IV) compounds are generally extremely sensitive to oxygen and moisture.

In the preparation of the MPc_2 complexes (M = Th, Pa, U), the electron donor-acceptor complexes (EDA complexes) $MPc_2 \cdot I_2$ are formed as intermediates. The sandwich configuration of the bis(phthalocyaninato) complex is thus formed immediately; by analogy with $SnPcI_2$[2], a monophthalocyaninatoactinide diiodide should have been expected as the first stage. The EDA complexes are also formed from MPc_2 and iodine in 1-chloronaphthalene. The black, completely insoluble compounds lose iodine at 250 °C. For EDA complexes of aromatic hydrocarbons with iodine, the excitation energy for the EDA band is a linear function of the ionization energy of the hydrocarbon. The EDA band of the $MPc_2 \cdot I_2$ complexes (λ_{max} = 530 nm) fits well into this system.

$ThPc_2$ and UPc_2 were the first actinide compounds having the sandwich configuration, and $PaPc_2$ is the only protactinium compound of this type known at present. Single crystals of $ThPc_2$ and UPc_2 have been grown, and structural determinations are in progress.

The IR spectrum from 400 to 4000 cm^{-1} for $PaPc_2$ is practically indentical with the corresponding spectra of $ThPc_2$ and UPc_2[1], and is characteristic of metal phthalocyanines. The electronic spectrum of $ThPc_2$ and UPc_2, like that of most phthalocyanatometal complexes, shows only *one* band between 600 and 700 nm[1]. In the spectrum of $PaPc_2$ this band is split.

It may be assumed from the IR spectra of the MPc_2 complexes between 4000 and 10000 cm^{-1} (absence of f-f transitions) and from their ESR spectra that the compounds have a center of symmetry.

Thorium tetraiodide reacts with perfluorophthalodinitrile at 240 °C to give a perfluorophthalocyaninato compound having the composition $ThPc^fI$. Thus in contrast to the reaction with phthalodinitrile, a monoperfluorophthalocyaninato compound is formed. In this compound thorium has the formal oxidation number III. It has been found by mass spectrometry that bis(perfluorophthalocyaninato)thorium(IV) ($ThPc^f_2$) is formed from the $ThPc^fI$ by thermal decomposition (molecular weight from mass spectrometry: 1830 ± 2). These compounds are the first known examples of the existence of the perfluorophthalocyanine ring[3].

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Independent Yields of Iodine Isotopes in Low-Energy Fission Reactions

By *H. O. Denschlag* (lecturer) and *S. M. Qaim*[*]

Fissionable material in aqueous solution was irradiated for a short time (approximately 50 msec) in a reactor or with a neutron generator. The samples were then ejected from the irradiation position by means of a special pneumatic tube system[1]. The fission iodine was separated from its genetic precursors – tin, antimony, and tellurium – within 2 sec by ion exchange on AgCl layers. From the ratio of iodine in the AgCl layer to iodine subsequently formed from the precursors in the filtrate, it was possible to calculate what fraction of the iodine isotopes ^{133}I, ^{134}I, and ^{135}I is formed directly by fission and what fraction is formed indirectly by decay of precursors (fractional independent and secondary yields, respectively)[2,3]. The fractional iodine yields were measured for the fission of ^{233}U, ^{235}U, and ^{239}Pu with thermal neutrons and for the fission of ^{232}Th with epi-Cd reactor neutrons and 14 MeV neutrons.

The results of the measurements provide interesting information on the charge distribution in the formation of fission products in the region of the closed nuclear shell with 82 neutrons ($^{135}_{53}$I, $^{134}_{52}$Te, and neighboring elements). The charge distribution is generally described by two parameters: Z_p, the most probable nuclear charge in an isobaric chain and σ, the width parameter of the Gaussian charge dispersion curve about the maximum value Z_p. It was possible to calculate both parameters for chain 135 in the fission of ^{233}U, ^{235}U, and ^{239}Pu, since experimental values of the fractional xenon yields[4] were also available. The width of the charge dispersion curve is $\sigma = 0.58 \pm 0.11$, in agreement with the value $\sigma = 0.59 \pm 0.06$ found outside the region of closed shells[5]. On the other hand, the Z_p values calculated from the experimental yields with $\sigma = 0.59$ show a fine structure, which can be understood as resulting from the tendency to achieve $N = 82$. The fine structure is particularly noticeable if the charge distribution curve is plotted as described by *Wahl*[5], but using the latest values for the evaporation of prompt neutrons from the fission fragments[6,7]. From the position of the fine structure and from the fact that the complementary fission fragment in the fission of ^{233}U exhibits an effect of the same type[8], we conclude that the existence of the 82-neutron shell influences both the division of the compound nucleus and the subsequent prompt neutron emission.

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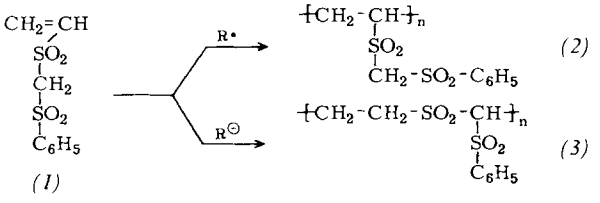
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Mass-Spectrometric Investigation of Poly-*S*-phenyl-*S'*-vinylmethylenedisulfones

By *H. Diefenbach* (lecturer), *H. Ringsdorf*, and *U. J. Zahorszky*[*]

S-Phenyl-*S'*-vinylmethylenedisulfone *(1)* has been polymerized with azodiisobutyronitrile and K-*tert*-butoxide in dioxane and DMF. The polymers *(2)* and *(3)* obtained by the free-radical and anionic methods differ in several of their properties. Owing to the acidity of the active methylene group and the strong tendency of the vinylsulfonyl group to enter into additions, an addition mechanism with proton migration is conceivable for the anionic polymerization of *(1)*.



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

The difference in structure was detected by mass spectrometry. Whereas the pyrolysis of the free-radical polymer *(2)* in the mass spectrometer yields CH_3—SO_2—C_6H_5 (m/e = 156) and SO_2 (m/e = 64), that of the anionic polymer *(3)* leads mainly to C_6H_5—S—S—C_6H_5 (m/e = 218).

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Novel Reactions of Hexachlorobutadiene

By *K. Gorzny, K. Grübel*, and *H. Drawe* (lecturer)[*]

The transfer of radiation-chemical syntheses from the preparative to the industrial scale involves economic and engineering considerations. The search for cheap products that are difficult to react by conventional methods led us to hexachlorobutadiene (HCB). HCB, which was formerly thought to be inert, occurs in large quantities as a waste product in the industrial production of chlorinated hydrocarbons.

We have so far carried out the following specific radiation syntheses with HCB:

1. The reaction with phosphites yields new phosphonates of the type

$$Cl_2C{=}CCl{-}CCl{=}CCl{-}P(O)(OR)_2$$

These are being tested for use as polymerization additives, and are to be produced on a pilot plant scale.

2. When elemental white phosphorus is dissolved in HCB, γ-irradiation yields a reactive red phosphorus that contains only about 50% of P. The possibility of preparing low molecular weight organophosphorus compounds from this reactive phosphorus is being investigated.

3. It has been shown for the example of cyclohexane (we synthesized 1,1,2,3,4-pentachloro-4-cyclohexyl-1,3-butadiene) that one Cl atom of HCB can in principle be replaced by a hydrocarbon group.

4. The radiation-chemical synthesis of telomers of styrene has also been achieved with HCB. Even small additions of HCB increase the overall polymerization rate of styrene; the molecular weight simultaneously shows a marked decrease. Since the reaction is completely suppressed by the addition

of diphenylpicrylhydrazyl, it must be free-radical in nature. In view of the observed dependence of the relative polymerization rate on the mole fraction of the mixtures, energy transfer is assumed to occur from styrene to HCB. This assumption is supported by the fact that the energy transfer is eliminated by the addition of quenchers (such as anthracene).

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Problems in the Blocking of Thiol Groups in Polypeptides

By *G. Ebert* (lecturer) and *Chr. Ebert*[*]

The investigation of keratin fibers often requires the reduction of the —S—S— bridges and blockage of the resulting SH groups. Examples of reagents used for this purpose are monoiodoacetate, monoiodoacetamide, *N*-ethylmaleimide, phenylmercury hydroxide, and methyl iodide. Most of these blocking agents contain hydrophilic, ionic, or polar groups and are also very much larger than the substituted H atom. Owing to interactions of the blocking groups with one another and with the amino acid side chains, as well as to steric effects, an additional change in the conformation of the protein molecules, which depends on the blocking agent, may occur.

The small, apolar CH_3 group (introduced by CH_3I, as suggested by *Harris*) appears to minimize disturbances of this type. A check showed, however, that a considerable proportion of the initially formed SCH_3 groups are further methylated to give the dimethylsulfonium salt of cysteine, which loses $(CH_3)_2S$ to give peptide-bound dehydroalanine. The double bond in this compound reacts to only a small extent with ε-amino groups of adjacent lysine units to give lysinoalanine, but even slight crosslinking of this nature can appreciably change the properties of the protein.

The order-disorder transition of partly reduced keratin fibers that had been blocked with CH_3I and ICH_2COO^- has been investigated by differential calorimetry and by shrinkage measurements. Very pronounced differences were found in the temperature at which the process occurred, the amount of heat absorbed, and the cooperativity of the process. These quantities are distinctly lower for the protein fibers in which ionic groups have been introduced to block the SH groups; this points to a considerable change in the conformation of the protein, in the sense of a decrease in order.

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Mechanism of the Formation and Isomerization of β-Lactams

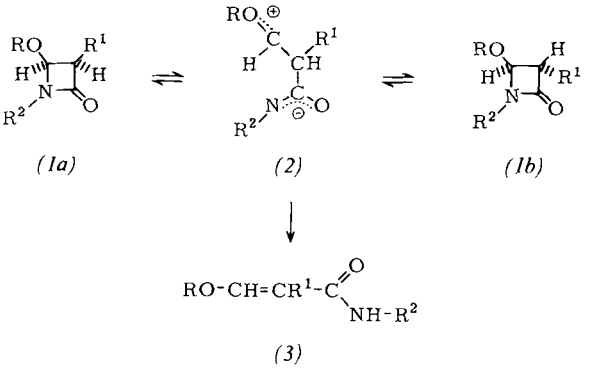
By *F. Effenberger* (lecturer) and *G. Prossel*[*]

Kinetic and stereochemical studies on the reaction of enol ethers with sulfonyl isocyanates lead to a deeper understanding of polar 2 + 2 cycloadditions.

The isocyanate adds stereospecifically to *cis*- and *trans*-enol ethers to give the β-lactams *(1)*.

The isomerization *(1a)* ⇌ *(1b)* and the irreversible formation of *(3)* proceed *via* the polar intermediate *(2)*. The isomerization rate is determined by the ring strain in *(1)* and the stabilization of *(2)*.

Information about the transition state of this cycloaddition can be obtained from the relative stabilities of the enol ethers used and of the β-lactams formed, the reaction rates in various solvents, and the activation parameters.



(1a) *(2)* *(1b)* *(3)*

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ESR-Spectroscopic Investigation of Radiation-Induced Electron Transfer Processes in Aqueous Solutions

By *K. Eiben*[*]

Radiation-induced electron transfer reactions in aqueous solutions have been studied directly by an *in-situ* ESR technique. The focused beam of a 2.8 MeV electron accelerator was directed toward a flat quartz cell centered in the ESR resonator. An aqueous solution was passed through the cell, and a stationary concentration of radicals (> 10^{-7} mole/l) was maintained in the solution during irradiation[1].

The hydrated electrons (e^-_{aq})[2] and H-atoms formed as intermediates in the radiolysis of water [eq. (1)] have been detected by this method.

$$H_2O \rightsquigarrow H;\ e_{aq};\ OH;\ H_3O^+;\ H_2;\ H_2O_2 \qquad (1)$$

In N_2O-saturated (approximately 2×10^{-2} mole/l) aqueous solutions which contained an aliphatic alcohol (approximately 10^{-1} mole/l), the primary radicals produced according to reaction (1) are converted quantitatively into hydroxyalkyl radicals [eq. (2)—(4)].

$$e^-_{aq} + N_2O \xrightarrow[-N_2]{} O^- \overset{+H_3O^+}{\rightleftharpoons} OH \quad p_K = 11.9 \qquad (2)$$

$$OH + CH_3OH \xrightarrow[-H_2O]{} {}^{\bullet}CH_2OH \overset{+OH^-}{\rightleftharpoons} {}^{\bullet}CH_2O^- \quad p_K = 10.9 \qquad (3)$$

$$H + CH_3OH \xrightarrow[-H_2]{} {}^{\bullet}CH_2OH \overset{+OH^-}{\rightleftharpoons} {}^{\bullet}CH_2O^- \quad p_K = 10.9 \qquad (4)$$

The ESR spectra of these hydroxyalkyl radicals disappear when suitable acceptors for an electron transfer [reaction (5) or (6)] are added to the aqueous solution in concentrations of 10^{-3}—10^{-4} mole/l.

$$CH_3NO_2 + R\dot{C}HOH \xrightarrow{H_2O} CH_3\dot{N}O_2^- + RCHO + H_3O^+ \qquad (5)$$

$$C_6H_5NO_2 + R\dot{C}HO^- \rightarrow C_6H_5\dot{N}O_2^- + RCHO \qquad (6)$$

The electron transfer reactions (5) and (6) yield the anion-radicals of several aliphatic and aromatic nitro compounds and the ketyl radicals of acetophenone and benzophenone [eq. (7)]. They were identified by their ESR spectra.

$$R^1R^2C{=}O + R\dot{C}HO^- \rightarrow R^1R^2\dot{C}{-}O^- + RCHO \qquad (7)$$

The dependence of the electron transfer on the dissociation and structure of the hydroxyalkyl radicals has also been studied. Hydroxyisopropyl, for example, is a more effective

electron donor than hydroxymethyl in acidic and neutral solutions, whereas the ionized hydroxyalkyl radicals do not differ in this respect in alkaline solutions.

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[1] *K. Eiben* and *R. W. Fessenden*, J. physic. Chem. *72*, 3387 (1968).

[2] *A. C. Avery, J. R. Remko*, and *B. Smaller*, J. chem. Physics *49*, 951 (1968).

The Reaction of Diborane and Boranecarbonyl with Nitrogen-Oxygen Compounds

By *U. Engelhardt* [*]

Attempts to prepare a hypothetical trihydridonitrosylborate (cf. [1]), $Na[H_3BNO]$, from diborane and "nitrosylsodium" $(NaNO)_x$ [2] gave sodium tetrahydridoborate as the principal product. When carried out without additional solvents as a heterogeneous solid-gas reaction or in suspension in liquid diborane at −100 to −130 °C, the reaction remains incomplete even after reaction times of several weeks (approximately 1/4 of the theoretically expected amount of diborane is consumed).

A small quantity of an unidentified compound, which is extremely sensitive to shock, is formed, and is obtained as a mixture with unreacted starting material and sodium tetrahydridoborate. The solid reaction products that remain when the unreacted diborane is pumped off give no gaseous decomposition products when slowly warmed to room temperature (similar results in suspension in pentane). If the solid starting material is suspended in ether and allowed to react with diborane at −78 to −110 °C, N_2O and H_2 are formed during the reaction and during subsequent warming to room temperature. The residue contains $Na[BH_4]$ as the only identified product containing a BH bond. The diborane consumption in these reactions is about 1 BH_3 per NaNO formula unit.

N_2O does not form a complex with diborane in the homogeneous gas phase between −105 °C and room temperature, as can be seen from pV/T curves. NO is also inert. It reacts slowly with diborane only at +90 °C with formation of H_2, N_2O, and H_3BO_3. The reaction becomes explosive at +120 °C.

Since boranecarbonyl decomposes primarily into CO and BH_3 even below room temperature, this compound seemed to be a particularly suitable starting material for the formation of borane complexes of the nitrogen-oxygen compounds at low temperatures. The required boranecarbonyl was partly prepared by a new method in normal glass apparatus without the use of pressure.

A gaseous mixture of diborane and carbon monoxide is heated on a hot finger at 200 °C, and the BH_3CO formed is simultaneously condensed in the bottom of the vessel at −150 °C. Attempts to prepare BH_3CO directly from $Na[BH_4]$ CO, and acid, on the other hand, have been unsuccessful. Boranecarbonyl begins to react with NO even at −135 °C with liberation of CO. Investigations in a low temperature IR cell showed that N_2O is formed even at this low temperature. A white coating of H_3BO_3 is also formed. The intermediate formation of BH_3NO could not be detected by IR spectroscopy. At higher temperatures (up to room temperature) the reaction with a large excess of NO leads almost quantitatively to N_2O, CO, and H_3BO_3. Mass spectra of a gaseous reaction mixture of BH_3CO and excess NO at very low pressures contained intense signals at mass numbers 28 (CO), 44 (N_2O), 26 ($^{11}B_2H_4$, $^{11}B^{10}BH_5$, $^{10}B_2H_6$), and 27 ($^{11}B_2H_5$ *etc.*). Very weak signals are also found at mass numbers 43 and 45, which can be interpreted as $^{10}BH_3{}^{14}N^{16}O$ and $^{11}BH_2{}^{14}N^{16}O$, and $^{11}BH_3{}^{15}N^{16}O$ (together with $^{14}N^{15}N^{16}O$) respectively. The species $^{11}BH_3{}^{14}N^{16}O$ (mass number 44) formed from the most abundant isotopes is, if present, masked by the N_2O, which has the same mass number and is always present.

Investigations on mixtures of N_2O with BH_3CO at room temperature in an IR gas cell have shown that the components do not react with each other. The boranecarbonyl decomposes quantitatively into B_2H_6 and CO in the course of several days with or without N_2O.

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[1] *L. J. Malone* and *R. W. Parry*, Inorg. Chem. *6*, 817 (1967). The work on "$(NaNO)_x$" (*cis*-$Na_2N_2O_2$) and diborane was done under the supervision of Prof. *R. W. Parry* during a post doctoral fellowship at the Dep. of Chemistry, Univ. of Michigan, Ann Arbor, Mich., USA; earlier results from our laboratory were probably in error [*J. W. Gilje*, Dissertation, Freie Universität Berlin 1965; Dissert. Abstr. *26*, 2458 (1966)].

[2] *J. Goubeau* and *K. Laitenberger*, Z. anorg. allg. Chem. *320*, 78 (1963).

Hydroformylation of Unsaturated Compounds with Carbonyltrialkylphosphinerhodium Catalysts

By *B. Fell* (lecturer) and *W. Rupilius* [*]

It is well known that the hydroformylation of an olefin is accompanied by double-bond isomerization, as a result of which even a compound having a definite double-bond position gives not only the aldehydes (or alcohols) corresponding to the olefin, but a mixture of all theoretically possible positional isomers. If the cobalt catalyst normally used is replaced by a complex carbonyltrialkylphosphinecobalt catalyst, even reactions with olefins having internal double bonds lead preferentially to the unbranched aldehyde.

In contrast with the cobalt-catalyzed reaction, the rhodium-catalyzed hydroformylation is accompanied by slight double-bond isomerization. This is completely suppressed by the use of a catalyst combination of a rhodium compound and excess trialkylphosphine. It is important to maintain a molar ratio of rhodium to phosphine of at least 1:50 to 1:60.

It is even possible with this catalyst system to hydroformylate compounds that formerly failed to undergo the reaction, owing to the formation of other products, *e.g.* allyl alcohol or 2-butene-1,4-diol, as a result of double-bond isomerization. 1,5,9-Cyclododecatriene reacts smoothly to form the tris-hydroformylated product. Other dienes and polyenes with isolated double bonds react similarly. The most important success achieved with this catalyst system was the first double hydroformylation of conjugated dienes such as 1,3-butadiene or 1,3-pentadiene.

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Determination of the Branching Ratio in the Disintegration of ^{242}Am

By *H.-J. Born, R. Gasteiger* (lecturer), *G. Höhlein*, and *W. Weinländer* [*]

In connection with the production of heavy nuclides by neutron irradiation of ^{241}Am, it is important to know the decay ratio of the resulting ^{242}Am, which decays by β^- emission into ^{242}Cm and by E. C. into ^{242}Pu.

Since the values in the literature exhibit considerable scatter, this ratio was redetermined by measurements on the two plutonium isotopes ^{238}Pu and ^{242}Pu. Unlike other methods, the method used here avoids sources of error such as losses on

prolonged irradiation as a result of fission and neutron capture, and inaccuracies in the determination of the neutron flux and in the absolute measurement of activities.

The most important requirement is a clean separation of the Pu isotopes formed from Am and Cm; the requirements concerning the decontamination of Am (factor 10^{-9}) are particularly rigorous, since the α energies of ^{241}Am and ^{238}Pu are practically identical. Ion-exchange separation satisfied the requirements for the purity of the Pu fraction only when anion exchangers and cation exchangers were combined.

The activity ratio of the Pu isotopes was determined by α spectroscopy, the α preparations being prepared electrolytically.

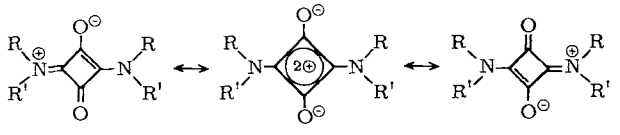
It was found that the ratio in the decay of the isotope ^{242}Am is β^-/E.C. = 4.8 ± 0.1.

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Condensation Products of Squaric Acid with Primary and Secondary Amines

By *J. Gauger* (lecturer) and *G. Manecke* [*]

Condensation of 1,2-dihydroxycyclobutenedione (squaric acid) with primary or secondary amines gave squaric acid 1,3-diamides *(1)*, which, as derivatives of 1,3-diaminocyclobutenediylium diolate, form a new class of intramolecular salts.

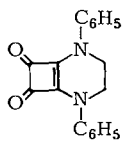


(1) R = H, Alkyl; R' = H, Alkyl, Aryl

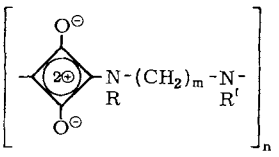
These compounds contain the resonance-stabilized cyclobutenediylium diolate system, which makes them very stable both chemically and thermally because of its quasi-aromatic character.

The structure of the squaric acid 1,3-diamides *(1)* was proved by synthesis of 1,3-bis(2,4,6-trimethylphenylamino)cyclobutenediylium diolate (exclusion of ring substitution in the aromatically substituted compounds) and by IR, NMR, and mass-spectroscopic measurements.

The chelating ability of the 1,3-diaminocyclobutenediylium diolates with donor groups in the *o*-position of the phenyl ring was investigated, the copper chelates of these compounds were prepared, and the Cu^{2+}: ligand ratio in these chelates was found to be 2:1. In the dialkali metal compounds of the three isomeric 1,3-bis(nitrophenylamino)cyclobutenediylium diolates, the deeply colored alkali metal salts of the *o*- and *p*-nitro compounds contain a novel quinoid dye system, in which the cyclobutenediylium diolate grouping is in resonance interaction with the aromatic nuclei and the nitro groups *via* N atoms. The *m*-nitro compound, on the other hand, gives a much weaker color deepening with alkali, since no resonance *via* quinoid structures is possible in this case.



(2)



(3)

(3a), R = C_6H_5; m = 2
(3b), R = H, alkyl; m = 6, 8, 10
(3c), R = H, alkyl; *p*-phenylene- or *p*-biphenylylene- in place of $-(CH_2)_m-$

Condensation of squaric acid with *N,N'*-diphenylethylenediamine led to the cyclic compound *(2)* and the chain polycondensate *(3a)*.

We were also able to prepare the polycondensation products *(3b)* and *(3c)*.

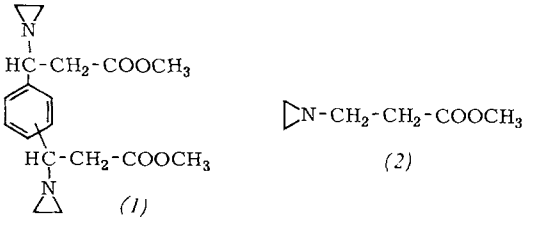
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Synthesis and Characterization of Amphoteric and Novel Weakly Basic Ion Exchangers with Strictly Uniform Structures

By *P. Gergs* (lecturer) and *G. Manecke* [*]

The amphoteric ion exchangers synthesized so far by copolymerization of aziridinylalkanecarboxylic acid esters with bisaziridinyl compounds followed by hydrolysis of the ester groups were not uniform in structure [1].

By copolymerization of dimethyl benzene-1,3- (or -1,4-)bis-(3-aziridinylpropionate) *(1)* [2] with methyl 3-aziridinylpropionate *(2)* followed by hydrolysis of the ester groups, we have obtained an amphoteric ion exchanger whose structure



(1) *(2)*

is perfectly uniform with respect to the functional groups. Crosslinking occurs only *via* the benzene rings built into the polymer chains. It was shown by elemental analysis that the composition of the hydrolyzed copolymer corresponds to the ratio of the components in the copolymerization. The occurrence of side reactions and degradation reactions during the copolymerization or hydrolysis can be ruled out. A crosslinker content of 25–30 mole-% has been found to be particularly suitable. The copolymers are light yellow, and exhibit excellent chemical and mechanical stability. They have good swelling properties; because of their amphoteric character, their swelling minimum occurs at pH = 3–4. The complexing properties of the copolymers have been examined with heavy metal ions (Cu^{2+}, Ni^{2+}, Zn^{2+}). 5 mequiv of Cu^{2+}/g of resin were taken up at pH = 6. The metal ions can be quantitatively eluted with acids.

Column-chromatographic separations of metal ions and of amino acids and peptides have also been tried on the new amphoteric ion exchangers. Good separations were obtained in some cases.

We have also prepared copolymers from aziridine and the crosslinking substances mentioned. These copolymers are novel weakly basic exchangers having very good chemical and mechanical stabilities, which form complexes with heavy metal ions and can be used for the column-chromatographic separation of weakly acidic amino acids.

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[1] *G. Manecke* and *H. Heller*, Makromolekulare Chem. *55*, 51 (1962); *G. Manecke* and *A. Grohmann*, *ibid.* *82*, 146 (1965); *G. Manecke*, *P. Gergs*, and *H. P. Aurich*, unpublished.

[2] *G. Manecke*, *P. Gergs*, and *H. P. Aurich*, Chem. Ber. *99*, 2444 (1966).

Unstable Carbonium Ions

By *R. Gleiter*[*]

Charge stabilization by interaction with neighboring groups is practically impossible in the phenyl cation and in bicyclic hydrocarbons carrying a positive charge on the bridgehead.

The possibility of a π-σ-π interaction[1] for the stabilization of these ions will be discussed here. In this type of interaction, two π orbitals are coupled *via* a σ bond. If the two π orbitals contribute only two electrons to the bond, the system is stabilized.

It was assumed in the calculation that the ion has a singlet ground state and has the same geometric structure as the parent hydrocarbon. As a measure of the stabilization, the energy required to remove a hydride ion from the hydrocarbon was calculated. In the presence of hetero atoms, the inductive effect leads to destabilization.

Results: In the case of the phenyl cation, hetero atoms such as N in the *ortho* position have a destabilizing effect, while in the *meta* position they have a stabilizing effect (approx. 0.1 eV). Vinyl and cyclopropyl groups have a stabilizing effect both in the *ortho* and in the *meta* position (approx. 0.1 eV). Of the three possible pyridyl cations, only the 4-pyridyl cation exhibits stabilization (0.25 eV). Among the bicyclic compounds, those having the quinuclidine structure are stabilized, whereas molecules derived from 1-azanorbornane are destabilized.

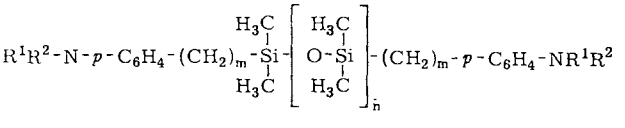
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[1] *R. Hoffmann, A. Imamura*, and *W. J. Hehre*, J. Amer. chem. Soc. *90*, 1499 (1968).

Preparation and Polycondensation Reactions of Aromatic Diamines Containing Siloxane Chains

By *G. Greber* (lecturer) and *D. Lohmann*[*]

By condensation of permethylated α,ω-dichloropolysiloxanes with 4-[*N,N*-bis(trimethylsilyl)amino]phenylmagnesium bromide or 4-[*N,N*-bis(trimethylsilyl)amino]phenyllithium and by addition of corresponding siloxanes with H instead of Cl to *N*-trimethylsilyl-4-allylaniline or 4-allyl-*N,N*-bis(trimethylsilyl)aniline, we have synthesized siloxane-modified *N*-silylated aromatic diamines *(1)*, *(2)*, and *(3)*, which can be converted into the free diamines *(4)* by hydrolysis or alcoholysis



(1), $R^1 = R^2 = (CH_3)_3Si$, m = 0, n = 1 - 3
(2), $R^1 = (CH_3)_3Si$-, R^2 = H, m = 3, n = 1 - 3
(3), $R^1 = R^2 = (CH_3)_3Si$, m = 3, n = 1 - 3
(4), $R^1 = R^2$ = H, m = 0 or 3, n = 1 - 3

The polycondensation of the fully silylated diamines *(1)* and *(3)* with acyl chlorides of dicarboxylic acids leads to loss of chlorotrimethylsilane and formation of interesting polyamides that are silylated on the amide groups, and which are soluble in benzene and tetrahydrofuran. On removal of the trimethylsilyl groups by hydrolysis, these give siloxane-modified, high-melting polyamides, which are soluble only in the typical polyamide solvents and are stable up to about 400 °C.

The fully silylated diamines *(1)* and *(3)* surprisingly also undergo polycondensation with pyromellitic dianhydride to give soluble and fusible polyimides having decomposition points between 430 and 500 °C. In contrast with the usual process, hexamethyldisiloxane is eliminated in this case instead of water, so that no hydrolytic degradation of the polyamidic acid molecules can occur.

Siloxane-modified polyimides having comparable properties can also be obtained by polycondensation of ordinary aromatic diamines with dianhydrides containing siloxane chains. Dianhydrides of this type are formed on reaction of α,ω-bis(4-trimethylsiloxyphenyl)siloxanes with trimellitic 1,2-anhydride 4-chloride, with elimination of chlorotrimethylsilane.

Soluble and fusible polymeric Schiff bases that are stable up to about 500 °C were obtained by polycondensation both of the free amines *(4)* and of the tetrasilylated diamines *(1)* and *(3)* with terephthaldialdehyde.

The thermal stability values indicated were determined in the presence of atmospheric oxygen by thermogravimetric analysis.

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Photochemical and Thermal Reactions of Carbonyliron Compounds with Halogenoalkanes and Halogenoalkenes

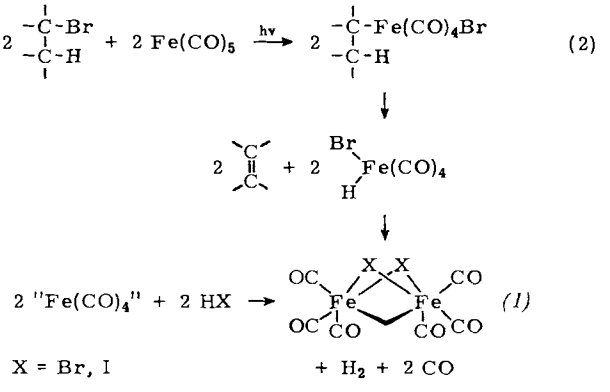
By *E. Koerner von Gustorf, F.-W. Grevels* (lecturer), and *J. C. Hogan*[*]

Organic halogen compounds with no readily abstractable β hydrogen can be photochemically dimerized by dehalogenation by $Fe(CO_5)$ [eq. (1)]. Alkyl halides with hydrogen in the

$$Fe(CO)_5 + 2\,RX \xrightarrow{h\nu} R_2 + FeX_2 + 5\,CO \qquad (1)$$

R = *e.g.* cycloheptatrien-7-yl

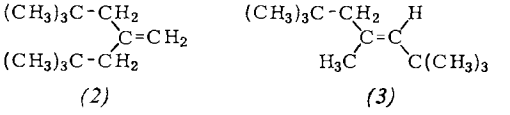
β position, such as *tert*-butyl bromide, react in accordance with eq. (2).



(2)

The novel dinuclear di-μ-halogenobis(tricarbonyliron) compounds *(1)* are also formed from "$Fe(CO)_4$" [from the photolysis of $Fe(CO)_5$ or from $Fe_2(CO)_9$] and hydrogen halide.

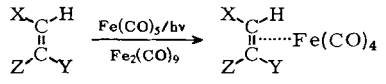
$Fe(CO)_5$ and *tert*-butyl bromide react photochemically to give isobutylene, which is converted mainly into the trimers *(2)* and *(3)*. Exposure of bromotricarbonyl-2-methallyliron or tricarbonyl(trimethylenemethyl)iron in *tert*-butyl bromide



(2) *(3)*

and isobutylene to light leads practically exclusively to *(2)* and *(3)*.

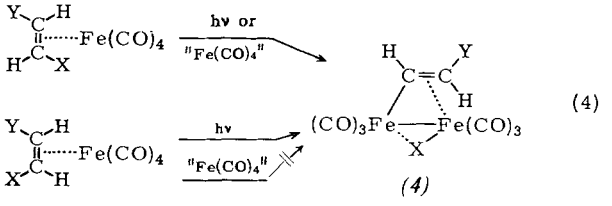
Halogenoethylenes react in accordance with eq. (3) to give the corresponding $Fe(CO)_4$ complexes.



(3)

X = F, Cl, Br, I; Y = H, Cl, Br, I; Z = H, Cl, Br, I

According to IR studies, the olefinic ligands are normally arranged equatorially in the trigonal-bipyramidal $Fe(CO)_4$ complexes, but appear to assume axial positions in the *trans*-1,2-dihalogenoethylene complexes. The carbon-halogen bond in the latter compounds is particularly reactive (cf. *e.g.* scheme (4)).



(4)

(4)

X = Cl, Br, I; Y = F, Cl, Br, I

(4) reacts with alcohols to give tetracarbonyliron complexes of acrylic esters, and tetracarbonyl-2-butene-1,4-dione-1,4-diyliron is formed in acetic acid. Both reactions probably proceed *via* an unstable acetylene complex.

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Quantitative Determination of Impurities in Boron Carbide by Neutron Activation Analysis

By *W. Gückel* (lecturer) and *H.-J. Born*[*]

When boron carbide is used in reactor technology, the nature and quantity of the impurities present should be accurately known. Chemical methods of trace analysis and spectral methods are of little value because of the great chemical and mechanical resistance of boron carbide. Activation analysis, on the other hand, offers a sensitive and non-destructive analytical procedure. However, the large cross section of boron for thermal neutrons presents considerable difficulties in activation and in the quantitative evaluation.

The first of three activation methods examined uses only nuclear reactions initiated by fast neutrons. This avoids the inhomogeneous activation of the sample caused by thermal neutrons and resonance neutrons. Since short-lived nuclides are formed in most cases, these investigations were carried out in the fast rabbit system of the Munich experimental reactor. The detection sensitivities that could be obtained in this way were unfortunately relatively low.

In the second method, thermal neutrons and resonance neutrons are used, and activation is practically confined to the surface of the sample. A correction factor is calculated to compensate for self-absorption effects. Good sensitivities could be obtained with this method, but it has the disadvantage that information about the sample as a whole must be deduced from the state of the surface layer.

In the third method, the inhomogeneous activation by thermal neutrons is avoided by irradiation behind a cadmium filter. The (n,γ) activations due to resonance neutrons are practically homogeneous in small specimens. The impurities throughout the volume of the specimen are found in this way, but the detection sensitivities are lower than with surface activation.

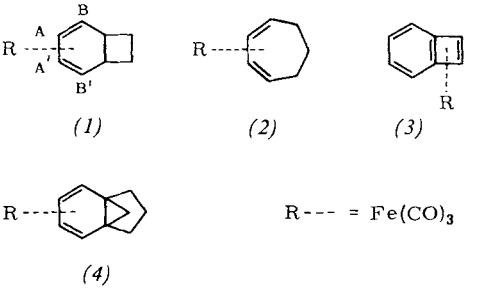
The trace content (ppm range) of Na, Al, Si, Sc, V, Mn, Cr, Fe, Co, and As were determined quantitatively. In some boron carbide specimens that had been purified by repeated zone melting, it was still possible to detect very small quantities (ppb range) of Na, Sc, Mn, and Co.

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NMR-Spectroscopic Studies on Olefin-Tricarbonyliron Complexes

By *H. Günther* (lecturer) and *R. Wenzl*[*]

The ^1H—NMR spectra of the tricarbonyliron complexes of bicyclo[4.2.0]octa-2,4-diene *(1)*, 1,3-cycloheptadiene *(2)*, benzocyclobutadiene *(3)*, and tricyclo[4.3.1.$0^{1,6}$]deca-2,4-diene *(4)* have been analyzed. The protons in the unsaturated part of the compounds give spectra of the AA'BB' type, which



(1) *(2)* *(3)* *(4)*

are perturbed by long-range coupling with protons on saturated C atoms, but can be calculated without difficulty (see Table).

Table: τ-values (in ppm) and coupling constants J (in Hz) for the olefinic protons in *(1)*–*(4)*

	$\tau_{AA'}$	$\tau_{BB'}$	J_{AB}	$J_{AB'}$	$J_{AA'}$	$J_{BB'}$
(1)	5.06	6.92	6.59	1.62	4.23	0.20
(2)	5.25	7.34	7.61	1.13	4.83	0.44
(3)	5.51	6.62	6.77	1.50	4.06	0
(4)	3.42 [a]	3.56 [a]	8.61	0.68	6.77	1.57

[a] assignment uncertain.

In the diene systems of *(1)* and *(2)*, the vicinal coupling constants are lower than the corresponding values in the free olefins. For J_{AB}, the change can be explained according to the equation [1]

$$^3J = -35.10\, R_{\mu,\nu} + 56.65$$

by the increase in the C—C distance $R_{\mu,\nu}$ in the complex. This correlation fails, however, for $J_{AA'}$. Other factors such as changes in the valence and dihedral angles and a substituent effect of the $Fe(CO)_3$ group must therefore be effective. The dependence of the ^3J values on the ring size as observed for cyclic olefins is confirmed in the complexes.

In *(3)*, the ^3J values exhibit considerably larger alternation in the six-membered ring than in benzocyclobutene (J_{AB} = 8.61, $J_{AA'}$ = 6.77 as against J_{AB} = 7.36, $J_{AA'}$ = 7.78 Hz), for which the strain effects are roughly comparable. It can therefore be concluded that partial bond fixation in the six-membered ring of *(3)* has occurred. This interpretation is supported by the magnitudes of the long-range coupling

constants ($J_{AB'}$ = 0.68, $J_{BB'}$ = 1.57 Hz). In the $Fe(CO_3)$ complex of anthracene analyzed by *H. Klose*[2], on the other hand, the complex formation evidently leads to isolation of a diene system. The NMR parameters in the uncomplexed part of the molecule are similar to those in naphthalene.

The norcaradiene complex *(4)* analyzed by *W. Bleck*[3] gives "normal" values for the H,H coupling constants, showing that the ligand is an olefin. On the other hand, a special bonding type evidently exists in the corresponding tricarbonylchromium complex, since the three-membered ring must also be involved in complex formation in this case.

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[1] *J. B. Pawliczek* and *H. Günther*, Tetrahedron, in press.

[2] *H. Klose* and *H. Günther*, unpublished.

[3] *W. Bleck*, Dissertation, Universität Köln 1969.

Homogeneous Precipitation of Halometalates from Anhydrous Acetic Acid

By *H. D. Hardt* (lecturer), *M. Fleischer*, and *G. Streit*[*]

Many heavy metals can be precipitated from solutions in glacial acetic acid *e.g.* in accordance with

$$M(CH_3COO)_2 \xrightarrow{CH_3COX} [MX_3]^- \xrightarrow{K^+,NH_4^+,\ etc.} Y[MX_3],\ Y_2[MX_4],\ etc.$$

M = metal, Y = cation, X = halogen

as halometalates, and the conditions for successive precipitations and/or heterogeneous transformations of the primary precipitate can be fixed by conductometric control. From solutions of trichlorocobaltate(II), for example, $NR_4[CoCl_3]$, $R=CH_3$, precipitates first, and changes on further addition of NR_4^+ into $(NR_4)_2[CoCl_4]$ (both compounds with tetrahedral crystal fields).

Precipitation with ammonium ions, on the other hand, after primary precipitation of $NH_4[CoCl_3]$ (blue, octahedral crystal field, hexagonal: a = 6.97 Å, c = 6.02 Å), leads directly to the pentachlorocobaltate, whose tetrahedral coordination is deduced from the reflection spectrum, and which should therefore be formulated as $NH_4^+\cdot(NH_4)_2[CoCl_4]\cdot Cl^-$. It decomposes thermally at 150 °C to give $NH_4[CoCl_3]$, which changes at 205 °C into $CoCl_2$.

This method can be used for the preparation of thermally unstable double salts, and yields *e.g.* the colorless tetramethylammonium trichlorochromate(II), $NR_4[CrCl_3]$.

Without the addition of alkali, acetic acid solvates of the corresponding halides, *e.g.* $CoCl_2 \cdot {}^1/_2CH_3COOH$ and $CrCl_2 \cdot {}^3/_2CH_3COOH$, are generally obtained; in the case of the chromium(II) halides, the dimeric solvate $Cr_2(CH_3COO)_4\cdot 2CH_3COOH$, which is structurally identical with $Cu_2(CH_3COO)_4\cdot 2\ CH_3COOH$, is formed[1].

Whereas the chlorochromate(III) ion in acetic acid solution exhibits characteristic splitting of the ${}^4A_{2g} \rightarrow {}^4T_{2g}$ transition, which points to C_{4v} symmetry, this splitting is absent from the reflection spectra of pentahalochromates(III), *e.g.* $(NR_4)_2[CrCl_5]\cdot CH_3COOH$, precipitated from such solutions. Their structure should therefore be characterized by practically regular octahedral crystal fields and probably by chains of $[CrX_6]$ units.

By comparison of the powder diffraction diagrams of the primary precipitates in the reaction medium with those of the dry samples, it is possible to decide whether acetic acid solvates are formed. Whereas the alkali metal halometalates (*e.g.* $K[CoCl_3]$, $NH_4[CoCl_3]$, $NH_4^+\cdot(NH_4)_2[CoCl_4]\cdot Cl^-$) generally precipitate out without solvation, acetic acid solvates of the pentahalogenochromates(III) are formed when they are precipitated as salts of organic nitrogen bases. The absorption due to the ${}^4A_{2g} \rightarrow {}^4T_{2g}$ transition, which occurs at 500–550 nm, shows a systematic red shift which increases with the cation in the order $K^+ < NH_4^+ < Rb^+ < Cs^+ = (NR_4)^+$.

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[1] *H. D. Hardt* and *G. Streit*, Naturwissenschaften *55*, 443 (1968).

Fatty Acids and Hydrocarbons from Extracts and Distillates of Bituminous Shales

By *W. Heller*[*]

The *Posidonomya shales* of Swabia have repeatedly attracted attention because of their bitumen content, though this is low. Where the shale material lies close to the surface, small smouldering fires often occur when the field is set alight. The object of the present investigations is to throw some light on the composition of the bituminous substance. The fats [triglycerides (neutral fats), esters of fatty acids, and free fatty acids] and hydrocarbons were examined. Even in bitumen extracted under mild conditions, the fatty acids are present mainly in the free state, but only in very small quantities. Triglycerides are, however, also present, and these were determined by methods for the determination of neutral fats. They are mainly derived from C_4 to C_8 fatty acids; there are no esters of long-chain fatty acids present. Micro methods are required for the detection of the individual fat fractions.

The gas chromatograms of the Posidonomya shale extracts show clearly that C_{15} und C_{17} *n*-hydrocarbons predominate. These can be definitely attributed to the corresponding physiologically important fatty acids, which have been decarboxylated in the sediment. Gas-chromatographic investigations on many petroleums lead to similar results. The strikingly high C_5 signal is very probably due to carbohydrates.

The aromatic components include benzene and its derivatives, particularly toluene, as well as polynuclear aromatic hydrocarbons such as anthracene, benzopyrene, phenanthrene, and pyrene. However, the aromatic hydrocarbons are present in much smaller quantities than the *n*-hydrocarbons.

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Properties of the Si—Si Bond

By *E. Hengge*[*]

It is well known that double Si—Si bonds using p orbitals cannot be formed. This agrees with the behavior of other elements with principal quantum numbers n = 3 and > 3. Strengthening of bonds by $(p \rightarrow d)_\pi$ bonding, such as occurs with phosphorus, sulfur, chlorine, *etc.*, is impossible for silicon because of lack of electrons.

The strength of the Si—Si bond nevertheless differs with the substituents. The force constant fSiSi in the hexahalogenodisilanes increases rapidly from iodine to chlorine. The strong influence of the substituents on the SiSi force constant can also be seen in a series of disilane derivatives with mixed substituents (methylchloro-, methylmethoxy-, and methyldimethylaminodisilanes), the value of the force constant changing in the order:

$$CH_3 < H < I \approx C_6H_5 < Br < Cl < OCH_3 < N(CH_3)_2$$

It is clear, therefore, that the strength of the Si—Si bond increases with the electron density on the silicon, which suggests that the additional bonding component is due to this increased electron density, presumably with participation of d states.

On the other hand, shifts in the UV spectrum in the sense of this series cannot be accurately detected. Bathochromic shifts occur preferentially on asymmetric substitution.

Comparable effects are also found for cyclic silanes. Several derivatives of cyclopentasilane (phenyl, methyl, methoxy, iodo, and butyl derivatives, as well as derivatives with mixed substituents) showed no appreciable shifts in the UV spectrum. Corresponding to the strong bathochromic shift of chain silanes with increasing chain length, however, bathochromic shifts into the visible region occur on polycondensation of rings.

The chemical properties of the Si—Si bond also change with the bond strength, though additional factors connected with the nature of the reaction must naturally also be considered in this case. Thus the Si—Si bond reacts preferentially with Grignard reagents only if the bond is asymmetrically substituted, if ring strain is present, or if additional halogen atoms are present on the Si.

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Activation Analysis of Boron and some Elements of the Rare Earths by Means of Prompt Neutron Capture γ Radiation

By *R. Henkelmann* (lecturer) and *H.-J. Born* [*]

The prompt γ quanta are emitted 10^{-14} to 10^{-12} seconds after neutron capture from the excited state of the intermediate nucleus, with liberation of the bonding energy of the neutron (6–8 MeV). The transition to the ground state generally proceeds *via* numerous intermediate states, so that very complex γ spectra are produced.

The prompt γ radiation is useful mainly for macroscopic analyses, and is suitable for trace determinations of only a few elements. The method can be used to advantage for the detection of elements whose determination by measurement of the (n,γ) reaction products is difficult either because no suitable γ spectrum exists or because the half-lives involved are too extreme. The method depends on the thermal neutron flux available and the reaction cross sections of the isotopes investigated. The isotope having the highest cross section and having a high abundance often forms a stable reaction product (B, Cd, Sm, Gd, Se, *etc.*).

Since the spectra contain very large numbers of lines, a planar Ge(Li) crystal of volume 13 cm^3 is used together with a 1600 channel pulse-height analyzer to record the γ spectra. The resolution of the detector is about 4.2 keV for the 661.6 keV line of ^{137}Cs. Owing to the low response probability of the detector for high-energy γ quanta, only the spectra in the region 0—1 MeV are recorded for analysis.

The γ spectra of 20 elements have been recorded, and the detection limits for these elements have been calculated from the spectra and checked experimentally. At the neutron flux of 1.5×10^7 n cm^{-2} sec^{-1} available, the detection limits for the elements B, Cd, Eu, Gd, and Sm are about 1 μg, those for Dy, Er, Hg, In, and Sc are about 10 μg, and those for all other elements are higher. This method can be used for the determination of lanthanides in minerals and boron in metals.

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Complex Formation Between Unsaturated Nitriles and Carbonylmetal Compounds

By *M. Herberhold* (lecturer) and *H. Brabetz* [*]

In solution cyanoolefins can add to the complex fragment $[C_5H_5Mn(CO)_2]$ formed photolytically ($\lambda > 300$ nm) from $C_5H_5Mn(CO)_3$. The question whether the cyanoolefin is coordinated *via* the olefinic π system [as in $C_5H_5Mn(CO)_2C_2H_4$] or *via* the free electron pair on the nitrogen atom of the cyano group [as in $C_5H_5Mn(CO)_2(NC—C_6H_5)$] depends both on the reaction conditions and on the steric conditions at the C=C double bond.

Direct irradiation of $C_5H_5Mn(CO)_3$ in the presence of acrylonitrile [1] or crotononitrile in benzene/hexane leads predominantly to π-complex formation. Coordination *via* the cyano group predominates when $C_5H_5Mn(CO)_3$ is irradiated in THF followed by displacement of the ether ligand in $C_5H_5Mn(CO)_2(OC_4H_8)$ by acrylonitrile or crotononitrile. Cinnamonitrile and fumarodinitrile form intensely red "nitrile complexes"; in both cases, the coupling constant of the olefinic protons in the ^1H—NMR spectrum points to a free *trans* double bond: $C_5H_5Mn(CO)_2(NC\text{-}CH'=CH\text{-}C_6H_5)$, $\tau = 5.47$ (C_5H_5 protons/s), 2.64 (1H/d), 3.81 (1H′/d) $J_{H,H'} = 16$ Hz; $C_5H_5Mn(CO)_2(NC—CH=CH—CN)$, $\tau = 5.39$ (C_5H_5 protons/s), 3.48 and 3.64 (2H/AB system with center at $\tau = 3.56$) $J_{A,B} = 16.5$ Hz; measurement in $[D_6]$-acetone. Tetracyanoethylene (TCNE), on the other hand, appears to be π-bonded through the olefinic double bond.

$C_5H_5Mn(CO)_2L$ compounds containing π-bonded cyanoolefins (L) exhibit a shift of the cyclopentadienyl proton signal toward lower field in the ^1H—NMR spectrum (in $[D_6]$-acetone), as compared to the corresponding complexes of σ-bonded nitriles. The shift is dependent on the number of cyano groups: $\tau(C_5H_5) = 5.35$ ($L = C_2H_4$), 5.10 ($CH_2=CH\text{-}CN$), 5.17 and 5.19 ($CH_3CH=CH—CN$), 4.84 (NC—CH=CH—CN), 4.48 (TCNE).

The force constant $k(C\equiv O)$ of the $C\equiv O$ stretching vibrations [2] in the IR spectrum is related linearly, to a first approximation, to the position of the C_5H_5 proton signal in the ^1H—NMR spectrum. If the cyanoolefin is coordinated *via* the free electron pair on the nitrogen atom of the nitrile group, the C_5H_5 proton signal always appears in the region $\tau \approx 5.35$-5.50. This is also characteristic of complexes of *p*-substituted benzonitrile of the type $C_5H_5Mn(CO)_2(NC\text{-}C_6H_4\text{-}Z)$ ($Z = CH_3O$, CH_3, H, CN, NO_2).

In compounds such as $(TCNE)Cr(CO)_5$ [3], the coordinated cyanoolefin partly retains its π-acid character. This is in agreement with the assumption that this compound is a true π-olefin complex.

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Structure of Dimeric Dimethylaminodimethylaluminum

By *H. Hess* (lecturer), *A. Hinderer*, *S. Steinhauser* (deceased), and *J. Weidlein* [*]

Dimeric dimethylaminodimethylaluminum has been investigated by X-ray analysis and molecular spectroscopy. The compound crystallizes in the monoclinic space group $P\ 2_1/a$ with the lattice constants $a = 12.85$, $b = 8.15$, $c = 7.63$ Å, $\beta = 117.7°$ and with 2 molecules in the unit cell. The structure was deduced from 711 reflection data *via* Patterson,

Fourier, and difference Fourier syntheses and refined by the method of least squares to an R value of 5.9% (anisotropic temperature factors, hydrogen atoms included). The molecules form planar, square 4-membered rings of alternating Al and N atoms. The following mean bond lengths were found: Al—N = 1.96, Al—C = 1.96 and N—C = 1.49 Å. In agreement with the centrosymmetry of the molecules, as found by crystallography, the IR and Raman spectra satisfy the alternative selection rules.

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Scavenger Experiments on the Mechanism of the Radiolysis of Ethylbenzene

By *H. Heusinger* (lecturer) and *H. Hofer* [*]

In the radiolysis of ethylbenzene, styrene (G = 0.031) and the possible side-chain dimers C_6H_5—$CH(CH_3)$—$CH(CH_3)$—C_6H_5 (G = 0.046), C_6H_5—CH_2—CH_2—$CH(CH_3)$—C_6H_5 (G = 0.0002), and C_6H_5—$(CH_2)_4$—C_6H_5 (G = 0.0001) were quantitatively determined.

Scavengers for free radicals and quenchers for excited states were used to clarify the mechanism. These investigations showed that styrene is formed independently of 2,3-diphenylbutane by elimination of molecular hydrogen from ethylbenzene. Various reaction paths must be considered for the formation of 2,3-diphenylbutane. Styrene and 2,3-diphenylbutane can account for only about 25% of the radiolytic liberation of hydrogen.

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Technological Observations in the Hardening of Varnishes with Electron Beams

By *H. Hinrichs* (lecturer) and *K. Wasem* [*]

The hardening of varnishes with electron beams at room temperature has attracted great interest, particularly since the varnish films harden thoroughly in seconds with practically no evolution of heat, and high throughputs are possible in continuous operations. The process is particularly recommended for the hardening of varnish films on heat-sensitive materials such as wood, paper, cardboard, plastics, and textile fibers.

The coating materials must be oligomers or synthetic resins with polymerizable double bonds activated by neighboring groups, which crosslink under the influence of the high-energy ionizing electron radiation.

These synthetic resins are adjusted to the desired working viscosity with polymerizable monomers such as styrene or esters of acrylic or methacrylic acids. The reactivity of a varnish system that can be hardened with electron beams depends both on the synthetic resin and on the monomer. The ratio of the quantities of synthetic resin and monomer is also of decisive importance for the tack-free hardening of a varnish film.

When the irradiation is carried out in air, the predominantly free-radical polymerization process is inhibited by oxygen, and the film surface remains tacky in many varnish systems. If the hardening is carried out under an inert gas (*e.g.* nitrogen), the surface crosslinking is improved and the radiation dose is reduced by 50—70 %.

Pigments do not interfere with the hardening process, provided that they are not affected by the radiation. Radiation-hardened, pigmented varnishes generally exhibit good gloss and smoothness. As expected, their solvent resistance and surface hardness are better than those of clear varnishes.

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Determination of Medium-Heavy Elements by γ-Excited X-Ray Fluorescence

By *M. Hollstein* [*]

The use of γ-excited X-ray fluorescence for the quantitative determination of medium-weight elements was investigated. The X-ray spectrometer used was a high-resolution semiconductor detector-preamplifier system in conjunction with a ^{241}Am source and conventional multichannel pulse-height analysis electronics. The energy resolution of the spectrometer was about 1 keV (FWHM) for photon energies of 8—60 keV.

The contents of alloying components in the concentration range 0.04—9 % in a series of NBS standards were determined by direct measurements. It was found that a non-destructive analysis can be carried out in a few minutes with an accuracy of a few percent and a sensitivity of approximately 1×10^4 counts min^{-1} $\%^{-1}$. The detection limit is about 0.01 %.

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Automatic Determination of Sulfur Dioxide in Atmospheric Air

By *J. G. Hoogland* (lecturer), *H. Zeedijk*, and *H. J. Brouwer* [*]

Highly sensitive methods are required for the analysis of gaseous impurities in the atmosphere. The impurities, which are often present in sub-ppm concentrations, must be recorded automatically for control purposes [1]. Since a fully automatic system capable of operating for 3 months or more without supervision was required, the coulometric titration of sulfur dioxide in KBr solution containing Br_2 [2] was chosen as the method.

After 3 years of development, the automatic measuring system is now in production [**] and is intended for a measuring network covering the whole of the Netherlands. The first section is being constructed in the industrial area at Rotterdam [3]. The SO_2 absorbed in the KBr/H_2SO_4 electrolyte containing Br_2 forms sulfate and bromide. The decrease in the bromine concentration leads to a decrease in the potential of a Pt electrode; an electrolysis current is produced electronically between two auxiliary electrodes. The electrolysis current liberates bromine at the anode until an equilibrium is reached in which the titration current is proportional to the SO_2 content in the air.

Even when the air sample contains no SO_2, the bromine concentration decreases as a result of evaporation. It is important to keep the resulting "zero current" (*i.e.* the bromine concentration in the solution) small, but in such a way that the other properties of the apparatus are not adversely affected. This is possible in dilute sulfuric acid, in which SO_2 and Br_2 react rapidly.

The potential measurement used for adjustment of the bromine concentration does not obey the Nernst law in the operating range (bromine concentration $< 10^{-7}$ mole/l), but is influenced by atmospheric oxygen and dissolved SO_2. This dissolved SO_2 displaces the operating point during the titration, so that the bromine concentration shows practically no decrease, and even increases in certain circumstances. It is thus possible to select a very low bromine concentration in the rest state.

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High and Low Coordination Numbers in Compounds of the Elements of Group IVa

By *F. Huber* (lecturer), *H.-J. Haupt*, and *E. Schönafinger* [*]

Organolead compounds $R_{4-n}PbX_n$ react with salts MX to give the complex anions $[R_3PbX_2]^-$, $[R_2PbX_3]^-$ (R = C_6H_5, CH_3; X = Cl, Br, $OCOCH_3$), and $[RPbX_4]^-$ (R = C_6H_5; X = $OCOCH_3$), which can exhibit considerable thermal stability provided that the ionic radius of M is sufficiently large [Cs^+, $(C_6H_5)_4P^+$, $(C_6H_5)_4As^+$]. (Some analogous tin compounds are also known.) R_3GeX and R_2GeX_2 (R = C_6H_5, X = Cl, Br, I), on the other hand, do not react with salts of bulky cations, and the reaction of $C_6H_5GeCl_3$ with $[(C_6H_5)_4El]Cl$ (El = P, As) leads to dismutation into $GeCl_4 \cdot 4\,[(C_6H_5)_4El]Cl$ and $(C_6H_5)_4Ge$. Organochlorosilanes $R_{4-n}SiCl_n$ (n = 1, 2, 3; R = C_6H_5, CH_3), like $SiCl_4$, react with $[(C_6H_5)_4P]Cl$ to give $SiCl_4 \cdot 4\,[(C_6H_5)_4P]Cl$.

In the presence of salts having cations not suitable for the formation of stable anionic organolead complexes, the inert pair effect causes R_2PbX_2 to give PbX_2 and RX, and $(CH_3)_3Pb$-hal to dismutate to $(CH_3)_4Pb$ and $Pbhal_2$ (hal = Cl, Br).

The new compounds $(CH_3)_3SiCl \cdot 3(C_6H_5)_3PO$, $RSiCl_3 \cdot 3(C_6H_5)_3PO$ (R = C_6H_5, CH_3), and $SiCl_4 \cdot 4(C_6H_5)_3PO$ have ionic structures (*e.g.* $CH_3SiCl_3 \cdot 3(C_6H_5)_3PO = [CH_3SiCl\{(C_6H_5)_3PO\}_3]Cl_2$), and so exhibit no unusual coordination numbers (in solution up to 5).

The same is true of $R_3SiCl \cdot phen$ (R = C_6H_5, CH_3), $(C_6H_5)_2SiCl_2 \cdot phen$, $SiCl_4 \cdot 2$ phen, and presumably also $C_6H_5SiCl_3 \cdot 3$ phen (phen = 1,10-phenanthroline).

In studies on the coordination of organoelement compounds in solution, UV spectroscopic and conductometric measurements showed that organolead compounds interact strongly with the solvent. Thus in solutions of R_2PbX_2, dissociation leads exclusively to complex ions with coordination numbers ≥ 3. In solvents having pronounced donor functions, *e.g.* pyridine or acetone, complexes of the type $R_2PbX_2 \cdot 4$ donor occur in equilibria in these complex species, the central atom (the ligand distance being not uniform) having a coordination number of 8 in the limiting case. $(C_6H_5)_2PbI_2$ in benzene forms EDA complexes with solvent molecules, these complexes being detected by dipole measurements.

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A High-Spin Isomer of ^{179}Hf

By *N. Kaffrell* (lecturer), *W. Herzog*, and *N. Trautmann* [*]

The existence of high-spin isomers for neutron-rich lutetium and hafnium nuclides in the region of mass numbers 177, 178, and 180 led us to look for isomeric states at mass number 179. On irradiation of enriched ^{179}Hf and ^{180}Hf with 14 MeV neutrons, a hitherto unknown component having a half-life of 25.3 ± 0.3 d was found. After irradiation of natural hafnium nitrate with 14 MeV neutrons, we separated lutetium and hafnium by partition between HDEHP [**] and 0.2 N hydrofluoric acid; the characteristic γ lines of the 25 d component could then be detected only in the Hf fraction.

Further investigation of the γ radiation with high-resolution Ge(Li) detectors and γ–γ coincidence measurements with two semiconductor detectors allowed the construction of a decay scheme. Of the twelve identified γ lines at 122.6, 146.3, 170.0, 192.7, 217.3, 236.5, 257.6, 268.9, 316.6, 362.7, 410.0, and 453.8 keV, eleven γ transitions can be fitted in the energy-level diagram of a rotational band based on the [624↑] ground state of ^{179}Hf.

The isomeric state could be a three-quasiparticle state of configuration p[514↑], p[404↑], n[624↑] with spin and parity of $J^\pi = 25/2^-$. This state is depopulated by a 257.6 keV γ transition, the multipolarity of which is assumed to be E3 on the basis of the indirectly determined conversion coefficient; this can be reconciled with the assignment of $J^\pi = 25/2^-$ for the isomeric state. Another γ transition (approx. 21 keV) that should be present according to the decay scheme could not be observed in the γ spectrum. Since this transition should be of type M2, its absence is understandable in view of the very high conversion coefficient.

To further clarify the assignment and to obtain carrier-free samples, attempts were made to prepare ^{179m}Hf by the reactions ^{181}Ta (γ, pn) ^{179}Hf and $^{181}Ta(d,\alpha)$ ^{179}Hf. When the irradiation had been completed, tantalum and hafnium were separated by partition between tributyl phosphate and 12 N nitric acid.

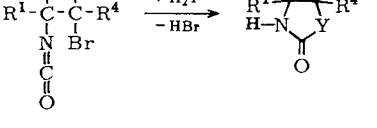
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[**] HDEHP = di-(2-ethylhexyl)orthophosphoric acid.

Rearrangement of *N*-Halogeno-β-lactams — A Simple Synthesis of β-Bromoalkyl Isocyanates

By *K.-D. Kampe* [*]

N-bromo- and *N*-chloro-2-azetidinones rearrange in the presence of CC-unsaturated compounds into β-bromo-*(1)* and β-chloroalkyl isocyanates respectively [1].



(1) *(2)*

The tendency of the bromine in the β position toward neighboring-group participation can be demonstrated by means of secondary cyclizations, *e.g.* to *(2)*, which occur in some isocyanate additions of the β-bromoalkyl isocyanates.

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[1] *K.-D. Kampe*, Tetrahedron Letters *1969*, 117.

Gas-Chromatographic Determination of the Purity and Polarization-Optical Quality Testing of Molecular Single Crystals of High Quality

By *N. Karl* [*]

For the investigation of semiconductor properties (particularly the mobilities and lifetimes of charge carriers), for the study of optical processes (particularly the singlet and

triplet exciton migration, fluorescence, and phosphorescence) and ESR of triplet excitons in crystals of organic compounds containing π-electron systems, *e.g.* naphthalene, anthracene, and fluorene, the requirements regarding the chemical purity of the crystals, special doping, and crystallographic quality have been steadily increasing in recent years.

Chemical purities of less than 1 ppm in all impurities, and of the order of magnitude of 0.01 ppm in special impurities, can often be achieved by zone melting and by crystal growth from the melt or by sublimation. The best crystals are of "optical" quality.

If a good separation can be achieved, gas-chromatographic analysis permits the determination of impurities and doping component concentrations down to the ppm range. The main problem is the detection of very similar substances that are difficult to separate. The systems thionaphthene (benzo[*b*]-thiophene)-naphthalene and phenazine-anthracene were investigated as typical examples. The former system can be quantitatively determined on a 5 m × 3/8" column with 20% LiCl on Chromosorb P—NAW at 150 °C down to about 50 ppm of thionaphthene in naphthalene with a flame ionization detector. Anthracene decomposes on this column. The phenazine-anthracene separation can be achieved on a 1.5 m × 1/8" column with 10% XE-60 on Chromosorb W-AW-DMCS at 140 °C. The detection limit for phenazine in anthracene is also about 50 ppm. The gas-chromatographic determination of the distribution coefficients is in progress.

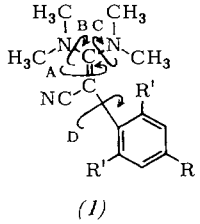
The crystallographic quality of aromatic single crystals can be judged conveniently from the interference diagrams obtained in monochromatic polarized convergent light. (These diagrams can also be used for the accurate orientation of the crystals.)

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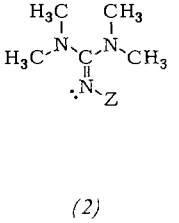
NMR Studies on Rotation and Inversion at Double Bonds

By *H. Kessler* [*]

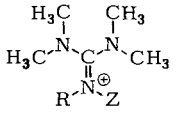
The thermal *cis-trans* and *syn-anti* isomerizations in the compounds *(1)*—*(4)* are being studied by means of the temperature dependence of the NMR spectra.



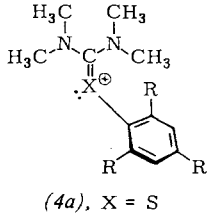
(1)



(2)



(3)



(4a), X = S
(4b), X = O

In the ketene aminals *(1)* (R′ = H, R = H, F, Cl, Br, $COOCH_3$, $COCH_3$, CN, NO_2), up to 4 rotation barriers (A, B, C, D) can be determined, and their values can be correlated with the Hammett σ_p constants of the substituent R. The Hammett reaction constants can be determined on the assumption that the activation entropy $\Delta S^{\neq}$ is zero. Their values are $\rho_A = +2.75$ (correlation coefficient $r = 0.99$) for the rotation about the CC double bond (A) in 1,2,4-trichlorobenzene as solvent; $\rho_B = -0.96$ ($r = -0.98$) and $\rho_C = -1.35$ ($r = -0.96$) for rotation about the two CN single bonds (B, C) in $CDCl_3$, and $\rho_D = -0.82$ ($r = 0.79$) for the rotation about the C-aryl bond (D) observed for R = $COOCH_3$, $COCH_3$, CN, NO_2 in $CDCl_3$. It is shown in the case of the *p*-bromo compound *(1)*, R′ = H, R = Br, that the rotation about the CC double bond becomes easier with increasing polarity of the solvent. On the other hand, the polarity has no measurable effect on the rate of inversion at the double-bonded nitrogen atom in the guanidines *(2)* [1]. This is however affected by protic solvents (CD_3OD, $CDCl_3 + CF_3COOH$) owing to protonation on the indicated unshared electron pair. In the guanidinium salts *(3)*, on the other hand, rotation about the CN double bond can be observed [1].

The *syn-anti* isomerization in the thiuronium salts *(4a)* [2] becomes more difficult with increasing size of the substituents R in the order R = H, CH_3, i-C_3H_7, which allows the conclusion that the isomerization at the CS double bond follows the rotation mechanism and does not involve inversion at sulfur.

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[1] a) *H. Kessler* and *D. Leibfritz*, Tetrahedron, in press; b) Tetrahedron, in press.

[2] *H. Kessler* and *D. Leibfritz*, Tetrahedron Letters *1969*, 427; *H. Kessler*, *H. O. Kalinowski*, and *C. V. Chamier*, Liebigs Ann. Chem. *727*, 228 (1969).

Separation of Alkaline Earth Metals on Cellulose Columns

By *H. Klamberg* (lecturer) and *W. Lohr* [*]

All six elements of Group IIa of the periodic system can be separated from one another quickly and reliably by paper chromatography. This method, in which the best results are obtained with methanol:water:concentrated hydrochloric acid = 80:10:10 vol-% as the solvent, and which allows easy detection of the elements in the presence of one another even in microgram quantities in UV light following treatment of the chromatogram with 8-hydroxyquinoline, was applied some time ago to thin layer chromatography using acid-washed cellulose powder as the layer material.

This separation method represents the starting point for development of a process for the rapid separation of beryllium, magnesium, calcium, strontium, and barium on cellulose columns and subsequent quantitative photometric determination. The columns used are 8 cm long and have diameters of about 12 mm. The adsorbent used was ultrafine cellulose powder No. 223 U manufactured by Binzer, Hatzfeld. To minimize the analysis time, the operation is carried out slightly above atmospheric pressure.

The samples for analysis are introduced at the top of the column by means of a microliter pipet (methanol:water:concentrated hydrochloric acid — 53:27:20 vol-% as eluent). For the quantitative determination, an ammoniacal solution of phthalein purple (Merck, Darmstadt) is added to the column eluate by means of a metering pump, and the complexes formed with magnesium, calcium, strontium, and barium are determined photometrically (flow-through cell, 578 nm). Beryllium, which leaves the column first, is determined indirectly by the formation of a carbonato complex and the reaction of the simultaneously liberated protons with the metal indicator. The extinctions of the eluate flowing continuously through the photometer are registered by a pen-type recorder and the resulting maxima are used, after calibration, for the quantitative determination of the elements.

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Chemical Lasers: Physicochemical and Technological Possibilities

By *K. L. Kompa* [*]

Chemical lasers are based on the occurrence of IR chemiluminescence in chemical reactions. Reactions known so far extend from photodissociations *via* bimolecular substituons to eliminations. Since their discovery (1965), lasers of this type have attracted interest as accurate probes for the investigations of the energy distribution in elementary chemical reactions and as gas lasers, sometimes with very high optical gain, that are independent, in principle at least, of auxiliary external energy sources. The latter aspect, for which fast, branched chain reactions such as occur *e.g.* in F_2/H_2 explosions are preferentially used, has received special attention in recent Russian work. We have followed the former aspect using the "pumping step" [1]

$$F + H_2(D_2) \rightarrow HF(DF)\ (v > 0) + H(D)$$

for the investigation of the vibrational and rotational energy distribution in the hydrogen fluoride or deuterium fluoride molecules formed and for the study of energy transfer processes. The fluorine atoms can be produced by flash photolysis of inorganic fluorides such as the hexafluorides of uranium, molybdenum, or tungsten, xenon tetrafluoride, antimony pentafluoride, or oxygen difluoride. Considerable demands are made on the flash photolysis equipment used in regard to time resolution (<1 μsec) and the possibility of vacuum UV photolysis.

The laser emission in these reaction systems takes place in $v = 3 \rightarrow 2$, $v = 2 \rightarrow 1$, and $v = 1 \rightarrow 0$ P branch transitions of HF or DF. The experimentally determined optical amplification of these emission lines can be used, together with the Patel equation [2], to determine the occupancies of the vibrational-rotational states involved in the emission. An interfering factor here, however, is the competition of very fast radiationless vibrational deactivation. The extent of this deactivation has been approximately determined by experiments on time-dependent energy storage in the hydrogen fluoride molecules by controlled switching of the laser resonator (q switching) at predetermined times during or after the pumping process. Experiments with a frequency-selective monochromatic resonator were also used for the investigation of coupling phenomena between the molecular energy states involved. When the parameters determined in this way are known, it should be possible to obtain correct amplification data and to determine state populations, which can be correlated with detailed reaction rate constants.

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[1] *K. L. Kompa, J. H. Parker*, and *G. C. Pimentel*, J. chem. Physics *49*, 4257 (1968); *K. L. Kompa, P. Gensel*, and *J. Wanner*, Chem. Physics Letters *3*, 210 (1969).

[2] *C. K. N. Patel*, Physic. Rev. *136*, A 1187 (1964).

Molecular Weight Distribution in Synthetic Resins

By *W. König* [*]

The technological properties and applications of macromolecular substances is largely determined by the shape, size, and size distribution of the molecules. The typical synthetic resins for coatings differ from high polymers in their structure and molecular dimensions. Various simultaneous or successive chemical reactions are usually involved in the formation of synthetic resins. The resulting molecules differ not only in their size but also in their chemical structure. The question of the molecular distribution was studied in this work with the aid of gel permeation chromatography.

Under certain conditions, gel chromatography gives elution curves that give a direct indication of the distribution characteristics of the resin. By calibration of the chromatographic system with suitable monodisperse substances, it is possible to use the data obtained from the elution curves for the construction of molecular distribution curves.

The resins studied included rosin derivatives, such as rosin itself, ester gum, modified phenolic resins, maleic resins, drying and nondrying alkyd resins of various structures, and cyclized rubbers. The resins had average molecular weights of about 1000 to 3000 and molecular weight distributions of from a few hundred to a few thousand or tens of thousands.

For the esterified rosin derivatives, irrespective of the nature of the modification by maleic acid or phenol, a pronounced maximum in the distribution curve always corresponds to the molecular weight of the pure glycerol or pentaerythritol ester of the resin acid. This maximum is followed on the high molecular weight side by plateaus or shoulders whose heights and widths depend on the modification. A separate maximum in the low molecular weight range is sometimes found for the free resin acids.

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Preparation and Electrical Properties of Polymers with Conjugated Polyene Structures Containing Aromatic, Substituted Aromatic, or Thiophene Rings

By *G. Kossmehl* (lecturer), *M. Härtel*, and *G. Manecke* [*]

Polymers containing arylene and vinylene units having the general structure

$$-[-Ar-CH=CH-Ar^1-CH=CH]_n-$$

(Ar = *p*-phenylene units, 2-nitro-, 2,5-dimethoxy-, or 2,5-dichloro-*p*-phenylene units; Ar^1 = *p*-phenylene or 2,5-thienylene units) were prepared, generally in good yields, from bis-Wittig salts and dialdehydes of the benzene or thiophene series.

We also prepared polymers containing *m*- and *o*-phenylene and containing 9,10-anthrylene units.

All the polymers were examined for crystallinity by X-ray methods, and their electrical conductivities were also investigated. Clear relations were found between the chemical structure, the crystallinity, and the electrical conductivity; for example, polymers containing *p*-phenylene units conduct electricity less efficiently than the polymers whose *p*-phenylene units have been replaced by 2,5-thienylene units.

Oligomers having the general formula

$$Ar^1-[-CH=CH-Ar^2-]_n-CH=CH-Ar^3$$

$Ar^1 = Ar^3$ = phenyl or 2-thienyl; Ar^2 = *p*-phenylene or 2,5-thienylene

with $n = 1, 2, 3$, and 5 were synthesized as model substances, and their spectral, X-ray, and electrical properties were compared with those of the corresponding polymers.

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Rapid Volatilization of Arsenic, Antimony, Selenium, and Tellurium as Hydrides from Mixtures of Fission Products

By *J.-V. Kratz* (lecturer), *H. Folger*, and *G. Herrmann* [*]

The radioactive tracer method was used for a systematic study of the optimum conditions for the volatilization of arsenic, antimony, selenium, and tellurium as hydrides from solutions of fission products. The hydride separations proceed

fastest on introduction of 1.6 g of zinc powder in 2 ml of concentrated hydrochloric acid with carrier quantities of about 10^{-4} mmole. Yields of 75—90 % were obtained for all four hydride-forming elements within one second. The decontamination factors for non-volatile fission products are greater than 10^3. For the investigation of short-lived fission products, the experimental procedure was fully automated in connection with the fast rabbit system of a TRIGA reactor[1]. The hydride mixture is separated on liquid or solid adsorbents; the arsenic and antimony fraction can be counted as early as 2 seconds after the end of irradiation, and the selenium and tellurium fractions after 5 seconds.

New delayed neutron precursors were detected in the selenium and tellurium fractions by neutron counting[2]. From selenium separations at various times after the end of irradiation and by counting the bromine daughters the half-lives of ^{87}Se and ^{88}Se were found to be 5.9 ± 0.2 and 1.7 ± 0.5 s respectively. Both isotopes are themselves weak neutron precursors with neutron yields of 0.35 ± 0.12 and 0.32 ± 0.16 neutrons/10^4 fissions respectively. Direct and indirect neutron measurements on the tellurium fraction gave half-lives of 20 ± 1 s and 3.5 ± 0.5 s for ^{136}Te and ^{137}Te respectively, and neutron yields of approximately 1.2 and approximately 0.7 n/10^4 fissions.

The fast separations made it possible to record γ spectra of short-lived isotopes of the hydride-forming elements. Using Ge(Li) semiconductor detectors, it was possible to confirm not only the known γ rays of $^{132-133}$Sb, $^{81-84}$Se, $^{131-134}$Te and their daughter products, but also to characterize γ rays of 11s-^{134}Sb, 33.7s-^{85}Se, 16.7s-^{86}Se, 16.6s-^{135}Te, 20.9s-^{136}Te, and 3.5 s-^{137}Te. The half-lives and mass assignments were confirmed in some cases by the growth of known γ rays of the daughter products, *e.g.* 1565 keV (^{86}Br) with $T_{1/2} \approx 16.1$ s, 1313 and 1321 keV (^{136}I) with $T_{1/2} \approx 21.6$ s precursor half-life.

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[1] *H. Folger, J.-V. Kratz,* and *G. Herrmann,* Radiochem. radioanalyt. Letters *1*, 3, 185 (1969).

[2] *H.-D. Schüssler, H. Ahrens, H. Folger, H. Franz, W. Grimm, G. Herrmann, J.-V. Kratz,* and *K.-L. Kratz,* 2nd Symp. Physics and Chemistry of Fission, I.A.E.A. Vienna, Contribution SM-122/22, July 1969.

Fast Separation of Fission Halogens by Recoil Reaction with Methane

By *K.-L. Kratz* (lecturer) and *G. Herrmann*[*]

The recoil-induced formation of volatile methyl halides when the fission products are stopped in methane was used for the separation of the halogens in the gas phase. The other fission products, present as aerosols, can be quantitatively retained either electrostatically or with a membrane filter.

The experimental procedure was fully automated in order to allow the determination of short-lived isotopes of iodine and bromine. Polyethylene capsules containing a uranium target and CH_4 as the stopping gas were subjected to pulse irradiation in the Mainz TRIGA reactor and transported rapidly to the separating apparatus by means of compressed air in a fast pneumatic tube system. The fission product/gas mixture is flushed out of the irradiation capsule with the carrier gas N_2 or CH_4 through two hypodermic needles (flow rate approximately 27 l/min) and forced through several successive adsorption vessels to achieve chemical separation. The adsorption vessels are then transported to the neutron detectors. In the most favorable case, 0.5 s elapses before the measurements can be started, *i.e.* isotopes with half-lives down to 0.2 s can be determined.

To test the selectivity of the separation, the contamination by the elements Se, Sb, and Te, which are known to form volatile compounds with CH_4 or H_2 that would pass through the aerosol filter, was determined by comparison of γ spectra of unseparated and separated samples recorded with semiconductor detectors. This fraction was found to be ≤ 1–3 %. To ensure that the halogens are decontaminated from inert gases and their daughter products, some of which are themselves neutron emitters, neutral adsorbents such as Sterchamol and silica gel with a few wt-% of $AgNO_3$, AgCl, KI or $KBrO_3$ are used. For further separation of the halogens from one another, iodine and bromine traps are filled with different adsorbents and use is made of the difference in the boiling points of methyl iodide (42.3 °C) and methyl bromide (4.5 °C). The iodine compound is retained in the first adsorption vessel, which is packed with Sterchamol/$AgNO_3$ and heated to 80 °C, while the more volatile methyl bromide is found mainly in the second trap, which contains silica gel/AgCl.

The half-lives and the contributions to the individual delayed neutron periods of the isotopes $^{87-91}$Br and $^{137-141}$I were determined by simultaneous measurement of the neutron decay curves.

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Alkylations with Tertiary Oxonium Salts

By *R. Kreher* (lecturer), *H. Hennige, G. Vogt,* and *A. Bauer*[*]

The trialkyloxonium tetrafluoroborates, which were introduced into preparative organic chemistry by *H. Meerwein*[1,2] exhibit surprisingly high selectivity despite their high chemical reactivity.

3-Arylisoindolin-1-ones are alkylated on the oxygen of the cyclic amide grouping by trialkyloxonium tetrafluoroborates to give the 1-alkoxy-3-arylisoindoleninium tetrafluoroborates. Deprotonation of these products yields 1-alkoxy-3-arylisoindolenines, which are of interest as tautomers of the hitherto unknown 1-alkoxy-3-arylisoindoles.

The *N*-alkylated isoindolin-1-ones also undergo *O*-alkylation with tertiary oxonium salts to give 1-alkoxy-*N*-alkylisoindoleninium tetrafluoroborates, which can also be prepared independently from 1-alkoxyisoindolenines by *N*-alkylation. Deprotonation yields the extremely reactive 1-alkoxy-*N*-alkylisoindoles.

The alkylation of 1,3-dimethyl-6*H*-cyclohepta[*c*]pyrrol-6-one takes place selectively on the oxygen of the vinylogous amide grouping. Deprotonation of the resulting oxonium-imonium salts yields 6-alkoxy-1,3-dimethyl-2-azaazulenes, which are easily accessible in this way.

Pyrazolin-5-ones with a cyclic acid hydrazide group are also alkylated on the oxygen of the carbonyl function; *N*-alkylation is also observed to an extent that depends on the substituents[3]. In the case of acyclic hydrazides the alkylating agent preferentially attacks the more strongly basic nitrogen atom in the β position. The isoelectronic *N*-alkoxybenzanilides are alkylated on the oxygen of the carbonyl function. Hydrolysis of the resulting oxonium-imonium salts leads to alkyl benzoates and, surprisingly, azobenzene.

The trialkyloxonium tetrafluoroborates are found in every case to be excellent alkylating agents for ambifunctional compounds.

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[1] *H. Meerwein* in *Houben-Weyl-Müller:* Methoden der organischen Chemie. Vol. 6/3. Thieme, Stuttgart 1965, p. 325.

[2] For a review of tertiary oxonium salts and their application see Chem. Ber. *100*, LXXX (1967), References 55 to 70.

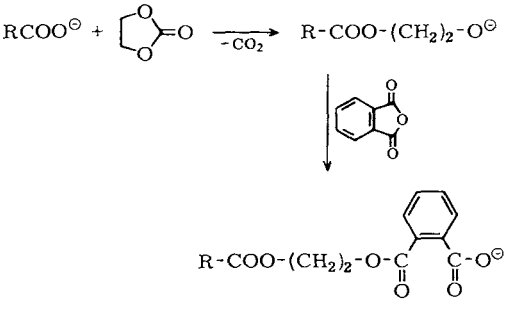
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Polymerization Reactions on Pigment Surfaces

By *K. Hamann* and *R. Kroker* (lecturer)[*]

The interactions between pigments and binders have until now been studied by investigation of the adsorption and desorption of low molecular weight and macromolecular substances on solid particles. A new line of investigation concerned with polymerization reactions on pigment surfaces has attracted interest in recent years. The object of these investigations is to bond macromolecules in which the pigment is embedded as firmly as possible to the pigment surface, by joint covalent bonds if possible.

An anionic copolymerization of ethylene carbonate and phthalic anhydride is initiated by sodium benzoate. The initiator molecules are incorporated into the polyester chains as end groups.



If the sodium benzoate is replaced by the sodium salt of a copper-phthalocyaninemonocarboxylic acid pigment, covalent bonds can be formed during the polymerization between copper-phthalocyanine and the polyester chains.

The polymerization is carried out in bulk at 200 °C. The reaction products isolated include, in addition to surface-treated pigments, soluble blue polyesters. These products were investigated analytically, thermogravimetrically, and IR-spectroscopically for characterization purposes.

The surface-treated pigments consist of about 15 to 40 % polyester. The soluble blue polymers have a number average molecular weight of 2000 to 4000, and contain up to 5 % of copper-phthalocyanine.

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Optimum Irradiation Conditions for the Production of Radionuclides with a Cyclotron

By *J. Lange* (lecturer) and *H. Münzel*[*]

For the optimum production of radionuclides and for the optimum use of the particle accelerator it is necessary to know the excitation function of the nuclear reaction in question. However, since this is frequently unknown, the irradiation conditions must be fixed arbitrarily in many cases. An investigation was therefore carried out to establish whether unknown excitation functions can be estimated in such cases from experimental data. It was found that the influence of the atomic number of the target nucleus on the shape, position, and maximum cross section of the excitation functions qualitatively corresponds to theoretical expectations. We were able to develop a method for the estimation of unknown excitation functions. The yields for the irradiation of thick targets were calculated for all elements using the estimated excitation functions.

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The Reaction between Phosphorus Pentoxide and Silicon Nitrides

By *I. Fränz* and *W. Langheinrich* (lecturer)[*]

Thin films of vitreous silicon nitride as produced from silane and ammonia can serve as diffusion masking layer in the fabrication of semiconductor planar devices. Phosphorus pentoxide acts on the silicon nitride at temperatures about 1200 °C in technical phosphorus diffusion processes. If oxygen is also present, the IR absorption spectrum of the diffused wafer contains the absorption peak of silicon dioxide at 1100 cm^{-1}, and the absorption of phosphorus pentoxide, recognized from the peak at 1335 cm^{-1}, as well as the absorption peak of silicon nitride at 900 cm^{-1}. The determination of the phosphorus concentration profiles after neutron irradiation of the samples shows that a homogeneous phosphorus glass containing 7—8 moles of SiO_2 per mole of P_2O_5 has been formed. Thus it appears that only the oxygen reacts with silicon nitride to form silicon dioxide, which then forms a glass with phosphorus pentoxide:

$$5\ Si_3N_4 + 15\ O_2 + 2\ P_2O_5 \rightarrow 15\ SiO_2 + 2\ P_2O_5 + 10\ N_2$$

This reaction is about 100 times as fast as the reaction in pure oxygen; this points to intermediate participation of the phosphorus pentoxide.

The intermediate product can be detected if the reaction is investigated in the absence of oxygen. The product is again a thin vitreous layer that is sharply separated from the underlying unreacted silicon nitride, and which has uniform phosphorus concentration, as is shown by tracer experiments with ^{32}P. The phosphorus concentration in these layers is appreciably higher than in the first case. The IR absorption in the NaCl range showed that the glass also contains silicon dioxide and phosphorus pentoxide. The second reaction product is indicated by the intense smell of phosphine which can be detected when the samples are chemically sectioned. Silicon phosphide must have been formed and can be detected by means of its absorption band at 475 cm^{-1}.

$$3\ Si_3N_4 + 4\ P_2O_5 \rightarrow 5\ SiO_2 + 4\ SiP + 2\ P_2O_5 + 6\ N_2$$

In the presence of oxygen the thickness of the silicon nitride layer that has been converted into phosphorus glass varies linearly with time. This indicates that the rate-determining step is probably not a diffusion-controlled process inside the phosphorus glass layer.

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Adsorption of Protactinium, Zirconium, and Niobium on Silica Gels and Vycor Glass from Solutions in Hydrochloric Acid[**]

By *M. Laser*[*]

The high-temperature chlorination of irradiated ceramic uranium-thorium breeder elements leads, on subsequent fractional condensation of the chlorides, to a uranium fraction that contains all the protactinium and considerable quantities of zirconium, niobium, ruthenium, molybdenum, tellurium, and other fission products. The fine purification of this fraction is effected by solvent extraction of the solution of the chlorides (Chlorinex process). However, it is first necessary to remove the protactinium. This is achieved by adsorption on silica gel or Vycor glass, a special glass containing 96.3 % of SiO_2.

Most of the protactinium is adsorbed on silica gel and Vycor glass from hydrochloric acid solution (optimum 4 M). Variation of the acid concentration has only a small effect.

Approximately 1–3 % of the protactinium is in a non-adsorbable form. This percentage is practically unaffected by variation of the acid concentration or of the temperature.

The adsorption mechanism is not yet known. It is probable, however, that at least two types of bonds are superimposed, since only part of the adsorbed protactinium can be desorbed by elution with oxalic acid.

The adsorption of niobium increases rapidly with increasing acid concentration, and so varies in the same direction as the precipitation of hydrated niobium pentoxide by strong acids.

In the case of zirconium, on the other hand, the adsorption decreases with increasing HCl concentration, and reaches a constant value for about 6 M hydrochloric acid.

Simultaneous separation of the protactinium, zirconium, and niobium, which would lead to a large reduction in the radiation level in the subsequent solvent extraction, is very difficult, since the optimum adsorption conditions for zirconium and niobium are very different. Nevertheless, the adsorption of more than 90 % of the zirconium/niobium activity has been achieved in a single pass.

The Vycor glass and the silica gels investigated differ only slightly in their adsorption behavior. The differences can be attributed mainly to the different surface areas of the products.

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Comparison of Organometallic Complexes of Aluminum and those of Some Transition Metals

By *H. Lehmkuhl* (lecturer) and *J. Čuljković* [*]

Potassium reacts with dialkylaluminum chloride in THF at −80 °C as follows:

$$2\,K \xrightarrow[-80°C]{THF} 2\,K^{\oplus} + 2e^{\ominus}_{solv.}$$

$$\xrightarrow[-2KCl]{2R_2AlCl/THF} R_2AlO(CH_2)_4AlR_2 \cdot THF$$

whereas aluminum is lost at +20 and +60 °C, with formation of a trialkylaluminum-tetrahydrofuran adduct. The cleavage of THF or the formation of Al are suppressed in the presence of benzene, naphthalene [1], or anthracene; the dihydroarene-diyl-bis(dialkylaluminum)-tetrahydrofuran adducts, *e.g. (1)* are formed instead.

$$2\,M + 2\,R_2AlCl + C_{14}H_{10} \xrightarrow[-2\,MCl]{THF} \text{H, AlR}_2\cdot\text{THF; H, AlR}_2\cdot\text{THF} \quad (1)$$

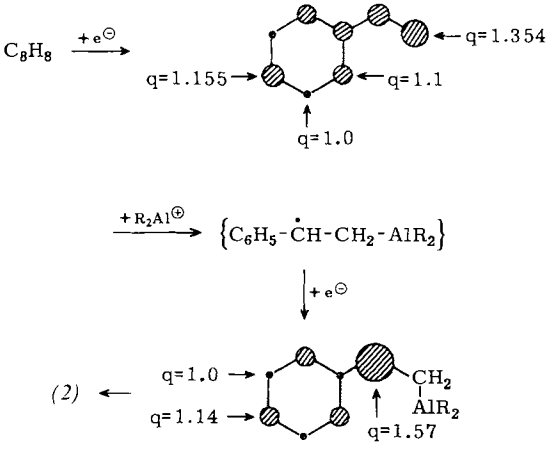
M = Na, K; with benzene only M = K; R = CH_3, C_2H_5

The analogous reactions with trialkylaluminums lead to equimolar mixtures of alkali metal tetraalkylaluminates and alkali metal dialkyldihydroarenediylaluminates [2]. The stability of the complexes increases with increasing electron affinity of the aromatic hydrocarbon. Olefins with similarly low reduction potentials (styrene, stilbene), 1,3-diolefins (butadiene [3], isoprene, myrcene, 1,3-cyclooctadiene), and electron-attracting alkynes (tolan) can react with alkali metal and trialkylaluminum to give the alkali metal dialkylaluminate complexes with hydrocarbons, *e.g. (2)*.

The course of the reaction and the products can be interpreted on the basis of HMO models of the initial hydrocarbons and their anions for all the systems investigated so far. The hydrocarbon anion is formed first, and a dialkylaluminum cation from the electrolytic dissociation equilibrium [4] then adds on in the position of highest charge order. This gives a new

$$2\,K + 2\,R_3Al + C_8H_8 \xrightarrow{THF} K^{\oplus}\left[\text{styrene-CH(AlR}_2\text{)-CH}_2\right]^{\ominus} + K^{\oplus}[AlR_4]^{\ominus} \quad (2)$$

π-electron system having a higher electron affinity, which rapidly takes over an electron from further alkali metal; the new carbeniate anion changes into an aluminate ion by formation of an Al—C bond. On the basis of HMO charge orders q, we obtain *e.g.* for the reaction of styrene, the following picture:



Organometallic complexes of transition metals were used for comparison in every case.

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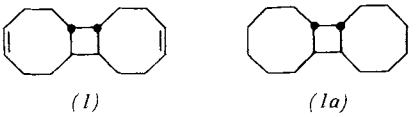
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The Thermal Dimerization of *cis-trans*-1,5-Cyclooctadiene

By *J. Leitich* [*]

Racemic *cis,trans*-1,5-cyclooctadiene dimerizes at room temperature in the dark by combination of two *trans* double bonds to form a cyclobutane ring. This reaction yields three stereoisomers, *i.e. trans-trans (syn) (1)*, *trans-cis (2)*, and *trans-trans (anti) (3)*, in proportions of about 10:4:1.



(1) *(1a)*

In *(1)* and *(3)*, the *trans* configurations of the reacting centers have been retained, while in *(2)* one inversion has taken place. The doubly inverted isomers are not formed (detection limit 0.1 %); the only by-products are about 3 % of *cis,cis*-1,5-cyclooctadiene and varying quantities of polymers. The rate of formation and the proportions of the dimers are independent of light or catalytic effects, and are practically independent of the solvent ($k_{cyclohexane}/k_{dimethylformamide} = 2.1$), and the proportions are practically independent of the temperature. Kinetic parameters [for *(1)* in DMF between 30 and 50 °C]: reaction order: 2; $\Delta H^{\neq} = 17.0 \pm 1.0$ kcal/mole; $\Delta S^{\neq} = -31 \pm 3$ e. u.

(R)-(−)-*cis,trans*-1,5-cyclooctadiene on the other hand, forms (+)-*(2)* and (+)-*(3)* in a ratio of 1:2.9 with no *(1)*.

Racemic *trans*-cyclooctene also forms small quantities of the analogous saturated dimers *(1a)*, *(2a)*, and *(3a)* in a ratio of 2:6:1 at 150 °C, together with polymers and isomers.

The question whether the *trans* or *cis* linkage is energetically more stable for an eight-membered ring condensed to a four-membered ring has also been investigated on the basis of equilibrium positions in the cyclobutanone and benzocyclobutene systems. The energy difference in the case of the saturated eight-membered ring is small: $c_c^{equ}/c_t^{equ} = 1$ and 3 respectively; in the case of the 5-*cis*-unsaturated eight-membered ring, on the other hand, the *trans* arrangement is clearly preferred ($c_t^{equ}/c_c^{equ} > 100$).

These observations lead to the following conclusions concerning the course of the reaction: The dimerization begins in every case with the formation of one bond to give a biradical intermediate (rate-determining step). Closure of the second bond with retention of all configurations then occurs so fast that monoinversion can compete only if it leads to an energetically more favorable end product [*(2a)* but not *(2)*], or if the reacting double bond is more highly twisted (as in *cis,trans*-1,5-cyclooctadiene). Nevertheless, it is concluded that a specific factor favoring monoinversion is operative which is not steric in origin and therefore must be stereoelectronic. Thus, the extent of formation of *(2)* and *(2a)* shows that the predictions of the Woodward-Hoffmann rules have some validity even in disconcerted cycloadditions.

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Determination of Copper, Lead, and Cadmium in Different Concentration Ratios by Various Voltammetric Methods

By *B. Lendermann* (lecturer), *H. Monien*, and *H. Specker*[*]

The determination of trace elements by voltammetric methods is influenced by the presence of other electro-active ions. The permissible excess concentrations of accompanying elements depend decisively on the electrochemical behavior both of the trace and of the excess element, as well as on the voltammetric method used.

In the determination of copper, lead, and cadmium in the systems Cu—Pb, Pb—Cd, and Pb—Cd—Cu, the concentration ratios at which one of the elements can still be determined in the presence of others without the measurement signal being affected and the determination limits for increasing excess concentrations are shown. The measurements were carried out with a conventional direct current polarograph, with a Davis cathode ray polarograph, and by inverse voltammetry on a hanging mercury drop electrode and on a carbon-paste electrode. By comparison of the results it is possible to estimate which method is most suitable for the analysis problem in question.

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Purification of Contaminated Exhaust Gases in the Combustion of Irradiated HTGR Graphite Nuclear Fuel Elements

By *M. F. Lepold*[*]

To remove graphite ballast, the reprocessing of HTGR nuclear fuel elements[1] is preceded by combustion at about 1000 °C. The exhaust gas consists of about 65—75 % vol-% of CO_2, 15—25 vol-% of CO, and 5—10 vol-% of O_2, and contains all the fission products that are volatile during the combustion. It is first prepurified by passage through sintered metal filters and fiber-glass filters, and is then converted into a gas consisting of more than 99.7 vol-% of CO_2 on a catalyst. The component CO or O_2 that is present in the smaller amount is added before the mixture is brought into contact with the catalyst.

^{131}I and ^{106}Ru are filtered out of this gas on active charcoal. At 80 °C and with a linear flow rate of the carbon dioxide of 5.2 cm/s, a decontamination factor $D \geq 10^5$ can be achieved for ^{106}Ru and ^{131}I, provided that the required bed depth of 4 cm can be displaced in the sense of a gas-solid chromatograph under the influence of the flowing carbon dioxide. The active charcoals examined have BET surface areas of between 950 and 2500 m^2/g; the capacity for iodine is 1.1 to 2.9 g per g of active charcoal at 80 °C when the CO_2 is saturated with I_2.

To separate the fission inert gases (concentration of the order of magnitude of 1 mg/Nm^3), CO_2 is reversibly fixed on a 5 Å molecular sieve zeolite, the interstitial volume of which is filled with argon, and which takes up fission inert gases. The argon and the accompanying fission inert gases are removed from the zeolite packing by flushing the interstitial volume with CO_2 after CO_2 saturation of the molecular sieve zeolite has been reached. The CO_2 desorbed by the molecular sieve zeolite is substantially free from activity, the decontamination factor for ^{85}Kr from CO_2 being 6×10^3, whereas the argon enriched with ^{85}Kr, as a concentrated gaseous waste, is fixed on active charcoal at −78 °C in aluminum cylinders. When the cylinders are warmed to room temperature, the internal pressure increases to 7 atm. The capacity of the molecular sieve zeolite for CO_2 between the extremes (25 °C, 600 torr during adsorption and 150 °C, 1 torr during desorption) is 20 % of the weight of the zeolite packing.

A pilot plant for the continuous purification of 2.5 Nm^3 of CO_2 per hour has been constructed in the hot cell at Jülich on the basis of these results.

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Absorption of Carbon Dioxide in Buffered Arsenite Solutions

By *A. Löwe* (lecturer), *N. Neth*, and *K. Dialer*[*]

The absorption, or more precisely the reaction, of carbon dioxide in water is accelerated by arsenite ions. This fact is utilized in industry for CO_2 washing in the "Vetrocoke" process. Apart from this application, the absorption system offers the interesting possibility of measuring specific interfacial areas in absorbers. For this purpose the catalyst concentration, which is pH-dependent, must be kept as nearly constant as possible by means of a buffer, to counter depletion phenomena in the absorption boundary layer. If, as is obvious, a carbonate buffer is used, the degree of dissociation of the arsenious acid at a buffer ratio (carbonate/bicarbonate) of 1, according to the thermodynamic equilibrium constants, is higher than 90 %.

Investigations on the equilibria in arsenite solutions with carbonate buffers have, however, shown that calculations based on thermodynamic constants, or using constants determined as a function of the ionic strength with large excesses of neutral salts (NaCl, KCl), lead to incorrect results for the compositions of the solutions.

The degrees of dissociation of arsenious acid are much lower in some cases than was formerly thought. Moreover, the hydrolysis constant of arsenite changes very rapidly with the degree of dissociation and with small additions of neutral salts. The specification of ionic strengths or buffer ratios, particularly if they are based on weighed portions, are

therefore of little value for the characterization of these absorption solutions.

The hydrolysis constant of the carbonate increases with increasing carbonation of a given solution, while that of the arsenite decreases. This is fortunate in view of the boundary layer depletion, since change is essentially confined to the buffer ratio, whereas the catalyst concentration remains practically constant.

In line with these results, kinetic measurements in a film absorber with various CO_2 pressures and contact times gave no indication of boundary layer depletion. For accurate evaluation of the measurements, it was necessary to make allowance for the fact that the "end effects" depend on the absorption rate, and cannot be predetermined by physical absorption measurements.

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The Lattice Vibration Spectra of Heavy Metal Thiospinels

By *H. D. Lutz*[*]

The *IR* absorption spectra of the thiospinels $MnCr_2S_4$, $FeCr_2S_4$, $CoCr_2S_4$, $ZnCr_2S_4$, $ZnAl_2S_4$, $CdCr_2S_4$, $HgCr_2S_4$, $CrGa_2S_4$, $CrIn_2S_4$, $MnIn_2S_4$, $FeIn_2S_4$, $CoIn_2S_4$, $NiIn_2S_4$, and $CdIn_2S_4$ have four generally very sharp absorption maxima in the regions 300–450, 230–350, 170–300, and 70–120 cm^{-1}, which correspond to the four IR-active vibrations of the type F_{1u}.

The vibration forms[1] of the lattice vibrations of the spinel lattice show that all the atoms in the unit cell are involved in each one of the IR-active vibrations. The modes of the IR-inactive vibration types can be rigorously separated on the basis of their symmetry properties into vibrations of $M^{II}S_4$ tetrahedra and vibrations of $M_4^{III}S_4$ cubes. The assignment of the absorption maxima to the IR-active vibrations was based on the influence of the mass of the atoms on the position of the vibrations, the ratios of the wave numbers of the maxima for corresponding oxo- and thiospinels, and the intensity of the vibrations.

The two short-wavelength, very intense lattice vibrations are displaced toward higher wave numbers from $MnCr_2S_4$ to $ZnCr_2S_4$, despite the increase in the mass of the metal atoms. This points to a marked increase in the force constant, which is connected with a corresponding decrease in the CrS and SS distances in the lattice, and an increasing compression of the $M^{II}S_4$ tetrahedra.

In the spectra of the indium thiospinels, which crystallize with the inverse spinel structure, the shortest-wavelength vibration is more intense than the next; this is the reverse of the relation found in the spectra of the normal chromium thiospinels. This reversal of the intensities of the two short-wavelength maxima can be interpreted as resulting from the replacement of the M^{II} ions in the tetrahedral positions by ions of higher valence.

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The α Radiation of $^{228}Ac(MsTh_2)$. A New α Branching in the Thorium Decay Series

By *F. Lux* (lecturer) and *N. Kaubisch*[*]

On the basis of the theories of α decay, α branching with a decay energy of about 4.6 MeV and a branching ratio of 0.8×10^{-8} or 3.5×10^{-8} has been estimated for $^{228}Ac(MsTh_2)$, a member of the thorium decay series.

For experimental checking, we had available a sample of 8 mCi of $^{228}Ra(MsTh_1)$, which also contained 10 mCi of ^{226}Ra. In the radiochemical separation and purification of ^{228}Ac, the ^{226}Ra had to be removed very carefully, since its 4.78 MeV α radiation would have interfered with the α-spectroscopic detection of the assumed α radiation of ^{228}Ac. The following decontamination factors (*DF*) had to be reached: 10^9 for radium, 10^5 for lead as $^{212}Pb(ThB) + ^{214}Pb(RaB)$ and for bismuth as $^{212}Bi(ThC) + ^{214}Bi(RaC)$, and 10^2 for $^{228}Th(RdTh)$. The following tracers were used for the evaluation of the separation process: ^{226}Ra, ^{140}La for ^{228}Ac, ^{228}Ac, ^{212}Pb, ^{212}Bi, $^{234}Th(UX_1)$. The separation and purification of ^{228}Ac was carried out in three steps.

1. Treatment of the ^{228}Ra sample by precipitation of $Ba(Ra)(NO_3)_2$ with fuming nitric acid; the radium content of the ^{228}Ac remaining in solution is reduced by a DF of 10^3.

2. Fine purification of the ^{228}Ac: Addition of thorium carrier, thorium hydroxide precipitation (quantitative coprecipitation of ^{228}Ac) with CO_2-free ammonia, single reprecipitation, DF for radium 10^4. Ion exchange separation (modification of the method given by *Cabell*[1]): Column 7.5×100 mm, cation exchange resin Dowex 50 WX8, 200–400 mesh, 60 °C. Application of preparation: 5 ml of 2 N HCl. Elutions: 10 ml of 2 N HCl (elution of lead and bismuth), 50 ml of 1.5 N HNO_3 (elution of radium), 10 ml of 3 N HNO_3, 20 ml of 6 N HNO_3 (elution of actinium). DF: for radium 10^2, for lead and bismuth 10^5 each, for thorium 10^4.

3. Preparation for α-spectroscopy: Electrolysis in nitric acid solution (pH = 2) after *Iyer et al.*[2], electrolysis time 30 min. The platinum cathode leaves with the actinium deposited on them are heated. Leaf diameter 16 mm, preparation diameter 10 mm. Total separation time 135 min, yield of ^{228}Ac 45 %.

The α spectra were recorded with the aid of a silicon semiconductor detector. The measuring chamber[3] was built between the pole pieces of a homogeneous electromagnet (magnet of a Varian ESR spectrometer) to deflect the interfering β radiation due to ^{228}Ac in the 9150 oersted magnetic field. The α line of ^{228}Ac was expected to appear on the low-energy flank of the 5.34 and 5.42 MeV α lines of ^{228}Th, which is formed in ^{228}Ac as a daughter product. A computer analysis was accordingly required to show that the α spectrum of the ^{228}Ac preparation contains an α line of energy 4.27 ± 0.04 MeV, which had not previously been observed for ^{228}Ac and its secondary products, and which must be assigned to the ^{228}Ac. Comparison of this line with that of ^{228}Th gives an α branching ratio of ^{228}Ac of $(5.5 \pm 2.2) \times 10^{-8}$.

Attempts were made to separate the ^{224}Fr resulting from the α decay of ^{228}Ac by α recoil and to identify it by decay measurements in an anticoincidence counter. The result was negative under the experimental conditions used. Therefore the half-life of ^{224}Fr seems to be considerably smaller than 2 min, which is the detection limit in the ^{232}Th-spallation experiments conducted by *Butement* and *Robinson*[4].

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Preparation, Structure, and Properties of Barium Phosphides

By *K.-E. Maass*[*]

We investigated the binary barium-phosphorus system at temperatures above 500 °C under 1 atm of argon. The phosphides were prepared from barium metal chips and red phosphorus vapor.

A melting point of higher than 3000 °C repeatedly given for the compound Ba_3P_2 since 1956 was found to be incorrect; Ba_3P_2 melts at 1340 °C. X-ray powder photographs show that Ba_3P_2 crystallizes in the Th_3P_4 structure and in the narrower sense in the anti-Ce_2S_3 type.

Very short metal-metal distances (3.81 Å) are found. The discussion of the atomic distances and coordinations leads to the conclusions that phosphorus as the anion does not carry the full negative charge of P^{3-}, the phosphorus-barium bond may be regarded as substantially ionic, and metallic bonds exist between the barium atoms, *i.e.* the substance exhibits mixed ionic-metallic bonding.

In addition to the stoichiometric compound Ba_3P_2, which is not formed preferentially in the system, there are seven other barium phosphides, which have been gathered together in a provisional phase diagram. The polyphosphide with the highest phosphorus content is BaP_3. All the phosphides are black and have a metallic luster, which decreases with increasing P content. Ba_3P_2 has a specific resistance of approximately 10^5 ohm·cm at room temperature. With the exception of BaP_3, all the phosphides decompose in air and in water and acids with loss of phosphines.

The insolubility of BaP_3 and the viscous softening of BaP_2 and $BaP_{1.82}$ suggest that the compounds are highly polymeric.

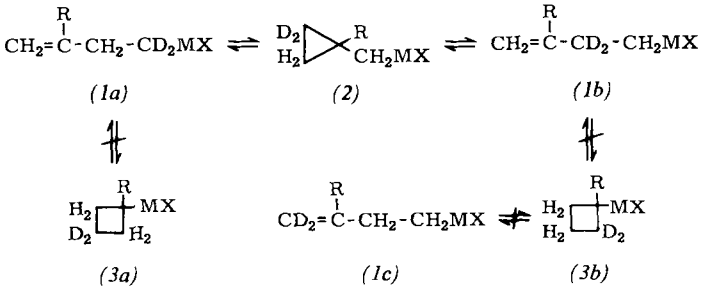
The phosphides of the alkaline earth metals occupy a distinct intermediate position between the sulfides and silicides in the transition from predominantly ionic bonding in the sulfides to predominantly metallic-covalent bonding in the silicides, magnesium phosphide exhibiting a closer relation to the sulfides, while the barium-phosphorus system shows a closer resemblence to the silicide systems.

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Kinetics of the Rearrangement of Allylcarbinyl Anions (3-Butenide Ions)

By *A. Maercker* (lecturer) and *K. Weber*[*]

In contrast with the unsubstituted allylcarbinyl Grignard compounds *(1)*, R = H, MX = MgBr, for which equilibration *(1a)*⇌*(1b)* can be readily followed by NMR spectroscopy even at room temperature[1], the rearrangement of the 3-substituted analogs *(1)*, R = C_6H_5, CH_3, MX = MgBr, proceeds at a comparable rate only at 80 °C. The β-deuterated Grignard compound *(1b)* is favored in the equilibrium ($K_p^{80\,°C} = 1.27 \pm 0.07$) because of a thermodynamic secondary isotope effect. The postulated cyclopropylcarbinyl intermediate *(2)* cannot be detected either chemically or by NMR spectroscopy. Rearrangement to give the four-membered ring *(3a)* or *(3b)* cannot be observed; nor can migration of the deuterium into the vinyl positions *(1c)*. A cyclobutyl intermediate *(3b)* in the equilibrium can therefore definitely be ruled out, even for R = C_6H_5.



(1a) *(2)* *(1b)*

(3a) *(1c)* *(3b)*

The rate of the equilibration *(1a)*⇌*(1b)* depends not only on the structure of the organic residue but also on MX, the solvent, the concentration, and the magnesium bromide content of the solution. Thus the rearrangement takes place more rapidly in diethyl ether than in tetrahydrofuran (THF). This is true of the Grignard and dialkylmagnesium compounds. The addition of small quantities of hexamethylphosphoramide to ethereal Grignard solutions leads to acceleration, whereas in the case of dialkylmagnesium compounds the presence of dioxane both in diethyl ether and in THF retards the rearrangement. The reaction rate is found to increase with increasing concentration and on addition of magnesium bromide. The transition from the alkylmagnesium bromide to the dialkylmagnesium compound in diethyl ether also leads to a distinct acceleration of the rearrangement.

The lithium compound *(1a)*, R = CH_3, MX = Li, rearranges particularly rapidly; in this case the establishment of the equilibrium can be followed even at 0 °C in diethyl ether. Since the by-products formed by decomposition of the ether influence the rearrangement rate, accurate kinetic measurements cannot be carried out over a long period. In nearly every case investigated, the rearrangement of the organomagnesium compounds exhibits a reaction order of <1; this indicates the participation of associates, presumably ate complexes, in the equilibria preceding the rearrangement.

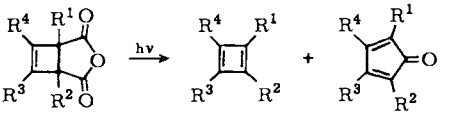
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Cyclobutadienes from Cyclobutenedicarboxylic Anhydrides

By *G. Maier* (lecturer), *U. Mende*, and *G. Fritschi*[*]

The photolysis of cyclobutenedicarboxylic anhydrides[1] appears to be a generally applicable method for the production of cyclobutadienes and cyclopentadienones.



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

	(1a)	*(1b)*	*(1c)*	*(1d)*	*(1e)*	*(1f)*	*(1g)*[2]
R^1	H	H	H	CH_3	CH_3	Cl	H
R^2	H	H	CH_3	CH_3	CH_3	Cl	H
R^3	H	CH_3	CH_3	CH_3	Cl	CH_3	$C(CH_3)_3$
R^4	H	CH_3	CH_3	CH_3	Cl	CH_3	$C(CH_3)_3$

On irradiation (low pressure Hg lamp) in a 2-methyltetrahydrofuran matrix at −196 °C, the unsubstituted anhydride *(1a)* remains practically unchanged, whereas the anhydrides *(1b)*—*(1g)* suffer photolysis. A yellow color appears, and very quickly disappears when the organic glass is warmed. All the observations indicate that the cyclobutadienes *(2b)*—*(2g)* and the cyclopentadienones *(3b)*—*(3g)* are frozen in as the monomers under the irradiation conditions. The steric hindrance of two *tert*-butyl groups is insufficient for appreciable stabilization of *(2g)* and *(3g)*.

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[1] *G. Maier* and *U. Mende*, Tetrahedron Letters, *1969*, 3155.
[2] *R. E. K. Winter*, unpublished.

Studies of Plutonium Dioxide by Chemical Analysis[1]

By *E. Mainka* (lecturer) and *A. v. Baeckmann*[*]

Very accurate and comprehensive chemical analyses are necessary for the supervision and control of fissionable material. To determine the accuracies that can be achieved under the conditions of routine analyses, the results for 160 samples were evaluated statistically. These samples were analyzed both in Hanford (USA) and by us in connection with the acceptance of the plutonium dioxide intended for the fast zero-energy unit at Karlsruhe.

The results show that the mass spectrometric determination of the isotope composition with respect to ^{239}Pu and ^{241}Pu, which is important for checking the material and for its value, was carried out with an accuracy of about 0.05%. The chemical determination of the plutonium contents gave an agreement of about 0.2%.

It is however interesting to note that our results were nearly always lower than those obtained at Hanford. Since we obtained the same results both gravimetrically and oxidimetrically, a systematic error on our part can be ruled out.

It must be mentioned that the material to be analyzed differs in its hygroscopicity according to its previous treatment. It was possible in one case in particular to explain the differences in the analyses on the basis of water absorption by the sample.

The hygroscopic behavior of the sample material is therefore the critical point to which special importance must be assigned in the sampling. We believe that this is the explanation of the systematic error.

Trace impurity determinations were also carried out on these samples at both laboratories by emission spectroscopy. The object of this investigation was to establish that the material corresponded to the given specifications. It was also important to obtain an estimate of the purity. Comparison of the values for up to 17 elements that were present as trace impurities gave an agreement of within 25% in most cases. Considerable differences were, however, sometimes found for the elements Al, Ca, Si, and Na. It is still necessary to check whether this could be due to inhomogeneity of the samples. Nevertheless, it may be said that these differences had no effect on the acceptance, since all the values were within the specification.

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[1] Work performed within the association in the field of fast reactors between the European Atomic Energy Community and the Gesellschaft für Kernforschung m.b.H., Karlsruhe.

Oxidation Kinetics of $NbSi_2$ and $MoSi_2$ at High Temperatures

By *E. Fitzer, K. Matthias* (lecturer), and *K. Wild*[*]

The resistance of $MoSi_2$ and $NbSi_2$ to oxidation in air at 1 atm between 1300 and 1700 °C is due to the formation of a vitreous SiO_2 surface film. The subsequent growth of the SiO_2 film is due to the fact that the oxygen diffusing through the SiO_2 selectively oxidizes the silicon from the hard material at the SiO_2/silicide phase boundary with formation of SiO_2 glass and an intermediate layer of a silicide having a lower silicon content. The rate-determining process in this selective oxidation of Si is the transport of oxygen through the SiO_2.

Conditions for the occurrence of this technically interesting kind of oxidation can be deduced from thermodynamic and kinetic considerations, and their validity has been checked in the cases of molybdenum silicides and niobium disilicide. The required oxidation kinetics for these silicides were quantitatively determined by thermogravimetric measurements. The weight changes due to uptake of oxygen could be used to find the growth of the SiO_2 layer, since the areas of the samples were known. The layer thicknesses found in this way were checked by layer thickness measurements on optical and electron micrographs.

X-ray studies and concentration measurements using an electron beam microprobe were used for the detection of the selective oxidation of silicon with formation of SiO_2 glass and silicides with lower silicon contents. Using a color picture technique it was also possible to show qualitatively the chemical composition of the layers in a single electron-scan photograph.

The satisfactory agreement of the theoretical calculations and the experimental checks in the establishment of the temperature range and the range of O_2 partial pressures for the technically interesting selective oxidation of Si in the molybdenum silicides and in niobium disilicide suggest that the oxidation behavior of other silicides can be estimated purely from characteristic material values.

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Preparation of Plutonium-238 from Americium-241

By *A. J. Blair, H. Ihle, H. Michael* (lecturer), and *A. Neubert*[*]

^{238}Pu can be obtained in macroscopic quantities by two methods: (i) from ^{237}Np by neutron capture and β decay, and (ii) from ^{241}Am by neutron capture, β decay, and subsequent α decay of the resulting ^{242}Cm. When prepared from ^{237}Np, the ^{238}Pu formed contains small quantities of ^{236}Pu (n, 2n; γ, n-reaction), as well as heavy plutonium isotopes[1]. ^{236}Pu is an isotopic impurity, which, owing to the γ activity of its daughter nuclei, affects the use of ^{238}Pu as an energy source for medical purposes (heart pacemakers, artificial hearts), even when present in very small concentrations[2]. ^{236}Pu should not be formed in measurable quantities in the production of ^{238}Pu from ^{241}Am.

Samples of 10, 50, and 100 μg of ^{241}Am were irradiated in the BR2 high-flux reactor (Mol, Belgium). Plutonium, americium, and curium were separated from one another and from the fission products by four ion-exchange separations. On the first column, americium, curium, and fission products were eluted with 8 N HCl from the anion exchanger AG 1—X4. The Pu^{IV}, which remains on the column under these conditions, is then reduced to Pu^{III} with HI and eluted. On the second column, the majority of the fission products, excluding the lanthanides, are eluted before the trivalent actinides with 1 N HCl from the cation exchanger AG 50W-X4. The actinide-lanthanide group separation is carried out on the third column at 80 °C with 12 M LiCl as the eluent and AG 1-X4 as the ion exchanger. Americium and curium are then separated on AG 50W-X4 with α-hydroxyisobutyric acid.

The radiochemical purity and the isotopic composition of the plutonium, americium, and curium fractions are examined by α analysis and mass spectrometry. The experimentally observed yields of the individual actinide nuclides are compared with the yields obtained by calculation for the formation of the various nuclides on neutron irradiation of ^{241}Am.

After completion of the chemical separation, the plutonium formed by α decay of the curium fraction is separated by anion exchange. Its isotope composition is determined by α analysis and mass spectrometry.

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The Analysis of Actinides Separated in a Mass Separator

By *A. J. Blair* and *H. Michael* (lecturer) [*]

In order to determine by emission spectroscopy the chemical impurities in actinide nuclide samples which have been separated in an electromagnetic mass separator, it is advantageous to separate them first from the actinide element. This can be carried out with a number of cation-exchange resin-hydrochloric acid systems [1, 2]. Many elements can be quantitatively separated from lanthanides by elution with 1.75 N HCl from Dowex 50W—X8 [3]. We have measured the partition coefficients of the elements Cs, Ba, Pm, Am, Cm, Cu, Au, Cd, Ta, Cr, W, Re, and Pt in this system. Complete separation, however, of the heavy alkaline earth metals from the actinides is not possible under these conditions. Therefore the partition coefficients of Sr, Ba, Y, Pm, Am, and Cm were determined in the system AG 50W—X4, 1.00 N HCl. Of all the elements examined, only the trivalent lanthanides could not be separated from the trivalent actinides. Contamination by lanthanides is not to be expected in actinides separated in a mass separator.

The partition coefficients K_d were determined by column experiments. If v is the volume of the eluate up to the elution maximum and V is the column volume, then

$$K_d = v/V$$

In the separation and determination of the impurities, the eluate collected up to the beginning of the elution of the actinides was analyzed.

To check the completeness of the separation and the recovery of the contaminating elements, samarium was used as stand-in for trivalent actinides. The elution position was determined radiometrically with ^{153}Sm. 12 elements expected to occur as typical impurities were added to the samples. The impurities were completely separated from the samarium by elution from the cation exchanger AG 50W—X4 with 1.00 N HCl, and were determined by emission spectroscopy. To within the limits of error of the emission-spectrographic analysis, the quantities found in the eluate agreed with those used.

The method allows a simple quantitative separation of nearly all impurities, with the exception of the lanthanides, from the trivalent actinides.

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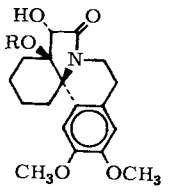
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A Reversible Skeletal Rearrangement in the *trans*-Erythrinane Ring System

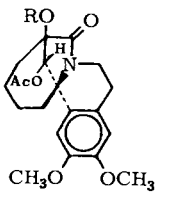
By *S. Mohr* (lecturer), *A. Mondon*, *G. Vilhuber*, and *Chr. Fischer* [*]

trans-Diol-*trans*-erythrinanelactam *(1a)* reacts exclusively at the tertiary alcohol function on monoacetylation or monomesylation to give *(1b)* and *(1c)*. Vigorous acetylation of *(1a)*, on the other hand, leads to rearrangement of the *trans*-erythrinane skeleton and formation of the diacetate *(2a)* with the10-azatetracyclo[10.4.1.0^{1,10}.0^{2,7}]heptadeca-3,5,7(2)-triene skeleton.

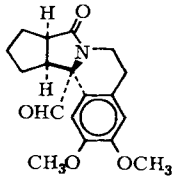
The rearrangement is reversed by hydrolysis, which leads back to the diol *(1a)*. The monomesylate *(1c)* also rearranges to give the mesylate acetate *(2b)*. On Zemplén hydrolysis,



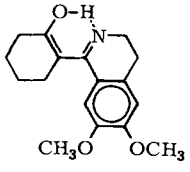
(1a), R = H
(1b), R = Ac
(1c), R = Ms



(2a), R = Ac
(2b), R = Ms



(3)



(4)

(2b) fragments to give the tertiary aldehyde *(3)*. The carboxylic acid corresponding to *(3)* is decarboxylated in concentrated sulfuric acid, with further substantial rearrangement to give the dihydroisoquinoline derivative *(4)*, the structure of which has been verified by independent synthesis.

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Preparation and Structural Chemistry of Mixed Oxo-Thio-Seleno Metalates

By *A. Müller* (lecturer) and *E. Diemann* [*]

By introduction of H_2S or H_2Se into aqueous solutions of $MoO_2S_2^{2-}$, $WO_2S_2^{2-}$, $MoO_2Se_2^{2-}$, and $WO_2Se_2^{2-}$ [*(1)* to *(4)*], it is possible to prepare the following compounds in the form of colored crystals in the presence of CsCl: Cs_2MoOS_3, Cs_2WOS_3, Cs_2MoOSe_3, Cs_2WOSe_3, Cs_2MoOS_2Se, Cs_2WOS_2Se, $Cs_2MoOSSe_2$, and Cs_2WOSSe_2.

The preparation depends on the facts that the more electronegative oxygen is replaced in the ions *(1)* to *(4)* in the first reaction step, and that the cesium salts are relatively sparingly soluble. All the salts indicated dissolve in water to give a deep color and have characteristic electronic spectra. The high extinction coefficients are indicative of M—X π bonds (M = Mo, W; X = O, S, Se). Characteristic ranges can be given for the ν (MX) stretching vibrations: ν (MO): 800 to 900 cm^{-1}, ν (MS): 450—480 cm^{-1}, ν (MSe): $\approx$ 300 cm^{-1}.

The bond orders estimated from the bond force constants according to *Siebert* also point to delocalized π bonds. Corresponding force constants have very similar values in different ions. The X-ray data were determined from single-crystal and powder photographs. All the compounds indicated above crystallize in the rhombic system with the space group D_{2h}^{16}-Pnma. The lattice constants vary only very slightly: a: 9.7—10.1 Å, b: 7.2—7.6 Å, c: 12.2—12.5 Å. The axial ratios are practically constant, $a : b : c \approx 1.35 : 1 : 1.67$. The similarity of the lattice dimensions and reflection intensities to those of other substances crystallizing with the β-K_2SO_4 structure suggests that these compounds crystallize in the pseudo-β-K_2SO_4 structure. The constant axial ratio a/b is particularly characteristic of such a structure.

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Investigation of Lattice Defects from the Diffusion Behavior of Argon in Neutron-Irradiated Potassium Chloride

By *F. W. Felix* and *M. Müller*[*] (lecturer)

Simple interstitial diffusion was formerly postulated for the movement of argon in potassium chloride. Later calculations by *Norgett* and *Lidiard*[1] showed that the measured activation energy of 0.4—0.6 eV[2,3] is too high in relation to that calculated for interstitial diffusion (0.14 to 0.2 eV). The increase in the activation energy is satisfactorily explained by assuming an additional interaction with cation vacancies, which hinder the diffusion of the inert gas through interstitial sites.

A value of $\Delta H = 1.28$ eV has been found for the binding energy of argon in vacancies. The defects resulting from the irradiation also interact with the inert gas and hinder its diffusion. The values found for the binding energy of these irradiation defects with the argon are $\Delta H = 1.9$ eV for a neutron dose of $\Phi t = 5.16 \times 10^{14}$ cm^{-2} and $\Delta H = 1.44$ eV for a neutron dose of $\Phi t = 3.09 \times 10^{17}$ cm^{-2}.

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[1] *M. J. Norgett* and *A. B. Lidiard*, Philos. Mag. *18*, 1193 (1968).

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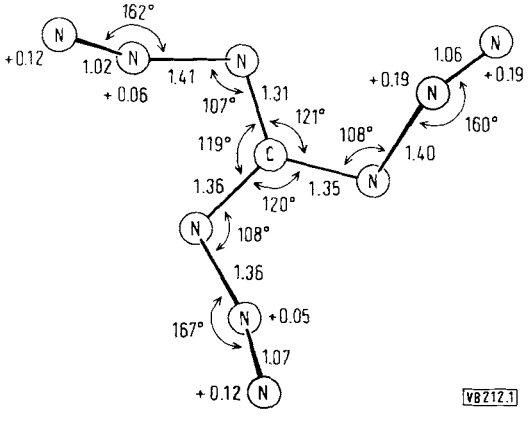
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The Crystal Structure of Triazidocarbonium Hexachloroantimonate

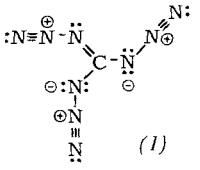
By *Ulrich Müller*[*]

Triazidocarbonium hexachloroantimonate, $[C(N_3)_3]^+SbCl_6^-$, is formed by reaction of antimony azide tetrachloride, $[SbCl_4N_3]_2$, with CCl_4[1]. Its vibration spectrum in both the solid and dissolved states contains 3 bands each for the symmetric and antisymmetric azide stretching vibration, so that the $C(N_3)_3^+$ ion does not have the point symmetry C_{3h} that seems probable at first sight. The crystal structure determination of $[C(N_3)_3]SbCl_6$ shows that the point symmetry C_3 is a good approximation for the $C(N_3)_3^+$ ion and that the deviation from C_{3h} is relatively small.

Single-crystal photographs showed a monoclinic unit cell of space group $P2_1c$ with four formula units, the lattice constants being $a = 9.27$, $b = 10.96$, $c = 15.30$ Å, and $\beta = 113.4°$. The structure was solved by three-dimensional Patterson and Fourier syntheses and refined by the method of least squares to an R value of 6.8% for the 1070 observed reflections. The structure consists of almost strictly octahedral $SbCl_6^-$ ions (average SbCl distance 2.353 Å) and propeller-like $C(N_3)_3^+$ ions assembled in such a way that each ion is surrounded by 8 nearest oppositely charged ions, so that there is some resemblance to the CsCl type. The geometry of the $C(N_3)_3^+$ ion is shown in the diagram, where the numbers with signs indicate the distance of the atom in question from the plane through the strictly planar $C(\alpha\text{-}N)_3$ basic skeleton (all distances in Å).



An unusually large difference is found between the two N—N distances in each of the three non-linear azido groups: The α-N—β-N bond must be formulated as a single bond, and the β-N—γ-N bond as a triple bond. The C—N bond lengths correspond to a bond order of 1.33, and thus compare with those in guanidinium salts. The bonding in the $C(N_3)_3^+$ ion can thus be represented by three resonance forms *(1)*.



(1)

The charge distribution leads to electrostatic interactions between the N atoms of adjacent azido groups within the $C(N_3)_3^+$ ion and between the β-N atoms and one of the neighboring $SbCl_6^-$ ions, which has three Cl atoms oriented toward the β-N atoms of the $C(N_3)_3^+$ ion. These interactions influence the geometry of the $C(N_3)_3^+$ ion.

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[1] *U. Müller* and *K. Dehnicke*, Angew. Chem. *78*, 825 (1966); Angew. Chem. internat. Edit. *5*, 841 (1966); *A. Schmidt*, Chem. Ber. *100*, 3725 (1967).

Isolation of ^{242}Cm for Use in a Radionuclide Battery

By *W. Müller*[*]

The nuclides ^{238}Pu, ^{242}Pu, ^{241}Am, and ^{242}Cm were isolated from samples of ^{241}Am that had been exposed to an integral flux of 1×10^{21} n/cm^2 in the BR2 reactor. At the beginning of the isolation, after a cooling time of about 250 days, 1 g of ^{242}Cm (> 3 kCi) and several grams of plutonium and americium were present.

On the basis of results obtained with samples that had been irradiated for longer times, a separation method based on ion exchange was chosen: The aluminum-encased irradiation samples were dissolved in NaOH, and plutonium (^{238}Pu and ^{242}Pu in a mass ratio of 3.6 : 1) and part of the fission products were removed from the mixture of trivalent actinides and lanthanides with 8 N HCl on Dowex 1X8. Americium and curium were separated from the lanthanides with 10 M LiCl. The decontamination factors of the principal fission products were around 10^3. The mixture of transplutonium elements (^{242}Cm, ^{241}Am) was precipitated from 0.1 N HNO_3 with oxalic acid; the oxalates were decomposed to oxides under nitrogen at 800 °C.

4.3 g of the oxide mixture with a curium content of 450 mg was sealed in a double-walled platinum capsule, transferred from the hot cell into a glove box shielded with 25 cm of water, and introduced into a thermoelectric converter.

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Structure and Conductivity of Organic Polymers

By *H. Naarmann*[*]

The polymeric organic semiconductors known at present cover a conductivity range of 16 orders of magnitude, from the insulators with specific electric conductivities of about

10^{-14} siemens/cm to *e.g.* products with graphite-like structures and values up to about 10^{+2} siemens/cm.

A distinction is made between (i) polymers with conjugated double bonds, (ii) polymers with hetero atoms in which the conjugation chain is interrupted by hetero atoms such as —S—, —O—, or —NR—, (iii) polymers with rings containing metals or with metal atoms in the chain, (iv) charge-transfer complexes, and (v) semiconducting plastics by electrically conducting additives.

Taking into account the relatively large intermolecular distances in organic substances, the mobility [μ] of the charge carriers *i.e.* π electrons, despite the possibility of overlap of π-electron clouds, is about 10^2 to 10^{-6} [$cm^2\ volt^{-1}\ s^{-1}$], *i.e.* distinctly lower than those of metals (10^3) or of inorganic semiconductors (10^3 to $10^{-3}\ cm^2\ volt^{-1}\ s^{-1}$). The following methods can be used to influence the conductivity of organic semiconductors:

1. Increasing the degree of polymerization, *i.e.* increasing the chain length, which is accompanied in every case by a deepening of color and an increase in conductivity.

2. Increasing the pressure. The energy barriers for the electron transition are lowered; depending on the type of semiconductor, the conductivity is found to increase by about 2 powers of ten per 1000 atm.

3. Raising the temperature. The specific electric conductivity and the thermal activation energy E are related as follows:

$$\sigma = \sigma_0\, e^{-E/2kT}$$

(σ = measured conductivity, k = Boltzmann constant, T = temperature in °K).

4. Irradiation (possibly in the presence of sensitizers). The conductivity is increased by 1—3 orders of magnitude. On exposure, *e.g.* to a tungsten filament lamp, a rapid increase in current ("primary photoelectric current") is observed, followed by a slower further increase ("secondary photoelectric current"). When the light is switched off, the primary photoelectric current quickly collapses, whereas the secondary photoelectric current decays with a half life of about 50 seconds. At higher light intensities, the primary photoelectric current increases proportionately.

5. Complex formation (formation of charge-transfer complexes). Conductivity increases of 1—3 orders of magnitude can be achieved by addition of monomeric electron acceptors (or donors) to polymeric electron donors (or acceptors).

The control of conductivity and the production of conducting, readily processable systems (as lacquers) by polymeric charge-transfer complexes in particular offers new possibilities for the production of products with values of 10^{+2} to 10^{+3} siemens/cm, corresponding to the specific electric conductivities of inorganic semi-conductors. Particularly suitable combinations are those in which electron-rich polyolefins are used as donors with polysulfonium picrates as acceptors. These systems and also polymers with added graphite, silicon, or metals such as arsenic or bismuth exhibit the thermoelectric force effect with values of between 4 and 250 μV/°C. The sign of the thermoelectric voltage shows that the conduction is of the p type.

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Calorimetric Temperature Measurements in Plasma Jets

By *R. Neubeck* [*]

Chemical reactions in plasma jets are gaining fresh importance as cheap electrical power becomes available from nuclear power plants. The term "plasma" refers here to partly ionized gases at high temperatures (2000—15000 °K), such as are formed by heating in an electric arc. To understand chemical processes in such plasmas, it is necessary, among other things, to know the local temperature distribution. This was formerly determined mainly by spectroscopic methods. These methods require expensive apparatus, and the accuracy attainable is frequently not very high. On the other hand, a special calorimetric method developed by *J. Grey* (Princeton, USA) has proved very suitable for temperature measurements in subsonic plasma flows.

In this method, a double-jacketed copper probe cooled with pressurized water and having an outside diameter of 1.5 mm is used, so that the local distribution of the temperature in plasma jets can be determined. To minimize errors due to radiation and thermal conduction, the measurement involves two steps. In the first no plasma gas is sucked through the inner tube of the probe, and only an external heat flow occurs from the plasma to the cooling water. A certain quantity of gas is then sucked through the inner tube so that an internal heat flow to the cooling water occurs as well as the external flow. The difference between the two measured quantities of heat gives the enthalpy of the plasma gas at the stagnation point of the probe by means of a simple heat balance if the gas enthalpy at the exit from the probe is known. The temperature can be calculated from the enthalpy. The stagnation pressure is measured at the same time as the enthalpy and used, with the Bernoulli equation, to find the linear velocity. From the velocity, the enthalpy, and the density calculated from the temperature, it is possible to determine the radial distribution of the mass and energy flow density.

The argon and nitrogen plasma jets used in the measurements are characterized by strong radial and axial temperature and velocity gradients. The mass flow density distributions obtained point to a swirl flow in the plasma jet. The local temperature measurements show that the hot plasma jet mixes very poorly with cold secondary gases.

Finally it is also possible to calculate the local equilibrium concentration from the temperature and mass flow density distributions.

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Nucleophilic Cyclic Carbenes as Complex Ligands on Transition Metals

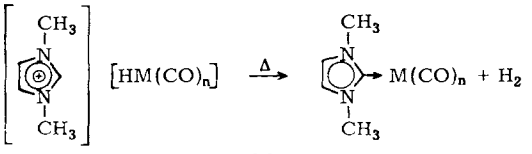
By *K. Öfele* [*]

A series of transition metal complexes with various cyclic carbenes have been prepared by three new methods.

The pentacarbonylchromium and tetracarbonyliron complexes of *N,N'*-dimethylpyrazolin-3-ylidene, 2,4-dimethyl-1,2,4-triazolin-3-ylidene, 1,4-dimethyltetrazolin-5-ylidene, and *N*-methylthiazolin-2-ylidene corresponding to *(1)* were formed in a similar manner in various yields.

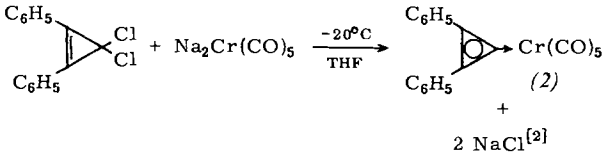
(2) and *(3)* are the first metal complexes in which a carbene that is not stabilized by hetero atoms is present as a ligand. Information about the bonding in *(2)* was provided by an X-ray structure determination [3].

All the complexes mentioned are perfectly stable in air and are characterized by high thermal and chemical stabilities, as is particularly noticeable on comparison of *(3)* with most of the organometallic Pd compounds prepared previously. The carbene ligands act as strong donors in every case. *(1)* and *(2)* do not undergo catalytic hydrogenation even at high pressures. It is interesting to note that all the Cr complexes and all the Fe complexes of type *(1)* with different heterocyclic carbene ligands have almost identical properties.

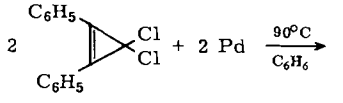


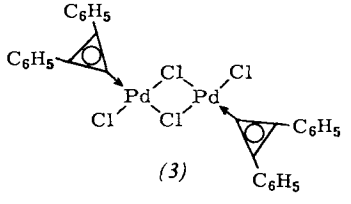
M = Cr, n = 5[1]
M = Fe, n = 4

(1)



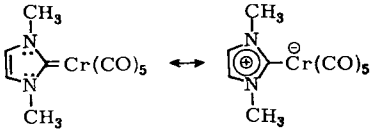
2 NaCl[2]





(3)

The behavior of these new transition metal complexes is evidently determined by the fact that the ligands are more or less aromatic in character, in accordance with (4).



(4)

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[1] *K. Öfele*, J. organometallic Chem. *12*, P 42 (1968).

[2] *K. Öfele*, Angew. Chem. *80*, 1032 (1968); Angew. Chem. internat. Edit. *7*, 950 (1968).

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Reactions of Thermalized Electrons in the Gas Phase

By *D. Perner* (lecturer) and *R. N. Schindler*[*]

Investigations on the reactivity of electrons in the gas phase have been carried out by two methods. In one experiment, the reactions of the electrons are followed by means of a microwave interferometer. A pulsed source giving 600 kV electrons is used for ionization. The arrangement permits the measurement of 10^{11} to 5×10^{13} electrons/cm^3 and their variation with time at a time resolution better than 10^{-7} s.

To obtain information that will be of interest to the radiation chemist, the experiments are carried out at pressures of up to 200 torr. At the electron and ion densities produced in this arrangement, which are relatively high for radiation-chemical conditions, combination of the ions with the electrons predominates in most cases. Rate constants are given not only for recombination reactions but also for the reaction of electrons with typical electron scavengers such as O_2 and SF_6.

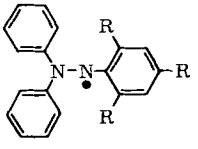
In a second experiment electrons are produced by photoionization of amines or NO in a windowless flow system with an inert gas as a carrier gas, and measured by EPR spectroscopy. This arrangement is suitable for the determination of rate constants for the reaction of electrons with substrate molecules

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Stable Triarylhydrazyls Containing no Nitro Groups as Polymerization Inhibitors

By *G. Peschk* (lecturer) and *D. Braun*[*]

Until recently, only stable triarylhydrazyls containing nitro groups such as diphenylpicrylhydrazyl *(1)* were known. When these compounds are used in studies of the kinetics of polymerization (*e.g.* for the determination of the rate of decomposition of free-radical forming inititators[1] and of the initiation rate[2]) relatively large errors occur, since in addition to the radical function the nitro groups present in the molecule also have a more or less strongly pronounced retarding effect on the reaction[3]. With the synthesis of new triarylhydrazyls containing no nitro groups, *e.g.* α,α-diphenyl-β-[2,4,6-tris(methoxycarbonyl)phenyl]hydrazyl *(2)*[4] and α,α-diphenyl-β-(2,4,6-tricyanophenyl)hydrazyl *(3)*, which was prepared independently by *Bretschneider* and *Wallenfels*[5] and by the present authors, compounds have become available that are better suited for kinetic purposes.



(1), R = NO_2
(2), R = $COOCH_3$
(3), R = CN

The hydrazyl *(2)* reacts in a strictly stoichiometric ratio with the free radicals formed by decomposition of initiators as well as with growing macroradicals, and so approaches the status of an ideal inhibitor.

Compounds of type *(1)* do not completely inhibit polymerization, as was determined by combining the ESR spectroscopic measurement of the consumption of the inhibitor radicals with the dilatometric determination of the chemical conversion. Compounds *(2)* and *(3)*, on the other hand, inhibit the polymerization reaction until they are completely consumed without affecting the subsequent polymerization, while the secondary reaction products of *(1)* formed during the induction period exhibit a strong retarding effect.

Whereas the decomposition of the initiator azoisobutyronitrile in the presence of oxygen yields peroxy radicals, which cleave the N—N bond of the hydrazyl, the products formed in the absence of oxygen are mainly substitution products of the hydrazyl, from which hydrazines are formed by hydrogen transfer. Products that can be reoxidized to hydrazyls are present after polymerization in this case.

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[1] *C. E. H. Bawn* and *D. Verdin*, Trans. Faraday Soc. *56*, 815 (1960).

[2] *M. Imoto, M. Kinoshita*, and *M. Nishigaki*, Makromolekulare Chem. *86*, 217 (1965).

[3] *Ch. Price* and *D. Durham*, J. Amer. chem. Soc. *65*, 757 (1943); *F. Tüdös, J. Kende*, and *M. Azori*, J. Polymer Sci. *A 1*, 1353 (1963).

[4] *D. Braun, G. Peschk*, and *E. Hechler*, Chimia *21*, 536 (1967).

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Preparation and Properties of Mixed Sulfides of the 4f Transition Elements

By *H. Pink* [*]

Ternary chalcogenides $M^{II}M_2^{III}X_4$ having various combinations of elements M^{II} and M^{III} with X = O or S have been known in large numbers for a long time. However, substances in which M^{III} is a lanthanide and M^{II} is Eu^{II} or an element of group IIa are relatively new.

These compounds are often prepared from the elements or by solid state reactions from the binary compounds. For example, the series $SrLn_2S_4$ (Ln = lanthanide) can be prepared by prolonged heating of SrS and Ln_2S_3. For the mixed sulfides $EuLn_2S_4$, EuS and Ln_2S_3 must first be prepared separately.

We found in an earlier investigation [1] that analytically pure and phase-pure europium(II) sulfide can be obtained in accordance with

$$Eu_2(C_2O_4)_3 \xrightarrow[T]{H_2S} 2\,EuS + 2\,H_2C_2O_4 + 2\,CO_2 \qquad (1)$$

from the oxalate, which is readily obtainable by precipitation of Eu^{3+} with $C_2O_4^{2-}$.

The precipitation of oxalate is well known as an accurate method of determination in the analytical chemistry of lanthanides. We have now precipitated the mixed oxalates from solutions containing Eu^{3+} and Ln^{3+} in a molar ratio of 1 : 2 and treated the resulting precipitates in accordance with eq. (1).

The products are dark brown to reddish brown powders whose composition corresponds to the empirical formula $EuLn_2S_4$. X-ray structure investigation shows that a change in structure from the cubic Th_3P_4-type to the orthorhombic $CaFe_2O_4$-type takes place with increasing atomic weight of Ln between Gd and Tb. The ratio of Eu^{2+} : Eu^{3+} was determined by the Mössbauer method from the isomerization shift of the 21.6 keV γ radiation of ^{151}Eu; the effective magnetic moments and the paramagnetic Curie temperatures were determined from susceptibility measurements between 4.2 and 500 °K.

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[1] *H. Pink*, Z. anorg. allg. Chem. *364*, 5, 248 (1969).

Use of Gas Chromatography for the Study of the Interaction Forces between Binders and Solvents in Paint Films

By *M. Schneider* and *K.-H. Reichert* (lecturer) [*]

Paint films may be regarded as multi-component systems composed of binders, pigments, and a series of different volatile and non-volatile substances. The interaction forces between the various components in the film are of great importance to the film properties. For example, the interactions between binders and solvents affect the film-forming process, which is responsible for a number of properties of the final paint film.

In order to investigate the relationship between different film properties and the interaction forces, attempts were made to obtain a suitable index for binder-solvent interactions using a gas-chromatographic technique. For this purpose the binders were applied to finely powdered inert support materials and were used in ordinary separating columns for the gas chromatographic measurement. On the resulting binder columns retention volumes of solvents were measured, which are dependent on the equilibrium distribution of the solvents between the carrier gas and the stationary binder phase, and are therefore closely related to the free energy of vaporization of the solvents from the corresponding binder phase.

Comparative studies on solvents of several homologous series on different binder systems have shown that the retention volumes of the solvents at adequate temperatures can be used as a measure of the interaction with the corresponding binder. For a given polar binder, the interaction forces generally decrease with decreasing polarity of the solvent, *e.g.* esters > aromatic hydrocarbons > aliphatic hydrocarbons.

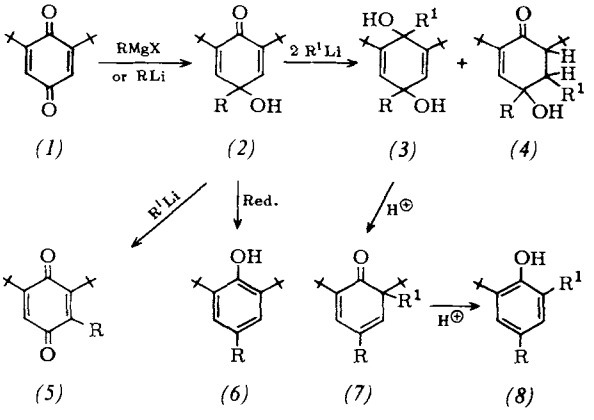
Binders can also be characterized according to their interactions with solvents by comparison of the retention volumes of polar and apolar solvents. It is possible by this method to distinguish not only binders of completely different types, *e.g.* urea resins and cyclized rubber, but also chemically very similar binders such as copolymers with different compositions. On vinyl chloride-vinyl acetate copolymer systems, for example, the interaction with polar solvents was found to increase with the acetate content of the copolymer.

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Reactions of Organolithium Compounds with Sterically Hindered Quinones, Quinols, and Quinonemethides

By *A. Rieker* [*]

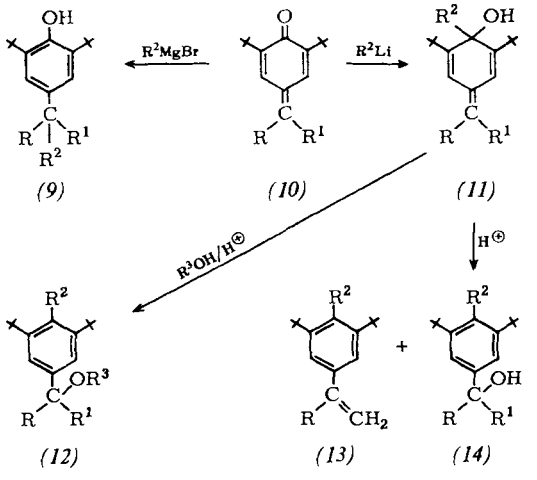
Experiments were carried out to establish whether the sterically hindered carbonyl group in 2,6-di-*tert*-butyl-substituted quinones, quinols, and quinonemethides undergo 1,2-addition with organolithium compounds.



R = C_6H_5

The reaction of *(2)*, R = C_6H_5, with 1 equivalent of R^1Li, R^1 = C_6H_5, CH_3, in ether at 30 °C leads after 12 hours and working up in air to 47% of the quinone *(5)*, R = C_6H_5, presumably as a result of 1,2-migration. With two equivalents of R^1Li (4 hours, 60 °C, diethyl ether or di-*n*-butyl ether, hydrolysis at pH > 7), on the other hand, the 1,2-addition products *(3)* are obtained, *e.g.* R = $C(CH_3)_3$, R^1 = CH_3: 90% (yield); R = $C(CH_3)_3$, R^1 = 4-$CH_3C_6H_4$: 50%; R = $C(CH_3)_3$, R^1 = C_6H_5: 46%; R = C_6H_5, R^1 = CH_3: 92%; R = C_6H_5, R^1 = 4-$CH_3C_6H_4$: 59%; R = R^1 = C_6H_5: 56%; R = R^1 = CH_3: 85%; R = CH_3, R^1 = 4-$CH_3C_6H_4$: 38%. The 1,4-addition products *(4)* are formed in smaller quantities. The proportion of *(4)* increases at higher concentrations, *e.g.* approximately 0.7 M, R = $C(CH_3)_3$, R^1 = C_6H_5: 60% of *(4)*. Similarly, the reaction of the quinone *(1)* with two equivalents of R^1Li also yields *(3)*; reactions with one equivalent of RLi or RMgX, on the other hand, leads only to *(2)*, R = C_6H_5, 2-, 3-, 4-$CH_3C_6H_4$, 2-, 3-, 4-$CH_3OC_6H_4$, 4-$C_6H_5C_6H_4$, 4-$(CH_3)_3C$—C_6H_4, 2,4,6-$(CH_3)_3C_6H_2$, 4-BrC_6H_4, α-naphthyl, β-naphthyl, cycloheptyl, in yields of 50—80%. The quinols *(2)* can be reduced to the phenols *(6)* in very good yields with Zn/HCl.

The diols *(3)* react with acids to give 2,4-cyclohexadienones *(7)*, which lose isobutylene to give the phenols *(8)* in yields of up to 90%. This reaction can be followed directly by UV and NMR spectrometry. In the case R = C_6H_5 and R^1 = 4-$CH_3C_6H_4$, *(7)* can be isolated as such.



Quinonemethides *(10)* generally give 1,6-adducts, *e.g.* *(9)*, R = R^1 = R^2 = CH_3 with Grignard compounds, whereas reaction with R^2Li leads preferentially to 1,2-adducts, *e.g.* *(11)* R = R^1 = CH_3, R^2 = C_6H_5; R = R^1 = R^2 = C_6H_5 (90%); R = H, R^1 = R^2 = C_6H_5 (57%). The adducts *(11)* are converted into the alcohols *(14)* by acids, and into the ethers *(12)* by acid and alcohol. For R = R^1 = CH_3 and R^2 = C_6H_5, styrene *(13)*, R = CH_3, R^2 = C_6H_5, is formed as well as *(14)* from *(11)*. It is therefore concluded that 1,2-addition predominates in the reactions of the 2,6-di-*tert*-butylated compounds *(2)*, *(1)*, and *(10)* with organolithium compounds, despite strong steric hindrance.

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Solid State Exchange Between Radiohalide and Ligands in Doped Hexahalo Complexes of Re^{IV} and Rh^{III}

By *K. Rössler* (lecturer) and *S. R. Upadhyay*[*]

Model experiments on ligand exchange in the solid state were carried out in hexahalo-complexes of Re^{IV} and Rh^{III} to obtain information on the annealing mechanism of recoil halogen produced by nuclear processes in the same systems (cf. abstracts *Bell* and *Stöcklin* in this collection).

Compounds of the type $K_2[ReX_6]$ and $K_3[RhX_6]$ (X = F, Cl, Br) were doped by coprecipitation with practically carrier-free radiohalides ($*X^-$ = $^{38}Cl^-$, $^{82}Br^-$, $^{131}I^-$). At temperatures between 80 and 250 °C it could be observed that the radiohalide-ions rapidly entered the ligand sphere, *e.g.*:

$$*X^- + K_2[ReCl_6] \rightarrow Cl^- + K_2[ReCl_5*X]$$

The identity of the products was confirmed by high-voltage electrophoresis.

Like the thermal annealing of recoil halogens in the corresponding systems, this solid state exchange proceeds approximately in accordance with first order kinetics and leads to temperature-dependent plateaus.

For a given matrix, the exchange velocity decreases with varying dopants in the sequence $^{38}Cl^- > {}^{82}Br^- > {}^{131}I^-$ *e.g.* (at 200 °C):

$^{38}Cl^-/K_2[ReCl_6]$: $k = 18.2\times10^{-2}$ min^{-1},
$^{82}Br^-/K_2[ReCl_6]$: $k = 5.0\times10^{-2}$ min^{-1},
$^{131}I^-/K_2[ReCl_6]$: $k = 3.0\times10^{-2}$ min^{-1}.

For the same dopant, the exchange velocity is higher in the hexabromo complex than in the hexachloro complex *e.g.* (at 200 °C):

$^{38}Cl^-/K_2[ReCl_6]$: $k = 18.2\times10^{-2}$ min^{-1},
$^{38}Cl^-/K_2[ReBr_6]$: $k = 48.0\times10^{-2}$ min^{-1};
$^{82}Br^-/K_2[ReCl_6]$: $k = 5.0\times10^{-2}$ min^{-1},
$^{82}Br^-/K_2[ReBr_6]$: $k = 36.5\times10^{-2}$ min^{-1}.

The exchange proceeds faster in the rhodium complexes than in the corresponding rhenium systems. These results can be attributed to steric and bond-energy effects.

The remarkable agreement of velocity constants and activation energies from the solid state exchange with those from thermal annealing of recoil atoms suggests that a very similar mechanism is operative in both cases. The very low activation energies (E_A = 3.5 kcal/mole for $^{38}Cl^-/K_2[ReCl_6]$ and E_A ≈ 7 kcal/mole for $^{82}Br^-/K_2[ReBr_6]$) indicate that the overall formalism of a first order reaction hides more complex processes. As a possible mechanism a lattice-defect promoted migration of ligand vacancies is suggested.

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Helix Formation in Oligopeptides of L-Proline

By *M. Rothe* (lecturer), *R. Theysohn*, *K.-D. Steffen*, *Hj. Schneider*, *M. Zamani*, and *M. Kostrzewa*[*]

We have prepared the hitherto unknown oligo-L-prolines up to the heptadecapeptide (n = 2–17) and co-oligopeptides of proline and glycine, such as H(Pro-Gly-Gly)$_n$OH with n = 1–8, by the conventional *p*-nitrophenyl ester method and by *Merrifield*'s method in a monodisperse and electrophoretically pure state. The properties of these compounds as collagen models[1] have been investigated.

Conformational studies by spectroscopic comparison (ORD, CD, IR, UV, NMR) with the corresponding polypeptides showed that helix formation starts with triproline[2].

Specific rotation measurements showed that beginning with this degree of polymerization, two conformations are present as in polyproline, *i.e.* a right-handed helix with *cis*-peptide linkages (form I) and a left-handed helix with trans-peptide linkages (form II). These conformations are stabilized in certain solvents, and can be interconverted by changing the solvents, as is shown by mutarotation in water to more negative final values (formation of form II) and in the opposite sense in *n*-propanol (back to form I).

The differences in specific rotation values increase rapidly to more than 400° at the decapeptide (in water). Beginning with hexaproline, forms I and II can be isolated and give conformation-dependent IR and CD spectra. It has thus become possible for the first time to prepare definite linear peptides with *cis*-peptide linkages. Their optical rotatory properties are similar to those of cyclotri-L-prolyl, in which, for steric reasons, only *cis*-peptide linkages are possible. The conformation of this 9-membered ring has been studied by CD and NMR spectroscopy.

The properties of the free and N-blocked[3] (*e.g.* *tert*-butyloxycarbonyl and benzyloxycarbonyl) oligoprolines approach those of the polymers as the chain length increases (with a marked change between the dipeptide and the tripeptide). The typical IR bands of polyproline I and polyproline II appear for the first time in the spectrum of pentaproline; N-blocked tetraprolines exhibit spectra nearly related to that of polyproline II.

In CD measurements in water, a weak positive and a strong negative Cotton effect is observed beginning with triproline (at 226 and 197 nm, respectively). They are shifted to higher wavelengths with increasing n, and at heptaproline the posi-

tions of the Cotton effects of polyproline II (230 and 205 nm, respectively) have practically been reached.

In the co-oligopeptides with glycine, on the other hand, no ordered structures are present even in the octatripeptide (24 amino acid residues).

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[1] *J. P. Carver* and *E. R. Blout* in G. N. Ramachandran: Treatise on Collagen. Academic Press, London and New York 1967, Vol. 1, p. 441.

[2] *M. Rothe, R. Theysohn, K.-D. Steffen, M. Kostrzewa, M. Zamani*, Proc. Tenth European Peptide Symposium, Abano Terme 1969; North-Holland Publ. Co., Amsterdam, in press.

[3] Cf. *T. Isemura, H. Okabayashi*, and *S. Sakakibara*, Biopolymers *6*, 307, 323 (1968).

IR and Raman Spectroscopic Studies on the Structure of TlF

By *A. Ruoff*[*]

In X-ray studies, *J. A. A. Ketalaar*[1] could not distinguish between the space groups Fmmm, Fmm, and F222 for the crystal structure of TlF, whereas *Alcock*[2] reported the space group to be Pm2a. However, since *Alcock* precipitated his products from aqueous solutions, it is not certain whether this was TlF or a hydrate of TlF. Using the method of factor group analysis, we obtained the selection rules given in the table for the IR and Raman spectra.

	No. of vibrations		
	IR and Raman active	Raman active only	IR active only
F mmm	—	—	3
F mm	3	—	—
F 222	3	—	—
Pm 2a	17	4	—
found	3	—	—

The spectra thus give the space group Fmm or F222. In the latter case, TlF would have the zinc blende structure. This would appear very unlikely because of the ratio of the ionic radii. The vibration frequencies can be readily correlated with the Tl—F distances by the Badger rule[3], since ν_1, ν_2, and ν_3 belong to different species. This correlation provides further confirmation of the space group Fmm, and allows an approximate determination of the position of the F atom (which is difficult to localize by X-ray methods). The following result is obtained:

Fmm Tl: 0; 0; 0; F: 0;0; 0.46

The Tl has a coordination number of 5+1 in this arrangement. This structure is similar to those of SnO, (isoelectronic) red PbO, and BiO^+.

A relatively sharp band in the IR spectrum at 474.5 cm^{-1}, which has no counterpart in the Raman spectrum, is very probably due to monomeric TlF, the content of which in the lattice may be estimated as about 5–10%.

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[3] *D. R. Herschbach* and *V. W. Laurie*, J. chem. Physics *35*, 458 (1961).

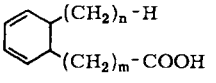
Cyclization of Long-Chain Trienoic Carboxylic Acids with Alkali

By *A. N. Sagredos* (lecturer), *J. D. von Mikusch*, and *V. Wolf*[*]

The cyclization of 9-*cis*,12-*cis*,15-*cis*-octadecatrienoic acid (linolenic acid), which has been observed to take place even under the conditions of alkali isomerization at 180 °C, is preceded by conjugation of the triene system. With tung oil, 80% of which consists of the glycerides of α-eleostearic acid (9-*cis*,11-*trans*,13-*trans*-octadecatrienoic acid) cyclization accordingly proceeds more rapidly than with linseed oil. However, since linolenic acid, which is present in linseed oil to the extent of about 54%, isomerizes to give a mixture of conjugated dienoic and trienoic acids, it was surprising to find that linseed oil gives a more uniform cyclization product than tung oil.

To elucidate the course of the reaction, 9-*trans*,12-*trans*,15-*trans*-octadecatrienoic acid (linolenelaidic acid) and 9-*trans*, 11-*trans*,13-*trans*-octadecatrienoic acid (β-eleostearic acid) as well as the above mentioned oils were treated with 6.5% KOH-glycol solution for 25 minutes at 180 °C, and the composition of the resulting isomeric cyclohexadiene derivatives was determined after aromatization, special attention being paid to the length of the side chains.

Cyclization of the *cis*,*cis*,*cis*-triene (linolenic acid) led primarily to compound *(1)*, $n = 3$, $m = 8$, whereas the three trienes with central *trans* double bonds gave mixtures of *(1)* with $n = 2$, 3, and 4 (from linolenelaidic acid) and $n = 3$, 4, and 5 (from the other trienes).



(1), n + m = 11

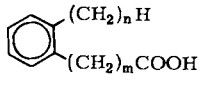
It may be concluded from these observations that the primary reaction is an ionic isomerization (allylic shifts and *cis-trans* rearrangements) of the trienecarboxylic acids into conjugated isomers. The ring-forming conjugated trienes with a central *cis* double bond subsequently cyclize by a multi-center mechanism leading to the cyclohexadiene derivatives.

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Aromatization of C_{18} Alkylcyclohexadienecarboxylic Acids

By *A. N. Sagredos*, *H. Scharmann* (lecturer), and *V. Wolf*[*]

In the presence of alkali, C_{18} trienoic carboxylic acids form alkylcyclohexadienecarboxylic acids after ionic isomerization. This cyclization is assumed to proceed by a multi-center mechanism. Aromatic carboxylic acids *(1)* are formed in a secondary reaction.



(1), n + m = 11.

It was shown by spectroscopic studies that all the isomers with $n = 0$–11 occur in the product. The mass-spectrometric fragmentation behavior in this series of isomers exhibits characteristic differences when n and m vary. Homologous ω-phenylalkanecarboxylic acids, alkanecarboxylic acids, alkylbenzenes and alkanes have been detected as by-products of this aromatization. The distribution of the homologous compounds shows a distinct dependence on the positions of the double bonds in the initial trienoic carboxylic acid. A

free-radical reaction and a base-catalyzed disproportionation of the initially formed alkylcyclohexadienecarboxylic acids is proposed.

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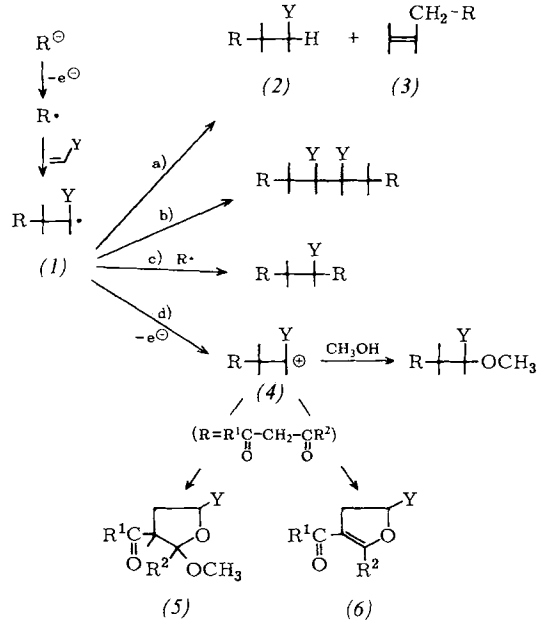
Oxidative Addition of Organic Anions to Olefins — Oxidative Dimerization of Olefins

By *H. Schäfer*[*]

Organic anions can be oxidatively added to unactivated double bonds at a platinum anode[1].

We have achieved the addition of the following anions (R^-) to olefins such as styrene, vinyl ethyl ether, butadiene, cyclooctene or cyclohexene: sodium salts of 1,3-dicarbonyl compounds, of aliphatic nitro compounds, and of nitriles; also Grignard compounds and sodium azide.

The electrolysis products can be readily explained if the following possibilities are assumed for the stabilization of the free-radical primary adducts *(1)*: (a) abstraction of hydrogen from the allyl position of the olefin to form alkyl *(2)* and alkenyl derivatives *(3)*, (b) dimerization, (c) mixed coupling, and (d) oxidation to give cations *(4)*, which are either solvolyzed or (in the case of 1,3-dicarbonyl compounds) intramolecularly cyclized to give tetrahydrofuran *(5)* or dihydrofuran *(6)* derivatives. Sodium azide leads by paths (a), (b), and (c) to monoazido-, 1,2-, and 1,4-diazidoalkanes, whose reduction yields the corresponding amines.



If the electrolysis is carried out on graphite instead of platinum anodes, these additions are almost completely suppressed and the dimers of the olefins are formed instead[2]. This oxidative dimerization of olefins allows the one-step preparation of 1,4-dimethoxybutane or butadiene derivatives from olefins and the coupling of aldehydes or ketones *via* the enol ethers to give 1,4-dicarbonyl compounds. The reaction is assumed to proceed by oxidation of the olefin to a radical-cation, which gives 1,4-dimethoxybutane and butadiene derivatives by dimerization and by S_N1 and E1 reactions respectively.

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Reactions of Electrophiles with Phosphonium Salts in the Absence of Auxiliary Bases

By *G. P. Schiemenz* (lecturer) and *J. Becker*[*]

Phosphonium salts are CH acid compounds. Under the influence of bases, the cations lose a proton from the α-position with respect to the phosphorus; the resulting carbanions react with many electrophiles. An auxiliary base has always been used in the past for the production of the carbanions. This should really be superfluous. The phosphonium cation is necessarily associated with an anion, which should be able, under suitable conditions, to take over the function of the base; this is particularly true of the fluoride ion, which is strongly nucleophilic in aprotic polar solvents. Phosphonium salts would then be both CH acids and bases.

Phosphonium fluorides were prepared in methanol solution from the bromides or chlorides on an ion exchanger charged with fluoride. The crystalline fluorides could be isolated in the case of cations of relatively low acidity; they have the typical properties of phosphonium salts: conductivity and molecular weight determinations showed that they are largely dissociated in polar solvents, but associated into ion pairs and higher aggregates in chloroform. In their NMR spectroscopic behavior they surprisingly show a greater similarity in $CDCl_3$ to the iodides than to the chlorides, possibly because of solvation of the anion. The α-proton signals appear as a doublet, *i.e.* deprotonation could not be detected in this way. In acetonitrile, however, they react with *p*-nitrobenzaldehyde in a sort of Wittig reaction to give good yields of olefins.

The reaction also takes place with more strongly acidic phosphonium salts, but the deprotonation to form the ylide takes place so readily that the fluorides can no longer be isolated. Mere evaporation of the methanolic solution often leads quantitatively to the ylide, *e.g.* in the case of triphenyl-*p*-nitrobenzylphosphonium fluoride, whose pale yellow methanol solution is stable for several months, the ylide is recognizable by its deep red color. Since the ylides here are not formed in a basic medium, they are stable for long periods; the phosphonium fluorides are regenerated by atmospheric moisture. The special role of the fluoride ion is seen in the NMR spectrum of acetonyltriphenylphosphonium salts in acetonitrile. The bromide has a doublet for the CH_2 protons; in the fluoride, the $^{31}P-^{1}H$ coupling is broken down by deprotonation-protonation equilibria. The particularly acidic cyanomethyltriphenylphosphonium cation enters into Wittig reactions even as the bromide.

The carbonyl olefination occasionally fails if one of the reactants is sensitive to the added base; for example, aldehydes may preferentially undergo the Cannizzaro reaction. The new variant, in which the reaction is not carried out in a basic medium, should be helpful in such cases. Moreover, the materials required do not include the auxiliary base, but consist entirely of substances of which groups are found in the desired products.

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Mechanism of the Anionic Catalysis of the Decomposition of Nitramide in the Light of New Views on Acid-Base Catalysis

By *Hermann Schmid*[*]

The elucidation of the course of general acid-base catalysis in the mutarotation of α-glucose in aqueous solution[1] also

leads to new views on the course of general base catalysis in the decomposition of nitramide ($H_2N{-}NO_2$) in aqueous solution. The entropy change ΔS_2 in the reaction of the hydrated anion $A^- \cdots H_2O$ with the hydrated oxonium ion $H_2O \cdots H_3O^+$ to give the hydrated acid $AH \cdots OH_2$ can be calculated from the catalysis coefficients of the anion (k_{A^-}) and of water (k_W) in the acid-base catalysis of the mutarotation of α-glucose with the same activation enthalpy:

$$\Delta S_2 = R \ln (k_{A^-}/k_W)$$

The entropy change ΔS_1 in the opening of the hydrogen bond $AH \cdots OH_2$ can also be calculated from the catalysis coefficients of the acid (k_{HA}) and of water (k_W) in the acid-base catalysis of the mutarotation of α-glucose with the same activation enthalpy:

$$\Delta S_1 = R \ln (k_{HA}/k_W)$$

In the general base catalysis of the decomposition of nitramide by anions such as formate, acetate, propionate, benzoate, primary phosphate, and hydroxide, on the other hand, the entropy change

$$\Delta S = R \ln (k_{A^-}/k_W)$$

corresponds to the entropy change in the reaction of $A^- \cdots H_2O$ with $H_2O \cdots H_3O^+$ to give the unhydrated acid AH.

This equation is interpreted as meaning that the anionic reaction, like the mutarotation of α-glucose, is preceded by the transfer of a proton from the nitramide (or from its tautomer respectively) to the water molecule of the hydrated anion $A^- \cdots H_2O$. The resulting H_3O^+ reacts with A^-, because of the immediate proximity of the two, without further activation enthalpy and with an entropy change of only ΔS. In contrast with the general acid-base catalysis of the mutarotation of α-glucose, this reaction leads not to $AH \cdots OH_2$ but only to AH.

The entropy change for the breaking of the hydrogen bonds

$$H_2O \cdots H{-}O{-}H \cdots H_2O$$

can thus be calculated from the OH^- catalysis of both reactions. This entropy value agrees with that found by *Walrafen* from the Raman spectrum of water. The Brönsted equation is replaced by the linear relation of ΔS_1 and ΔS_2 to the logarithm of the base constant K_B[1]. In comparison with

$$\Delta S_2 = \beta R \ln K_B$$

it is

$$\Delta S = R \ln K_B$$

β is therefore equal to 1. The deviations from this relationship are clarified by thermodynamics.

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[1] Recent publications: *H. Schmid*, Mh. Chem. *99*, 1932 (1968); *100*, 851, 1654 (1969).

Elucidation of the Mechanism of the Reaction of Epoxides with Carboxylic Acids by Kinetic Studies and Model Analysis Using a Digital Computer [1]

By *W. W. Schmitt* [*]

The primary step in the acid-catalyzed reaction of α-epoxides with carboxylic acids (hydroxyalkylation), which leads to 1,2-diol esters, was subjected to a comprehensive kinetic analysis in an inert solvent without additional catalysts.

The systems studied were propylene oxide + benzoic, formic, acetic, and chloroacetic acid.

From the kinetic results, it was possible to distinguish two parallel paths leading to the same reaction product β-hydroxypropyl ester, since it was found *e.g.* that the reaction order with respect to the acid component, independent of the system and temperature, showed sliding transitions from 1.0 to 2.0, the order with respect to epoxide converging to zero.

From these results and independent spectrometric observations, it was shown that both steps take place from a fast H-association equilibrium that precedes the actual reaction, the "true" reactants of the individual steps still being unknown at that time because of interplay of dimerization and association equilibria of the acids.

All but two of the formal reaction possibilities were eliminated as nonsense reactions by a selection strategy with the aid of a digital computer, so that the following quantitative interpretation can be given.

The parallel elementary steps of the process are the unimolecular reaction by rearrangement of the epoxide-acid associate and the bimolecular reaction of two epoxide-carboxylic acid associates with one another which are described by time equations of the type

$$v_R = -(dx/dt) = k_1 \times c_a + k_2 \times c_a^2$$

where c_a is the equilibrium concentration of the associate in question.

The rate constants for the two steps were determined for all systems by congruence analysis, and the "true" activation entropies were calculated from the dependence on T. In agreement with the unimolecular reaction course, $\Delta S^{\neq}$ values of about —40 e.u. were obtained for k_1.

The purely associate-controlled reaction course is contrary to ionic A and S_N mechanisms described earlier for the systems investigated. The Brønsted law is formally satisfied with $\alpha = 1$; it seems necessary, however, to reformulate its applicability as a criterion of catalysis in non-aqueous systems.

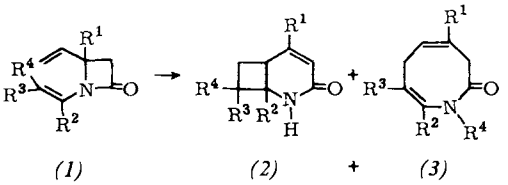
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[1] *W. W. Schmitt*, Z. physik. Chem. N.F. *59*, 217 (1968).

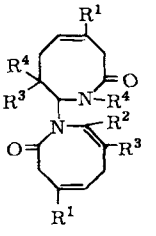
The Cope Rearrangement of 1,4-Divinylazetidin-2-ones

By *H. Schnabel* [*]

1,4-Divinylazetidinones *(1)* rearrange when heated at 160 to 210 °C. Depending on the nature of the substituents R^1—R^4 (H, CH_3), the products are compounds of the types *(2)*, *(3)*, and *(4)*, single or mixed in various ratios.



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



(4)

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Dependence of the Stress Birefringence of Rubber-Elastic Substances on Temperature and Degree of Swelling

By *J. Schwarz* [*]

It follows from the *Kuhn-Grün* statistical theory of photoelasticity that the birefringence exhibited by an amorphous rubber-elastic substance at constant deformation is independent of temperature. It also follows that the photoelastic coefficient, *i.e.* the ratio of the birefringence to the stress, remains constant when these substances are swollen in solvents, provided that a correction is applied to allow for the possible change in the average refractive index of the material on swelling.

We found that for crosslinked polybutadiene and crosslinked styrene-butadiene copolymer (26% styrene), the birefringence at constant deformation decreased by 23 and 12% respectively with rising temperature between 0 and 75 °C.

The corrected photoelastic coefficients of the polymers also decreased on swelling in carbon tetrachloride, the maximum decreases being 35 and 30% respectively.

Deviations from the predictions of the simple theory are to be expected if the mean conformation of the polymer, *i.e.* that of the main chains and that of side groups, changes with temperature and degree of swelling. The addition of optically anisotropic solvent molecules to the polymer during swelling can also cause deviations; in order to prevent this, carbon tetrachloride was used as the swelling medium.

In the case of polybutadiene it is certain that the decrease in birefringence with rising temperature and with swelling is not due to side group effects; this is also fairly certain in the case of the styrene-butadiene copolymer.

This decrease must therefore be due to an effect of the mean conformation of the main chains. It can be concluded that in amorphous polymers, instead of complete randomness, certain positions of chain segments in relation to one another are preferred as a result of the interaction forces, and this leads to a short-range order in the sense that the chains tend to be roughly parallel to one another. This deviation from randomness should decrease or disappear entirely with rising temperature and with swelling of the polymers.

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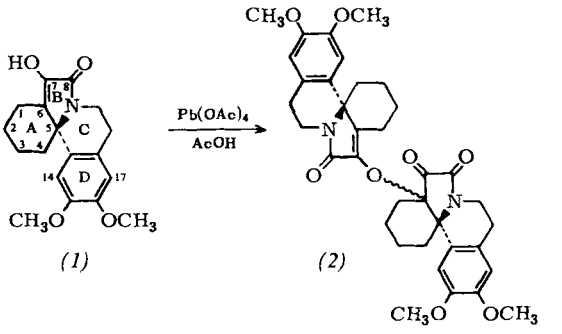
Synthesis of *trans*-Erythrinanes

By *P.-R. Seidel* (lecturer) and *A. Mondon* [*]

All the erythrinanes described prior to 1960 have been shown to belong to the *cis* series (with respect to the linkage of rings A and B) [1]. *trans*-Erythrinanes were unknown until now, though models of these compounds can be readily constructed.

A *trans*-linked erythrinane derivative has been obtained on the preparative scale for the first time from the enol lactam *(1)* by oxidation with $Pb(OAc)_4$. The reaction product can be separated by fractional crystallization into two isomeric "double molecules" *(2)* (m.p. 240 and 270 °C).

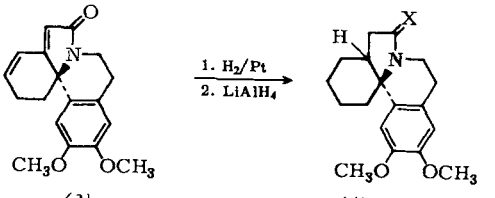
These compounds, which are no longer enolizable, are remarkably readily hydrogenated. They smoothly take up 3 moles of H_2, and after hydrogenolysis of the enol ether linkage, they both give *cis*-15,16-dimethoxy-7β-hydroxy-erythrinan-8-one, which is obtained directly under the same



(1) *(2)*

conditions from *(1)*. This confirms the existence of *cis,trans*-isomeric erythrinane derivatives.

trans-Erythrinanes that are not substituted on C-7 are obtained by hydrogenation of the diene lactam *(3)* with Pt in methanol or glacial acetic acid. The known *cis* base *(5a)* and the new *trans* base *(5b)* are obtained by chromatographic separation of the lactams *(4a)* and *(4b)* and reduction with $LiAlH_4$.



(3)

(4), X = O
(5), X = H_2
(a), *cis*; *(b)*, *trans*

Proof of the structure is provided by the UV and mass spectra, which are identical for the two steroisomers. The NMR spectra of the *trans* series show a strong deshielding effect for the aromatic proton on C-14. For chemical proof of the configuration, the quaternary ammonium bases of *(5a)* and *(5b)* were subjected to Hofmann degradation until the chirality center on C-6 was eliminated. The two stereoisomers gave the same biphenyl derivatives after three steps.

Pharmacological studies on the isolated, chronically enervated rat diaphragm showed no difference in activity between *(5a)* and *(5b)* and their optical antipodes. The curare-like action of the erythrinanes is thus neither structure-specific nor configuration-specific [2].

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[2] *H. Lüllmann, A. Mondon*, and *P.-R. Seidel*, Naunyn-Schmiedebergs Arch. Pharmakol. exp. Pathol. *258*, 91 (1967).

Preparative Scope of the Reduction of Higher Transition Metal Chlorides in Anhydrous Methanol

By *H. J. Seifert* [*]

In solution in methanol containing HCl, VCl_3 can be electrolytically reduced to V^{2+}, and $TiCl_4$ to Ti^{3+}.

$ZrCl_4$ is not reduced in pure methanol; the alcoholysis equilibrium is displaced toward the formation of methoxy compounds by discharge of the H^+ ions. The reduction of WCl_6 is concentration-dependent: in dilute solution it yields trivalent tungsten, while in concentrated solutions, reduction plus alcoholysis lead to green $W_2Cl_4(OCH_3)_4 \cdot 2\,CH_3OH$.

Reduction of $VOCl_3$ at a controlled potential yields a solution of $VOCl_2$.

Solid methanol adducts have been isolated from the resulting solutions in some cases. Complexes with other organic ligands have also been prepared by displacement reactions and investigated.

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Determination of Trace Elements in Plastics by Neutron Activation and Gamma Spectrometry

By *H. Sorantin* [*]

To assess the suitability of a plastic for special applications *e.g.* in electrical engineering, nuclear engineering, and medicine, the nature and quantity of the trace elements present must be accurately known.

Since the concentration of foreign elements is very low, neutron activation analysis was chosen because of its sensitivity and the fact that no interfering activations of the matrix with neutrons occur, except in Teflons and PVC's.

A further advantage of the selected method was the elimination of any errors due to the escape of volatile compounds during ashing or due to reagents used in chemical procedures. In a series of commercially available plastics 23 elements could be identified, after neutron activation, by their radioisotopes. The quantitative analysis covered 16 elements (Na, Cl, Ca, Se, Cr, Mn, Fe, Cu, Zn, Sc, Br, Sb, Au) and ranged from 10^{-4} to 10^3 ppm [1].

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Behavior of Neptunium and Plutonium in Various Oxidation States on a Cation Exchanger

By *S. Specht* (lecturer), *G. Höhlein*, and *H.-J. Born* [*]

Plutonium in mineral acid solutions can exist simultaneously in four oxidation states: Pu^{3+}, Pu^{4+}, PuO_2^{2+}, and in a very low equilibrium concentration as PuO_2^{+}. The proportions of the valence states can be altered by disproportionation and radiolysis; in solutions with pH $\geq$1.5, part of the Pu^{IV} may be present in the colloidal state. Neptunium exhibits similar behavior though to a lesser degree; the oxidation states Np^{4+}, NpO_2^{+}, and NpO_2^{2+} are again readily obtainable.

In an attempt to find the simplest possible method for the separation and identification of microconcentrations of Pu^{III}, Pu^{IV}, Pu^{VI}, and the colloidal component, as well as of Np^{IV}, Np^{V}, and Np^{VI}, the behavior of these species on the cation exchanger AG50WX8 was investigated with HCl as the eluent. This investigation was based on work by *Diamond*, *Street*, and *Seaborg*.

The arrangement used consisted of chromatographic columns [1] developed by the present authors and operated by hose pumps and tubular plastic scintillators [2], which were used for the continuous monitoring of the α-activity in the solutions. The elution curves could be recorded automatically in this way.

The partition coefficients and the separation factors of the individual ions and the HETP values of the columns were determined as a function of the acid concentration. We found that the ions containing plutonium in various valence states were best separated in the range 1N–3N HCl and could be definitely identified on the basis of the position of the band. Pu^{III} and Pu^{IV} could not, however, be separated in the region around 6N HCl, and could be separated only with difficulty in the range up to 12N HCl. Colloidal plutonium always appears as a relatively sharp band after the first three column volumes.

In the case of neptunium the separation conditions are more favorable. Thus the oxidation states of synthetic mixture can be eluted with 1 N HCl in the order Np^{V}, Np^{VI}, Np^{IV} with separation factors of *ca.* 3 and 5. The separation factors increase with decreasing acid strength. Np^{IV} and Np^{VI} cannot be separated by elution with 4–5 M HCl for at this acid strength these two oxidation states of Np exhibit the same elution behavior.

The HETP values of the ion exchange columns used increase considerably with increasing acid concentration, and this again makes it advisable to carry out the separations in the dilute acid range.

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[2] *S. Specht*, *G. Höhlein* and *W. Weinländer*, Z. analyt. Chem. *244*, 161 (1969).

Addition of Mixed Epoxides in the High Pressure Range

By *E. Staude* [*]

The addition of ethylene oxide-propylene oxide mixtures to β-phenoxyethanol (monophenyl monoethylene glycol) has been investigated using sodium phenoxide as the catalyst at pressures up to 1000 atm. The four possible competing reactions were investigated kinetically as single reactions. The basic addition of epoxide proceeds in bulk by a multi-center reaction. If the reaction product has an end group similar to that of the initial alcohol, the reaction rate above an epoxide-alcohol ratio of 1 depends only on the concentration of the catalyst. On the other hand, when a secondary alcohol is formed from a primary alcohol and a corresponding epoxide or *vice versa*, the OH component also appears in the kinetic equation.

This means that it is not possible to calculate the dimensionless reactivity parameter normally used to describe a copolymerization reaction. The incorporation of the monomer into the product can however be determined *via* the relative rates as a function of the initial monomer composition. Closed expressions are given for the overall conversions of the two monomers. Since the constants of the individual reactions of ethylene oxide at high pressures cannot be determined for experimental reasons, the effect of pressure on these reactions can be determined *via* the kinetic equation set up for the overall conversions in mixed reactions. An increase in pressure leads to an increase in the ethylene oxide conversion. The high negative activation volume rules out an ionic reaction.

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The Phase Behavior of Ethylene-Polyethylene Mixtures (under the Conditions used in the Industrial High-Pressure Synthesis of Polyethylene)

By *R. Steiner* (lecturer) and *K. Horle* [*]

The occurrence of a phase separation is of considerable importance for the control of the industrial high-pressure polymerization of ethylene, since the separation into a monomer phase and a polymer phase can not only influence the kinetics

of the reaction, but can also lead to deposition of polymer films on the inside wall of the reactor.

The phase behavior of ethylene-polyethylene mixtures has therefore been investigated in the range 1200—2000 atm and 180—240 °C by an optical method [1], the measurement being carried out during the polymerization to avoid measuring errors due to delayed dissolution of the polymer [2]. The principle of this method is that the intensity of light passing through the reaction mixture is very strongly reduced in the two-phase region by scattering, and a switch from light to dark consequently occurs on phase separation. A special micro-stirrer vessel with two opposing pressure-resistant sapphire windows 3 mm in diameter was constructed for this investigation. This reactor can be operated continuously and is connected on the one hand to a compression system and on the other to product separators and analytical equipment.

Since the polymer concentration in the reaction mixture cannot be specified in advance, but is determined by the pressure, temperature, and initiator concentration, the conversion was determined by weighing the polymer collected, or, if the reaction time was insufficient for such a determination, was calculated from kinetic equations [3].

The results show that a miscibility gap occurs, and extends into the industrially interesting range above 1500 atm. At constant temperature, the phase separation curves have an upper critical phase separation point above which polyethylene and ethylene are miscible in all proportions. This critical phase separation point is displaced toward lower pressures and higher polymer concentrations with rising temperature. The displacement is however limited, since polyethylene and ethylene decompose at excessively high temperatures, and the polymer crystallizes at excessively low temperatures. No dependence of the phase separation curves on the average molecular weight could be detected in the range investigated.

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[1] *G. Schneider*, Z. physik. Chem. N.F. *37*, 333 (1963); *R. Steiner* and *E. Schadow*, *ibid. 63*, 297 (1969).

[2] *P. Ehrlich*, J. Polymer Sci. *73*, 131 (1963).

[3] *R. Steiner* and *J. W. Thies*, Chemiker-Ztg./Chem. Apparatur *92*, 665 (1968).

The Crystal Structure of Molybdenum Nitride Trichloride, $MoNCl_3$

By *J. Strähle* [*]

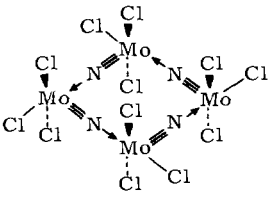
Molybdenum nitride trichloride crystallizes in the triclinic system (space group $P\bar{1}$) with four formula units per unit cell and with the lattice constants $a = 9.14$, $b = 7.67$, $c = 8.15$ Å, $\alpha = 108.8°$, $\beta = 99.3°$, and $\gamma = 108.6°$. The crystal structure was deduced with the aid of three-dimensional Patterson and Fourier syntheses and refined by the method of least squares to an R value of 5.8% (1600 reflections, MoKα-radiation).

$MoNCl_3$ molecules are present in the crystal structure, but these are strongly associated *via* nitrogen bridges to form tetramers. The tetramers are in turn loosely linked *via* chlorine bridges and form undulating layers parallel to (010). Each Mo atom is surrounded by four Cl and two N atoms to give a strongly distorted octahedron. The individual molecules, which are strictly speaking asymmetric, have a pseudo-reflection plane containing one Cl atom and the Mo and N atoms. The association of the four molecules of the unit cell to give the tetrameric unit is such as to give approximately the point symmetry 4/m (pseudo-reflection plane m parallel to $(03\bar{1})$). The Mo atoms form approximately a square with the N atoms on its sides.

Angles: Mo(1)-N(1)-Mo(2′) = 167.3°, Mo(2)-N(2)-Mo(1) = 178.1°.

Mo-N-distances: Mo(1)-N(1) = 1.64 Å, N(1)-Mo(2′) = 2.20 Å; Mo(2)—N(2) = 1.67 Å, N(2)-Mo(1) = 2.14 Å

These data point to the bonding scheme indicated for the tetrameric unit.



Atomic coordinates for $MoNCl_3$.

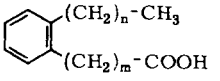
Atom	x	y	z
Mo(1)	0.2257	0.5164	0.5555
Mo(2)	0.3640	0.3624	0.1337
Cl(1)	0.1179	0.1755	0.4546
Cl(2)	0.0619	0.5840	0.7349
Cl(3)	0.2996	0.8110	0.5188
Cl(4)	0.3393	0.0484	0.1021
Cl(5)	0.1345	0.2741	−0.0788
Cl(6)	0.4909	0.6928	0.1490
N(1)	0.3900	0.5649	0.7082
N(2)	0.3070	0.4320	0.3210

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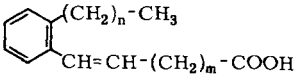
Metal-Catalyzed Aromatization of Unsaturated C_{18} Carboxylic Acids

By *H. J. Strauss* (lecturer), *W. R. Eckert*, and *J. D. von Mikusch* [*]

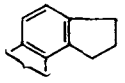
When unsaturated fatty acids are heated with palladium or platinum catalysts, aromatic fatty acids are formed, as is shown for the methyl esters of linseed oil fatty acids, tung oil fatty acids, linoleic acid, oleic acid, and elaidic acid. The aromatic fatty acids are isolated by treating the product with urea to remove straight-chain fatty acids by adduct formation. They consist essentially of the 11 isomers *(1)* having $n = 0$—10. The products *(2)* and *(3)* are also observed.



(1), n + m = 10



(2), n + m = 8



$R^1 = CH_3$ or C_2H_5
$R^2 = (CH_2)_7COOH$ or $(CH_2)_6COOH$

(3), R^1 and R^2

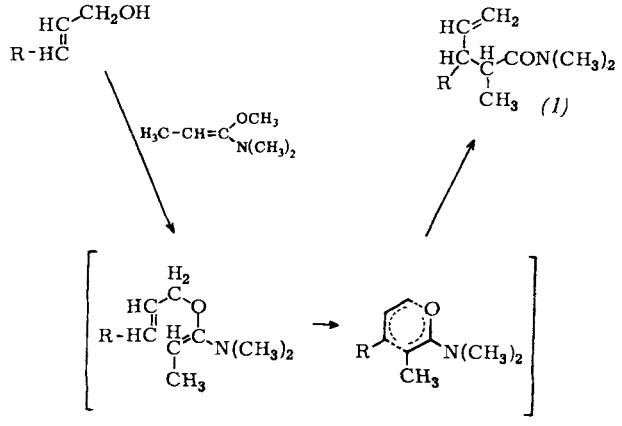
The course of the reaction with time has been studied for the methyl esters of linseed oil fatty acids and of oleic acid with Pd/C as the catalyst at 270 °C. Rapid *cis-trans* isomerizations and double bond shifts occur at first, as shown by IR and UV spectroscopy as well as by oxidation of the unsaturated straight-chain carboxylic acids. The aromatization involves dehydrogenation, the hydrogen being taken up by an unsaturated C_{18} carboxylic acid. Polyunsaturated acids first yield aromatic fatty acids of all types and octadecenoic acids. The monoenoic carboxylic acids are subsequently disproportionated at 270 °C, leading to the formation of aromatic fatty acids *(1)* and stearic acid. If the aromatization is carried out at 180 °C, monoenoic acids remain in the final product.

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Formation of Amides by Claisen Rearrangement of Ketene *O,N*-Acetals; Stereochemistry

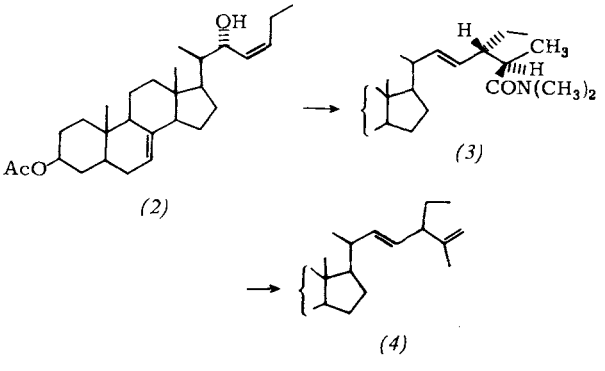
By *W. Sucrow* (lecturer) and *B. Girgensohn* [*]

We have recently applied the rearrangement of allylketene *O,N*-acetals, which was studied by *Eschenmoser* [1], to methylketene *O,N*-acetal in the synthesis of santolinatriene [2]. The reaction leads predominantly to one of the two epimers of *(1)*, R = $(H_3C)_2C{=}CH$



With 2-buten-1-ol as a model (R = CH_3), it can be shown that the rearrangement proceeds stereoselectively. *trans*-Butenol gives mainly (about 85%) *erythro-(1)*, while *cis*-butenol gives mainly (about 90%) *threo-(1)* (recognizable from the NMR spectra, confirmed by Lemieux degradation and hydrolysis to the dimethylsuccinic acids). Since the configuration of the ketene *O,N*-acetal double bond is unknown, this result can be explained either by a chair-form transition state (cf. [3], ketene acetal then having the Z configuration), in which both methyl groups would be quasi-axial with *cis*-butanol as the starting material, or by a boat-form transition state (ketene acetal then having the E configuration).

In the synthesis of the sterol side chain of *(4)*, the rearrangement proceeds practically stereospecifically. The Δ^{23}-*cis*-steroid alcohol *(2)* forms a practically uniform amide *(3)*, which has the *threo* configuration if the rearrangement mechanism corresponds to that of butenol. The configuration of the alcohol group in *(2)* (probably 22 β_F) must be transferred to C-24 of *(3)*, according to model considerations. Reduction with $LiAlH_4$ and Cope degradation gives the sterol of natural configuration as in pumpkins. The epimeric alcohol of *(2)* leads to the 24-epimeric sterol *(4)*.



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[1] *A. E. Wick, D. Felix, K. Steen,* and *A. Eschenmoser,* Helv. chim. Acta *47,* 2425 (1964); *D. Felix, K. Gschwend-Steen, A. E. Wick,* and *A. Eschenmoser, ibid. 52,* 1030 (1969).

[2] *W. Sucrow,* Angew. Chem. *80,* 626 (1968); Angew. Chem. internat. Edit. *7,* 629 (1968).

[3] *P. Vitorelli, T. Winkler, H. J. Hansen,* and *H. Schmid,* Helv. chim. Acta *51,* 1457 (1968).

Temperature Dependence of the Reaction Rate of Enzymes

By *G. Talsky* (lecturer) and *W. Müller* [*]

The investigation of the temperature dependence of the reaction rates of a series of native and modified enzymes with their substrates, including lipase [1], xanthine oxidase [2] urease [3], papain [4], trypsin [5], chymotrypsin [5], and ribonuclease showed that the deviations observed in the Arrhenius diagram, *i.e.* the curvature of the line or two intersecting straight lines, can be resolved into a trend line if measurement is carried out over sufficiently small temperature intervals. It is therefore impossible to give a uniform experimental activation energy for an enzyme substrate system over a large temperature range in the absence of larger amounts of buffers and salts; it is necessary instead to distinguish in addition to practically linear sections, temperature ranges in which temperature anomalies occur.

The ranges of anomalous temperature behavior can be displaced or made to disappear by variation of the reaction medium. The results led to the conclusions that enzymes exist in more than one active conformation, and that these conformations can change into one another within a few degrees. Assuming an equilibrium between pairs of active forms of the enzyme and a cooperativity of 80–100 interactions per enzyme molecule, the experimental course of the curve can be satisfactorily calculated. The anomalous temperature behavior is demonstrated for the case of the systems ribonuclease A/cyclic cytidine phosphate and RNase/ribonucleic acid.

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[1] *F. Patat* and *G. Talsky,* Z. Naturforsch. *22b,* 524 (1967); *G. Talsky, ibid. 22b,* 1111 (1967).

[2] *G. Talsky* and *G. Fink,* Hoppe-Seylers Z. physiol. Chem. *348,* 1141 (1967).

[3] *G. Talsky* and *G. Klunker,* Hoppe-Seylers Z. physiol. Chem. *348,* 1372 (1967).

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[5] *G. Talsky,* Tagungsberichte der Biophysikalischen Tagung in Baden bei Wien, Verlag der Wiener Medizinischen Akademie, 1968.

Preparation and Investigation of Zirconium Phosphate Exchangers Exhibiting Separation Properties for Lanthanides and Actinides

By *J. Treplan* (lecturer) and *H.-J. Born* [*]

In the search for ion exchangers having high resistances to radiation, attempts were made to vary *Amphlett*'s method in such a way as to give products having the highest possible ion exchange capacity for the trivalent actinides and lanthanides.

Particular attention was paid to fixing the conditions for the preparation so that reproducible products could be produced. The chemical and physical properties of the zirconium phosphate preparations obtained by variation of the conditions were investigated.

A capacity of 0.12 to 1.81 mequiv/g was found at pH = 4 for the trivalent ions (test substance Eu^{3+}). The capacity for monovalent elements is between 0.19 and 2.3 mequiv/g. These values were also confirmed by potentiometric titration.

The partition ratios of some lanthanide and actinide elements in the system zirconium phosphate-HCl were determined in batch experiments, the dependence of the partition ratios on the acid strength corresponding to the theoretical values. It was found advantageous to use higher temperatures.

To elucidate the structure of the product the ratio Zr : phosphate was first determined. The gravimetric and activation analysis method gave a ratio of 1 : 2 which agrees with the

structure suggested by *Blumenthal*. The loss on drying and the change in capacity were determined for the various preparations at 30, 45, 75, and 105 °C, as were the losses on heating between 105 and 1000 °C. Solubility studies with hydrochloric acid at various concentrations gave an average loss of 6% when the exchanger was in the NH_4^+ form.

Preliminary values for the radiation resistance of the preparations was obtained by γ irradiation in the Munich research reactor. Surprisingly, it was found that for radiation times of up to 16 hours at a dose rate of 10^8 rad/h, the capacity for Cs^+ increased by up to 30%, depending on the irradiation time. The capacity for europium on the other hand reaches a maximum, also corresponding to an increase of about 30%, after irradiation for 4 hours, and then falls back to its original value.

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Quantitative Separation of Several Fission Products with Ion Exchangers

By *H. Völler* (lecturer), *H.-J. Born*, *G. Höhlein*, and *W. Weinländer*[*]

A process is described in which several fisson products from neutron-irradiated ^{241}Am can be separated with the aid of ion exchangers in a single separation step and determined spectroscopically.

A simple combined ion-exchange separation unit with an anionic first column (Dowex 1X8, 200—400 mesh) followed by a cationic column, (Aminex, marketed by Biorad Laboratories, grain size 15 μm) was designed. With a view to operation in a glove box, this method involves only a few, uncomplicated steps. Extensive investigations on elution conditions and their parameters as well as on operating procedures were therefore necessary. For the optimization of the separation steps, series investigations were carried out, *e.g.*, on the influence of the grain size of the exchanger, the flow rate of the eluate, the activity in the columns, and the construction of the columns. The separation method has been tested with a mixture of the radionuclides ^{95}Zr, ^{95}Nb, ^{106}Ru, ^{110m}As, ^{137}Cs, ^{115}In, ^{115}Cd, ^{133}Ba, ^{154}Eu, and ^{140}La in tracer quantities.

^{95}Zr and ^{95}Nb were quantitatively absorbed, together with most of the ^{106}Ru (up to 98%), in the strong oxalic acid solution on the anion exchanger. The other nuclides pass quantitatively and are retained on the following cationic column. Zirconium and niobium can be selectively desorbed from the anion exchanger with a mixture of very dilute oxalic acid and dilute nitric acid. The ruthenium in the anion column appears in the eluate with dilute sodium hydroxide solution or very concentrated hydrochloric acid, sodium hydroxide solution being preferred because of its more favorable elution band (greater symmetry, smaller width). A group separation of the monovalent, divalent, and trivalent cationic fission products is carried out on the Aminex column with nitric acid. Owing to the small grain diameter of the Aminex resin, the elution bands of the nuclides are very narrow, and a relatively good separation of the elements within the individual groups is possible with suitably chosen elution conditions.

Owing to the large quantity of the target material ^{241}Am in relation to the fission products, a broad americium band, which overlaps with neighboring elution bands, occurs in the lanthanide-actinide group. This is avoided by oxidation of the Am to Am^V, whose elution band appears sooner.

The elements of the important lanthanide group are separated on the cation exchanger Aminex by the "pH gradient method" with α-hydroxyisobutyric acid.

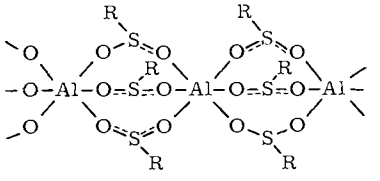
The investigations were carried out in a glove box, which was fitted with a gamma- and an alpha(beta)-through flow measuring device for following the elutions and with special devices that allow the removal of the resulting nuclide fractions without contamination for spectroscopy.

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Cleavage of Aluminum-, Gallium-, and Indium-Carbon Bonds with SO_2, CO_2, COS and CS_2

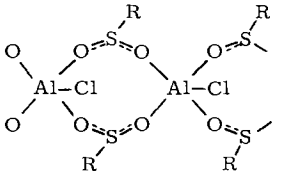
By *J. Weidlein*[*]

The reaction of trialkylaluminum or its ether adducts with gaseous or liquid SO_2 leads to alkanesulfinates of aluminum. All three Al—C bonds are broken with strong evolution of heat. The products are pure white, highly polymeric solids, which are completely insoluble in organic solvents and whose hydrolysis leads in good yields to alkanesulfinic acids, which can otherwise be obtained only with difficulty[1]. On the basis of the IR spectra, the structure *(1)* with hexacoordinate Al atoms and —O—SR—O— bridges can be postulated.

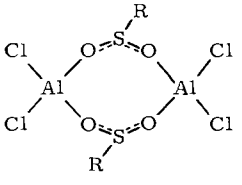


(1)

Halogen- or pseudohalogen-monosubstituted dialkylaluminums (R_2AlX with R = CH_3, C_2H_5 and X = Cl, Br, SCN) react with SO_2 to form white hygroscopic solids, which are insoluble in apolar solvents but dissolve readily in liquid sulfur dioxide. Alkylaluminum dihalides ($RAlHal_2$ with R = CH_3, C_2H_5 and Hal = Cl, Br) can be converted by SO_2 into highly viscous, colorless, thermally very unstable, and hygroscopic oils, which also dissolve in organic solvents (dimeric in benzene). The IR and Raman spectra of the compounds are compatible with the structures *(2)* and *(3)*.



(2)



(3)

The reactions of trialkylgallium[2] and trialkylindium with SO_2 lead to the cleavage of only one metal-C bond. The products are dimeric, liquid or solid dialkylmetalalkanesulfinates, which are soluble in organic solvents, and whose vibration spectra (IR and Raman) as well as ^1H-NMR measurements point to 8-membered ring skeletons similar to *(3)*, presumably with only slight undulation. Halogen-substituted organogallium and organoindium compounds do not react with SO_2.

Gaseous CO_2 (at normal pressure and elevated temperatures) can cleave only one metal-carbon bond in Al-, Ga-, and In-trialkyls. Whereas only dimeric dialkylmetallocarboxylic acid derivatives are formed in the case of Ga and In, with Al trimeric and more highly associated oligomers can be isolated. Dimeric molecules are the sole products of reaction of the trialkyls (or their addition compounds with ether) with the amount of pure carboxylic acid calculated for exchange of one alkyl group for a RCOO group. (Formation of one mole of alkane.) IR, Raman, and ^1H-NMR spectra show that the

eight-membered parent system of the dimeric dialkylcarboxylic acid compounds of Al, Ga, and In is isosteric with the ring system of the dialkylsulfinates of Ga and In.

Cleavage of the metal-carbon bond in the trialkyls of Al, Ga, and In can also be achieved with COS and CS_2. The thermally unstable and hygroscopic solids formed in this reaction can be assigned a structure analogous to the SO_2 and CO_2 "insertion compounds" on the basis of physical measurements.

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[1] *K. Ziegler, F. Krupp, K. Weyer*, and *W. Larbig*, Liebigs Ann. Chem. *629*, 251 (1960).

[2] *J. Weidlein*, Z. anorg. allg. Chem. *366*, 22 (1969).

Experience in the Isolation of ^{242}Cm in the Kilocurie Range

By *H.-J. Born, G. Höhlein, D. Pabst, B. Schütz, S. Specht, H. Völler*, and *W. Weinländer* (lecturer) [*]

A method for the separation of ^{242}Cm on the kilocurie scale from neutron-irradiated americium targets has been developed and tested. It was particularly important to prepare the curium free from impurities and to obtain the ^{241}Am and the plutonium isotopes quantitatively. After dissolution of the aluminum irradiation capsule with 8 N NaOH followed by filtration, the oxides of Am, Cm, Pu and the fission products are dissolved in 12 N HCl. Approximately 0.1 N I^- is added to ensure that the Pu is trivalent after dissolution.

The solution is then pumped through an anion exchanger (AG 21 K); Zr (Kd $\approx$ 100) and Nb (Kd $> 10^4$) are completely adsorbed while Ru (Kd $\approx$ 20—30) is partly adsorbed. The remaining ions pass through the exchanger.

After subsequent dilution the entire solution is pumped through a cation exchanger. Most of the monovalent ions largely pass through immediately. The rest of the monovalent ions, the divalent ions, and the remainder of the Ru are then eluted with 1 N H_2SO_4. In order to bring the plutonium into the tetravalent state traces of NO_2^- are added to the sulfuric acid. 9 N HCl (20% methanol) is then used for desorption of Pu^{IV}, Am^{III}, and Cm^{III}, while the lanthanides still remain on the column. The Pu^{IV} is quantitatively removed from the solution by adsorption on a second anion exchange column. After concentrating the solution and adjusting its acid strength to 1 N, the solution, containing mainly Am and Cm together with traces of lanthanides, is adsorbed on top of a cation column, and then Am and Cm are separated with α-hydroxyisobutyric acid. This step had been checked earlier with approximately 100 Ci of ^{242}Cm.

The separation process was tested and optimized in inactive runs. The "hot" experiment showed that great difficulties were created by the radiolysis of the solvent and of the ion exchanger. Since cation exchangers are completely destroyed by a dose of 10 Wh/g, and anion exchangers by much smaller doses, special attention must be given to this point. However, the decomposition of the solvent and the consequent formation of gas bubbles, which interferes in particular with the operation of the anion exchanger, is even worse. In the case of the cation exchanger this problem could be largely overcome by the addition of methanol.

The Cm fraction obtained is then converted into the oxide by readsorption on a cation exchanger followed by ashing of the exchanger bed at about 800—1000 °C. The Cm is obtained as the oxide in a very clean state; yield about 90%.

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ESR Studies on the Mechanism of the Radiolysis of Polystyrene

By *J. Wilske* (lecturer) and *H. Heusinger* [*]

The formation of free radicals and radical-pairs in polystyrene under the action of ionizing radiation has been investigated as a function of temperature.

It has been shown that the radical-pairs formed in polystyrene do not consist of radicals that were accidently formed close together; on the contrary, the two radicals are formed almost simultaneously as a result of the same primary act of absorption. The average distance between these radicals is about 20 Å; this distance remains approximately constant as the dose is increased.

The following reactions, which were proposed by *Voevodskii* [1] and *Libby* [2], are possible for the formation of these radicals:

$$R_aH^+ + e^- \rightarrow R_a^\bullet + H_{kin}$$
$$R_bH + H_{kin} \rightarrow R_b^\bullet + H_2$$
$$R_aH^+ + R_bH \rightarrow R_aH_2^+ + R_b^\bullet$$
$$R_aH_2^+ + e^- \rightarrow R_a^\bullet + H_2$$

In the first case the closely adjacent radicals R_a and R_b are formed by the reaction of a "hot" hydrogen atom, and in the second case by an ion-molecule reaction.

When polystyrene is heated to 20 °C, the radical-pairs recombine in a first order reaction. It is assumed that this involves chain cross-linking:

$$R_a^\bullet + R_b^\bullet \rightarrow R_aR_b$$

The formation of free radicals and of radical-pairs at −196 °C is not influenced by the addition of pyrene. Even when the polystyrene is warmed to 20 °C, the free-radical concentration remains independent of the pyrene content; the recombination of the radical-pairs is also unaffected by pyrene.

On irradiation at 20 °C, the free radical formation decreases by a factor of 10 at a pyrene content of 3% in the polystyrene, whereas the formation of chain crosslinks is independent of the pyrene content.

To explain these results, it must be assumed that the free radical formation proceeds by two different mechanisms at high and low temperatures. At high temperatures (20 °C) the radicals are formed mainly *via* excited states of the polystyrene (energy transfer to pyrene possible), while at low temperatures they are formed *via* ionized states.

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[1] *V. V. Voevodskii* and *Yu. N. Molin*, Radiation Res. *17*, 366 (1962).

[2] *W. F. Libby*, J. chem. Physics *35*, 1714 (1961).

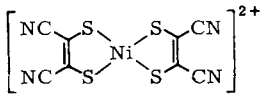
Polymers from Tetracyano Compounds

By *D. Wöhrle* (lecturer) and *G. Manecke* [*]

We have examined several possibilities for the synthesis of conjugated polymers from tetracyano compounds and compared the semiconductor properties of these polymers.

Some of the monomeric tetracyano compounds have poor electric conductivities; tetracyanobenzene, tetracyanothiophene, tetracyanofuran, and tetracyanoethylene: $\sigma_{300\,°K} < 10^{-15}$ ohm^{-1} cm^{-1}. Other monomers, on the other hand, exhibit good semiconductor properties, *e.g.* some bis(*cis*-1,2-dicyanoethylene-1,2-dithiolato)metalates [1] such as *(1)*, for which $\sigma_{300\,°K} = 5.0 \times 10^{-2}$ ohm^{-1} cm^{-1}.

Polymers having hemiporphyrazine-like structures [2] have been synthesized by reaction of the tetracyano compounds



Cu^{2+} *(1)*

with diamines such as 2,6-diaminopyridine. In the presence of metal salts at higher temperatures, tetracyano compounds give polymers with phthalocyanine-like structures[3,4]. The reaction of the tetranitriles in basic reaction media, *e.g.* in quinoline, led at high temperatures to polymers with a triazine-like structure[4].

The products in every case were perconjugated, dark, infusible polymers, mostly characterized by good electric properties: $\sigma_{300\,°K} = 3.9 \times 10^{-2}$ to 7.2×10^{-14} ohm^{-1} cm^{-1}. In the case of the polymeric phthalocyanines it was found that the conductivities increase with increasing aromatic character of the polymer unit from furan *via* thiophene to benzene. It was also possible, for polymeric phthalocyanines containing different metals, to describe the influence of the ionization potential of the metal on the conductivity.

The phthalocyanines are better conductors than the hemiporphyrazines, since the phthalocyanine system is more strongly aromatic, and so exhibits a stronger electronic ring current, than the hemiporphyrazine system. In the case of the highly conducting polymers obtained from the bis(*cis*-1,2-dicyanoethylene-1,2-dithiolato)metalates, the nature of the metal atom has no great influence.

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[2] *G. Manecke* and *D. Wöhrle*, Makromolekulare Chem. *120*, 192 (1969).

[3] *G. Manecke* and *D. Wöhrle*, Makromolekulare Chem. *102*, 1 (1967).

[4] *G. Manecke* and *D. Wöhrle*, Makromolekulare Chem. *120*, 176 (1969).

Energy and Isotope Dependence of the Chemical Behavior of Molybdenum Recoil Atoms in Hexacarbonylmetal Compounds Following Nuclear Reactions

By *E. Henrich* and *G. Wolf* (lecturer)[*]

As has been shown by numerous investigations, the chemical behavior of recoil atoms produced by nuclear reactions can be influenced by the recoil energy, and also varies from isotope to isotope of an element. In most experiments, recoil atoms having different energies have been produced by different nuclear reactions (n, γ; n, 2n; γ, n reactions). However, these reactions always led to different isotopes of an element, so that the energy effect and the isotope effect could not be clearly separated. To avoid this, a series of target elements (Mo to In) were bombarded with 600 MeV protons. Both ^{90}Mo and ^{93m}Mo were formed together with other products. The recoil energies of these two species varied with the mass number of the target element.

The targets were irradiated in close contact with hexacarbonylmetal compounds so that some of the recoiling Mo atoms could penetrate into the carbonyl. A selective reaction took place between some of the Mo recoil atoms and the catcher, with formation of hexacarbonylmolybdenum, which could be separated from the other products, together with the catcher, by sublimation or extraction.

The yield of this reaction was always the same for a given isotope irrespective of the target, *i.e.* irrespective of the recoil energy within the limits considered. Moreover, the ^{93m}Mo yield was always about 10% higher than the ^{90}Mo yield, irrespective of the target. Similar results were obtained on irradiation of hexacarbonylmolybdenum with fast neutrons having energies of up to 50 MeV, in which the same Mo isotopes are formed.

This energy-independent isotope effect is explained as follows: ^{90}Mo is still in an excited nuclear state after being slowed down in the catcher, and some of the bonds already formed are broken again as a result of its decay by γ emission or electron conversion. ^{93m}Mo, on the other hand, has no nuclear level that is sufficiently long-lived to cause such a delayed effect.

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Radio Frequency Polarographic Studies on Semiconductors and Reactor Materials

By *I. Büker* and *G. Wolff* (lecturer)[*]

Modern polarographic methods have recently assumed increasing importance alongside emission spectroscopy, mass spectrometry, and activation analysis for the trace analysis of semiconductor materials and of light metals and steels used as structural materials for modern reactors[1]. One of these new methods, in which the detection of the polarization current is based on the rectification effect caused by the non-linearity of the current-voltage curve, is radio frequency polarography.

It is possible with the aid of the rectification technique to reach detection limits of a few 10^{-9} to 1×10^{-8} mol/l for metal ions. Accordingly, with suitable preparation of the sample material and careful choice of the electrolyte, impurities in the solids can be detected down to the range of 5—10 ppb, *i.e.* 5 to 10×10^{-9} g of impurity/g of sample. In the electrochemical technique used here a very simple preparation of the sample is often sufficient, so that the introduction of impurities with impure chemicals is largely avoided. On the other hand, the method requires a fairly accurate knowledge of the relations between signal size, signal position, and double layer parameters. Thus an optimum detection limit is obtained, *e.g.*, only if the high frequency amplitude over the double layer is accurately adjusted to suit the ion being analyzed. Another factor that has an important effect on the step height is the pH value of the electrolyte, which must be kept within very narrow limits in some cases, particularly in the analysis of light metal.

If due attention is paid to all these points, this method is as effective as the others mentioned above.

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[1] *G. Wolff* and *H. W. Nürnberg*, Z. analyt. Chem. *224*, 332 (1967).

Inverse-Voltammetric Determination of Tin and Lead in the Presence of each Other

By *K. Zinke* (lecturer) and *H. Monien*[*]

The determination of tin and lead in the presence of each other is difficult both by the hanging mercury drop and by the dropping mercury electrode, since the electrochemical properties of the two elements differ only slightly. The elements can, however, be determined in the presence of each other by the use of the carbon paste electrode. Lead is determined by oxidation at an electrolysis potential of +1.4 V. The PbO_2 formed accumulates on the electrode surface and redissolves on subsequent reduction with a current wave. The

current maxima are proportional to the quantity of Pb deposited. In a tartrate-buffered electrolyte, 20—100 ng of Pb/ml can be determined in this way in the presence of a 100-fold excess of tin.

Another possible method of concentration is the adsorption of a metal-dye complex on the electrode surface. In this case there is no need to apply a potential to the carbon electrode. Tin is determined *via* the oxidation of a tin-dye complex, which is adsorbed on the electrode surface after the electrode has been in the solution to be analyzed for 5—10 minutes. On subsequent scanning of the anode potential, an oxidation signal that is proportional to the quantity of tin adsorbed is obtained at +0.720 V. Out of several complexing agents that react with Sn but not with Pb, hematein has proved to be particularly suitable. The complexing agent dissolved in dioxane reacts at pH 3.7 to 4.0 both with Sn^{2+} and with Sn^{4+} ions to form a precipitate. A method is described for the determination of 10—100 ng of Sn/ml in the presence of a 10^5-fold excess of lead and zinc with a relative standard deviation of 7%. The permissible excess of Fe^{3+} is 10^3, of Cu^{2+} is 10^2, and of Sb^{3+} is 10. In a standard Pb alloy containing 0.005% of Sn, the Sn could be determined with a relative standard deviation of about 5%. [VB 212 IE]

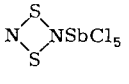
German version: Angew. Chem. *81*, 908 (1969)

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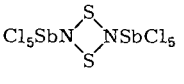
SELECTED ABSTRACTS

The first allowed triplet-triplet absorption band of benzene has been detected by *R. Astier* and *Y. H. Meyer* at 430 nm. It was detected in the flash photolysis of a 3×10^{-2} M solution of benzene or hexadeuteriobenzene (425 nm) in methanol-ethanol (1:3) in a 20 cm cell at about 100 °K. By simultaneous measurement of the lifetimes of the phosphorescence and the 430 nm absorption at various temperatures it was established that a triplet-triplet absorption was involved. The extinction coefficient of the 430 nm band may be of the order of 10^4. / Chem. Physics Letters *3*, 399 (1969) / —Hz. [Rd 82 IE]

The reactions of disulfur dinitride with antimony pentachloride and with boron trihalides have been studied by *R. L. Patton* and *W. L. Jolly*. A solution of S_2N_2 in CH_2Cl_2 reacts with an excess of $SbCl_5$ to give the diadduct *(2)*, which is converted into the monoadduct *(1)* by further S_2N_2. Compound *(1)* adds $SbCl_5$ to form the diadduct *(2)*, any excess of S_2N_2 dimerizing to S_4N_4. *(1)* (orange needles) melts at 108—109 °C (decomp.) in a sealed tube and sublimes in a vacuum at 60 to 70 °C; *(2)* (yellowish crystals) melts at 130—131 °C with decomposition. The IR spectra show that the S_2N_2 ring remains intact in both compounds; in *(1)* it is planar or folded, and in *(2)* planar. S_2N_2 reacts with *(1)* in CH_2Cl_2 to give the known compound $S_4N_4SbCl_5$, containing the eight-membered S_4N_4 ring, as well as $(S_4N_4SbCl_5)_x$.



(1)



(2)

In CH_2Cl_2, S_2N_2 reacts with BCl_3 to yield $S_4N_4BCl_3$, $S_2N_2(BCl_3)_2$, and $(S_2N_2BCl_3)_x$. At 0 °C, the diadduct corresponding to *(2)* affords the monoadduct, which gives the diadduct on renewed addition of BCl_3 at −78 °C. $SbCl_5$ can displace BCl_3 from $N_2S_2BCl_3$ to yield $N_2S_2(SbCl_5)_2$ *(2)*. The sole product formed on reaction of BF_3 and N_2S_2 is $S_4N_4BF_3$./ Inorg. Chem. *8*, 1389, 1392 (1969) / —Kr. [Rd 85 IE]

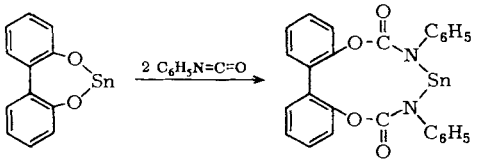
Dichlorodimethylpentanedionatoantimony(v) *(2)* (and two similar stable methylantimony(v) complexes) have been prepared by *N. Nishii, M. Shindo, Y. Matsumura*, and *R. Okawara* at low temperature from chlorodimethylstibine, sulfuryl chloride, and Na pentanedionate (Na-acac).

$$(CH_3)_2SbCl + SO_2Cl_2 \rightarrow \underset{(1)}{(CH_3)_2SbCl_3} \xrightarrow{\text{Na—acac}} (CH_3)_2SbCl_2(acac)$$

(2), m.p. 176 °C (decomp.)

The stable trichlorodimethylantimony(v)-DMSO, m.p. 147.5 °C, crystallizes on addition of DMSO to a solution of the unstable compound *(1)* in methanol. Trichloromethylpentanedionatoantimony(v) was obtained from CH_3SbCl_2, SO_2Cl_2, and 2,4-pentanedione (m.p. 110—111 °C). / Inorg. nuclear Chem. Letters *5*, 529 (1969) / —Kr. [Rd 86 IE]

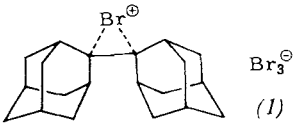
Phenyl isocyanate inserts into the tin^{II}-oxygen bond, as has been found by *P. G. Harrison* and *J. J. Zuckerman*. These authors obtained grayish-white *(2)*, which decomposes at ≈300 °C, in 97% yield after refluxing 5,7-dioxa-6-stanna^{II}-dibenzo[*a,c*]cycloheptene *(1)* (prepared from SnO and 2,2-dihydroxybiphenyl) in toluene for 50 hours. *(2)* appears to be



(1) *(2)*

the only compound known having an Sn^{II}-N bond. No final distinction can be made between *(2)* and an alternative form containing the —O—C(=NC$_6$H$_5$)—O—Sn grouping [instead of —O—CO—NC$_6$H$_5$—Sn— as in *(2)*] on the basis of the IR or Mössbauer spectrum. / Inorg. nuclear Chem. Letters *5*, 545 1969) / —Kr. [Rd 87 IE]

The isolation of the stabilized bromonium compound *(1)* has been accomplished by *J. Strating, J. H. Wieringa*, and *H. Wynberg*. Compound *(1)*, which is a comparatively stable yellow substance, precipitates on treatment of biadamantylidene with bromine in CCl_4, and could not be recrystallized owing to its insolubility. If the suspension is heated to 40 °C



(1)

with a KI solution, bromine and the hydrocarbon are liberated again. This finding, together with the empirical formula and the fact that no bromine-substitution products are present (mass and IR spectrum), suggested the bromonium structure. / Chem. Commun. *1969*, 907 / —Kr. [Rd 88 IE]

The reactions of methyl radicals with silane, disilane, phenylsilane, and their Si-deuterated analogs, which proceed *via* H or D abstraction, have been studied by *O. P. Strausz, E. Jakubowski, H. S. Sandhu,* and *H. E. Gunning*. The methyl radicals were produced by photolysis of azomethane and the product distributions determined by mass spectrometry and gas chromatography. Silanes are more reactive than hydrocarbons; the activation energies of the reactions are lower, while the pre-exponential factors are equal. The reactions

$$CH_3^{\bullet} + CH_4 = CH_4 + CH_3^{\bullet} \quad (1)$$

and

$$CH_3^{\bullet} + SiH_4 = SiH_3^{\bullet} + CH_4 \quad (2)$$

are compared as an example: the activation energies are 14.65 kcal mole^{-1} for eq. (1) and 6.99 kcal mole^{-1} for eq. (2); the logarithms of the pre-exponential factors are 11.83 cm^3 mole^{-1} s^{-1} for eq. (1) and 11.80 cm^3 mole^{-1} s^{-1} for eq. (2). / J. chem. Physics *51*, 552 (1960) / —Hz. [Rd 102 IE]

Trimethyltin isothiocyanate is reported by *R. A. Forder* and *G. M. Sheldrick* to consist of zig-zag chains containing linear S · · · Sn—N—C—S units arranged along the *z* axis of the orthorhombic unit cell (a = 13.20, b = 10.28, c = 12.01, all ±0.01 Å; Z = 8; $d_{calc.}$ = 1.82 g/cm^3), the bond angle at the S atom being 97 ± 2 °. The C_3Sn unit is almost planar with d SnC = 2.13 ± 0.03 Å. The interatomic distances are S · · · Sn 3.13 ± 0.02, SnN 2.15 ± 0.06, NC 1.15 ± 0.07, and CS 1.64 ± 0.07 Å; the bond lengths in the NCS group lie between those in HN=C=S and CH_3S—C≡N and thus suggest resonance of the kind

$$=S\cdots Sn-N=C=S\cdots Sn-N= \leftrightarrow -S-\overset{\ominus}{Sn}-\overset{\oplus}{N}\equiv C-S-\overset{\ominus}{Sn}-\overset{\oplus}{N}\equiv$$

which requires no contributions from $(p\rightarrow d)_\pi$ bonding to explain the stereochemistry. / Chem. Commun. *1969*, 1125 / —HB. [Rd 104 IE]

The IR spectrum of CO in zeolites has been subjected to investigation by *P. J. Fenelon* and *H. E. Rubalcava*. It can be deduced from the differences between the spectra of pure $^{12}C^{16}O$ and a mixture of $^{12}C^{16}O$ and $^{13}C^{16}O$ that CO can rotate relatively freely in the cavities of Na zeolites (diameter of cavity in Na zeolite 11.4 Å, effective diameter of the rotating CO molecule approx. 4.5 Å). The spectrum corresponds approximately to that of CO gas at 50 atm. In Ca zeolites, where considerably stronger adsorption forces occur, the spectrum resembles that of liquid CO. It can be interpreted if a relatively high threshold potential is assumed for the rotation. / J. chem. Physics *51*, 961 (1969) / —Hz. [Rd 107 IE]

The conductivity of aqueous electrolyte solutions in shock waves has been studied by *S. D. Hamann* and *M. Linton*. The molar conductivity of KCl does not change significantly in shock waves up to 140 kbar; although the temperature jump should increase the mobility of K^+ and Cl^-, this effect is cancelled by the simultaneous increase in the density. On the other hand, the conductivities of KOH and HCl are increased several-fold, signifying that the additional mobilities of H_3O^+ and OH^- increase by a factor of 3 to 4 under shock-wave conditions. The ionic product of water is estimated as 0.09×10^{-6} mole^2 g^{-2} at a shock-wave pressure of 133 kbar. A careful extrapolation permits the assumption that water is almost completely dissociated at 200 kbar and then possesses properties similar to a fused salt. A discontinuity in the compressibility curve of water in the region around 150—200 kbar lends further support to such a concept. / Trans. Faraday Soc. *65*, 2186 (1969) / —Hz. [Rd 108 IE]

BOOK REVIEWS

Carbene, Carbenoide und Carbenanaloge (Carbenes, Carbenoids, and Carbene Analogs). By *W. Kirmse*. Vol. 7 of "Chemische Taschenbücher", edited by *W. Foerst* and *H. Grünewald*. Verlag Chemie GmbH., Weinheim/Bergstr. 1969. 1st Edit., 260 pp., 4 figs., 26 tables, paperback DM 18.—.

One of the focal points of organic chemical research during the past decade has been the detection of short-lived intermediates and this has simultaneously given a new impulse to preparative work. This intimate mixture of theory and practice is illustrated in *Kirmse*'s book on Carbenes, Carbenoids, and Carbene Analogs. The author is an expert and successful research worker in the outlined field and has mastered his task in the concise style required by a pocket book.

He begins with an introduction to the theory of particles containing bivalent carbon, passes to their reactivity in the gas phase (where carbenes have been demonstrated beyond dispute), and then turns to their reactions in solution. Here there is a high probability that occurrence of carbenes must be taken into account, so far as they are produced by photolysis or thermolysis of diazo compounds. Their characteristic reactions are set out briefly and clearly with a large number of examples.

The critical basis for the probability of production of carbenes or carbenoids is also presented. This is important for the evaluation of reaction mechanisms with carbenoids prepared by different methods, particularly those which are organometallic. The next chapter concerning intramolecular reactions introduces the reader to the role of carbenes and carbenoids in synthetic planning, to the extent that one recognizes that they permit access to unusual ring structures which are otherwise scarcely obtainable. — In the preparative section, the synthesis of cyclopropane derivatives is given prominence. These structures are able, in turn, to give interesting transformations, either during the process of formation or thereafter. The final chapter deals with carbene analogs. Fascinating studies are described here concerning the reactivity of carbon in the vapor phase and of the nitrenes. The chemistry of these species corresponds in many respects to that of carbenes.

The art of omission, which will not please everyone, is here well warrented. The essential points (literature up to 1968 inclusive) have been clearly brought out by the author. Apart from some misprints, the book can be warmly recommended to all scientists, particularly to organic and organometallic chemists.

G. Wittig [NB 827 IE]

Organometallic Chemistry. By *P. L. Pauson*. Edward Arnold (Publishers) Ltd. Maidenhead 1967. 1st Edit., 202 pp., stitched 30s., bound 50s.

According to the author, who is Freeland Professor of Chemistry at the University of Strathclyde, Glasgow, this book is intended, not for specialists, but as a general introduction for advanced students.

A general, very concise introductory section on structure, bonding, and thermochemical data is followed by skillfully

presented chapters dealing with methods of preparation, properties, and reactions of organic compounds of metals of the main groups and of the triads. In the chapter on catalytic processes, insufficient attention is given to exchange and reorientation phenomena in intermediate complexes, *i.e.* the dynamic aspects of the metal-catalyzed reactions. The reader making his first contact with organometallic chemistry may find the book difficult to read because of the large numbers of individual facts mentioned in some sections.

P. Heimbach [NB 826 IE]

Experimental Methods in Catalytic Research. By *R. B. Anderson.* In the series "Physical Chemistry". Academic Press, New York-London 1968. 1st Edit., xii + 498 pp., numerous illustrations and tables, bound, $ 22.50.

In the past four decades methods have been developed for studying the alteration to molecules activated on a catalyst and the physicochemical properties required in a catalyst for specific processes of heterogeneous catalysis. A series of such experimental methods is described in this book. Since an introduction into the theory and the experimental bases of these methods requires very varied experience, *R. B. Anderson* has recruited several well-known scientists with special experience to present the extensive material in eleven chapters.

In the first chapter *Anderson* himself describes the study of the kinetics of catalytic reactions in 40 pages. The 2nd chapter, by *W. B. Innes*, concerns physical adsorption and chemisorption, also the determination of surface area and pore structure of the catalyst (49 pages). In the 3rd chapter, comprising 65 pages, *P. M. Gundry* and *F. C. Tompkins* treat the determination of surface potentials and their use for problems in catalysis. The 4th chapter, by *R. S. Hansen* and *N. C. Gardner*, provides a summary, in 45 pages, of field electron and field ion microscopy. The 5th chapter is devoted to chemisorption in ultra high vacuum systems; here, in 45 pages, *R. S. Hansen* and *V. J. Mimeault* describe flash desorption spectrometry and give a brief section on evaporated films and electronic action between their surface and adsorbed foreign molecules. Diffraction of slow electrons is treated in chapter 6 (20 pages) by *H. E. Farnsworth*. In the 7th chapter *T. J. Gray* concerns himself with measurement of semiconduction and photoconduction and the catalyst properties connected therewith (34 pages). The study of vibration and electronic spectra of adsorbed molecules is described by *G. Blyholder* in chapter 8 (36 pages). In chapter 9, *W. S. Goldstein* devotes 38 pages to the measurement of the acidity of catalyst surfaces. In the 32 pages of chapter 10, *L. J. E. Hofer* describes the magnetochemical methods and their use in research on catalysis. *R. J. Kokes* presents electron spin resonance and its use in problems of catalysis (37 pages).

The older methods of investigating catalysts by diffraction of X-rays and fast electrons are not reported, nor are applications of the electron probe microanalyzer, X-ray absorption, or the Mössbauer effect, or the study of electrode reactions. Each chapter is provided with a list of references, treating English-language literature up to about 1966 but (with three exceptions) the German only up to 1960.

As a whole the book gives a useful comprehensive survey of modern physicochemical methods for research on catalysis.

R. Suhrmann [NB 831 IE]

Solid Phase Peptide Synthesis. By *J. M. Stewart* and *J. D. Young.* W. H. Freeman and Co., San Francisco-London 1969. 1st Edit., xi + 103 pp., 28 illustrations, bound 48s.

Within a few years of the first publication, solid-phase peptide synthesis, often called Merrifield synthesis after its discoverer *Bruce Merrifield*, has achieved a firm place in most laboratories concerned with the synthesis of peptides or proteins. The culmination to date is the synthesis, by *Merrifield* and *Bernd Gutte* early in 1969, of an enzyme preparation with ribonuclease activity. As is now well known, the principle of this method is to build a linear peptide by chain-lengthening, unit by unit, from the carboxyl end while keeping the peptide chain anchored covalently, *e.g.*, by an ester bond, to a solid phase until the synthesis is complete. Sequence-pure peptides, *i.e.* peptides with the desired sequence throughout, can, however, be obtained only if each peptide bond is formed in 100% yield and if the selective protecting groups on the *N*-terminal amino acid are completely removed while the side-chain functions remain protected until the end of the synthesis.

Merrifield syntheses have split chemists working on peptide synthesis into two camps: one group hopes for rapid solution of all the synthetic problems by the new method and sees the time coming when sequence-pure peptides will be synthesized automatically in gram quantities; the other considers it impossible in principle to prepare sequence-pure peptides with more than a definite but as yet undetermined number of amino acid units.

The present is thus a very opportune time for *Stewart* and *Young*'s book. It will help everyone wanting to synthesize peptides by the Merrifield method, not only by explaining the theoretical basis of each operation (pages 1—26) but also by providing clear experimental details (pages 27—70) for this method. The book is written with exemplary clarity and the illustrations are of excellent quality. It is directed in the first place to those interested in solid-phase synthesis, but the Reviewer recommends this "Gattermann of peptide synthesis" to everyone with any interest in amino acids and peptides. Although we already have excellent textbooks and reference works for peptide chemistry, such as those by *Bodansky* and *Ondetti* (1966) and *Schröder-Lübke* (1965, 1966), we must nevertheless welcome a laboratory book that covers the literature between those dates and the beginning of 1968 and describes, *e.g.*, in detail *Sakakibara*'s method for removal of almost all protecting groups by means of hydrofluoric acid.

This unrestricted recommendation is not weakened by mention of the very fragmentary citation of European literature; this can be remedied in the next edition if Merrifield specialists will heed the author's request to keep them informed of new papers.

H. Zahn [NB 834 IE]

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Editorial office: Ziegelhäuser Landstrasse 35. 6900 Heidelberg 1, Germany, Telephone 4 50 75, Telex 4 61 855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

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ANGEWANDTE CHEMIE
International Edition
VOLUME 8 · NUMBER 12
DECEMBER 1969
PAGES 933–1022

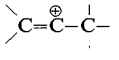
Acid-Catalyzed Cyclodimerizations *via* Vinyl Cations as Intermediates[1]

By K. Griesbaum[*]

The electrophilic addition of hydrogen chloride and bromide to allene and of hydrogen bromide to methylacetylene at −70 °C leads not only to the simple Markownikoff adducts but also to cis- and trans-1,3-dihalo-1,3-dimethylcyclobutanes. These cyclodimerizations, which evidently proceed via vinyl cations, have opened up new short routes for the synthesis of cyclobutane-, cyclobutene-, and bicyclobutane derivatives starting from substrates that are industrially readily accessible.

1. Introduction

Vinyl cations have long been considered to be species of particularly high energy and thus unstable. This view, which has even been presented in recent textbooks[2], is probably based on the inertia of vinyl halides toward silver nitrate in alcoholic solution[3].



In recent years, however, other methods have been used to verify the existence of vinyl cations. Though they have not yet been definitely detected as such by spectroscopic methods in solution, there are now convincing arguments for their occurrence as intermediates in many reactions. Examples of such reactions are the solvolysis of arylvinyl-[4a] and cyclopropylvinyl halides[4b], vinyltrifluoromethanesulfonates[4c], and homoallenyl-[4d] and homopropargyltosylates and -bromosulfonates[4e], the nitrosation of some vinylamines[5], and particularly some electrophilic additions to alkynes[6–9] and to allene[10].

2. Electrophilic Cyclodimerization of Allene and Methylacetylene with Hydrogen Bromide

The addition of acids to allene is a particularly suitable example for the necessity of a re-appraisal of ideas on the reputed instability of vinyl cations. Unlike in the addition to alkynes, two reaction paths, *i.e.* one *via* the vinyl cation *(1)* and one *via* the alkyl cation *(4)*[11], are possible in this case. However, all the hitherto studied electrophilic additions of compounds of the type HX to allene have proceeded in such a way

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[1] Based on the Habilitation Thesis by *K. Griesbaum*, Universität Karlsruhe 1968.

[2] See, *e.g.*, *R. L. Shriner*, *R. C. Fuson*, and *D. J. Curtin*: The Systematic Identification of Organic Compounds, Wiley, New York 1956, 4th Edit., p. 141.

[3] This reaction is inadequate as a test for the existence of vinyl cations, since it would necessitate the cleavage of a very strong vinyl chloride bond. The preferential protonation of allene at one of the termini of the cumulative system by acids could, on the other hand, suggest the opposite conclusion, *i.e.* that vinyl cations are formed preferentially. Hence, it is not sufficient to consider only one parameter, but both the kinetic and the thermodynamic factors must be taken into account.

[4] a) *C. A. Grob* and *G. Czeh*, Helv. chim. Acta *47*, 194 (1964); *L. L. Miller* and *D. A. Kaufman*, J. Amer. chem. Soc. *90*, 7282 (1968); b) *S. A. Sherrod* and *R. G. Bergman*, J. Amer. chem. Soc. *91*, 2115 (1969); *M. Hanack* and *T. Bässler*, J. Amer. chem. Soc. *91*, 2117 (1969); c) *P. J. Stang* and *R. Summerville*, J. Amer. chem. Soc. *91*, 4600 (1969); d) *R. S. Bly* and *S. U. Kook*, J. Amer. chem. Soc. *91*, 3292, 3299 (1969); e) *J. W. Wilson*, J. Amer. chem. Soc. *91*, 3238 (1969).

[5] *D. Y. Curtin*, *J. A. Kampmeier*, and *B. R. O'Connor*, J. Amer. chem. Soc. *87*, 863 (1965).

[6] *R. W. Bott*, *C. Eaborn*, and *D. R. M. Walton*, J. chem. Soc. (London) *1965*, 384.

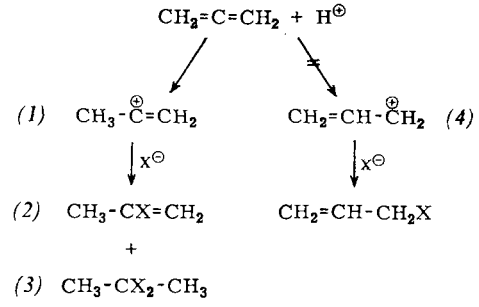
[7] *D. S. Noyce*, *M. A. Matesich*, *O. P. Melvyn*, and *D. Schiavelli*, J. Amer. chem. Soc. *87*, 2295 (1965).

[8] *R. C. Fahey* and *D. J. Lee*, J. Amer. chem. Soc. *88*, 5555 (1966).

[9] *R. E. Peterson* and *J. E. Duddey*, J. Amer. chem. Soc. *88*, 4990 (1966).

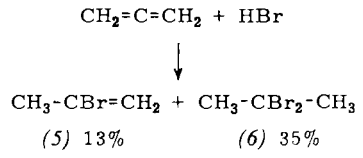
[10] For a review of these reactions, see *K. Griesbaum*, Angew. Chem. *78*, 953 (1966); Angew. Chem. internat. Edit. *5*, 933 (1966).

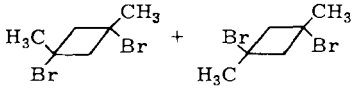
[11] The incipient cation *(4)* is not a resonance stabilized allyl cation but a primary cation, owing to the perpendicular arrangement of the two double bonds in allene.



that it is possible to formulate a vinyl cation intermediate *(1)*.

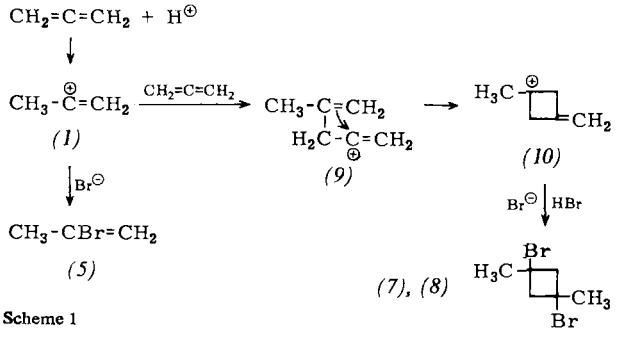
Whereas it has long been assumed that only the simple Markownikoff adducts *(2)* and *(3)* are formed in these additions, we have found that the reaction of hydrogen bromide with allene at −70 °C and in the dark yields a mixture of adducts containing four components instead of the expected two. These were the Markownikoff adducts 2-bromopropene *(5)* and 2,2-dibromopropane *(6)* as well as the previously unknown *cis*- and *trans*-1,3-dibromo-1,3-dimethylcyclobutanes *(7)* and *(8)* [12].





A free-radical cyclodimerization to form *(7)* and *(8)* was unlikely in view of the reaction conditions and it could be definitely ruled out on the basis of detailed investigations [13]. A second possibility was the radical-induced or electrophilically induced head-to-tail cyclization of the 2-bromopropene *(5)* formed in the free-radical and electrophilic additions of hydrogen bromide to allene. It was also possible to rule out this reaction path by model experiments.

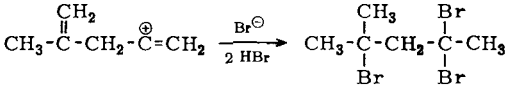
We therefore assumed that this was the first case of a purely acid-induced [14] cyclodimerization *via* vinyl cations, which possibly proceeds by the following steps (Scheme 1):



Scheme 1

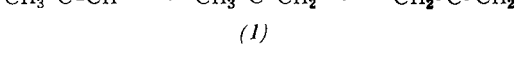
In the first step, allene is protonated at a terminal carbon atom to form the 2-propenyl cation *(1)*. Cation *(1)* can either react further with the nucleophile Br^- to give the Markownikoff adduct *(5)* or it can alkylate another molecule of allene to form the new vinyl cation *(9)* [15a]. This intermediate *(9)* cyclizes as indicated by the arrow to give the presumably more stable tertiary cation *(10)* [15b]. The cyclic dibromide *(7)*, *(8)* is finally formed by attack of bromide and addition of hydrogen bromide to *(10)*.

To obtain experimental evidence for this postulated reaction course, it would be necessary *e.g.* to try to intercept the dimeric vinyl cation *(9)* by formation of acyclic adducts such as *(11)*.



It is quite conceivable that the reaction leads not to a true intermediate of the form *(9)*, but directly to the tertiary cation *(10)* *via* a transition complex between the vinyl cation *(1)* and allene. It is also uncertain whether the observed isomer ratio reflects the stereochemical course of the reaction or merely a post-isomerization.

Despite their incompleteness, these views have proved to be a useful working hypothesis for the further investigation of these cyclodimerizations. The next substrate to be considered was methylacetylene, the protonation of which should give the same 2-propenyl cation *(1)* as the protonation of allene:



[12] *K. Griesbaum*, J. Amer. chem. Soc. *86*, 2301 (1964).

[13] *K. Griesbaum, A. A. Oswald*, and *D. N. Hall*, J. org. Chemistry *29*, 2404 (1964).

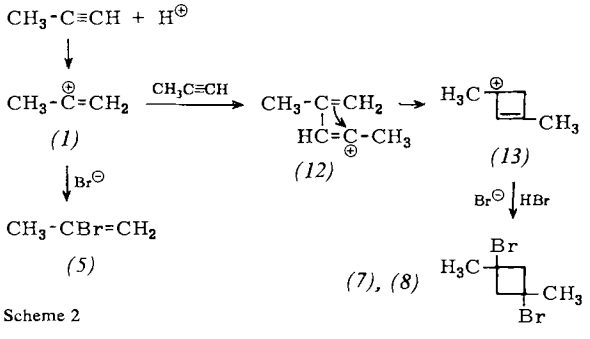
[14] When this work was being carried out we knew of only one example of a cyclodimerization *via* vinyl cations, *i.e.* the boron trifluoride-catalyzed cycloaddition of chlorine to 2-butyne with formation of dichlorotetramethylcyclobutene: *R. Criegee* and *A. Moschel*, Chem. Ber. *92*, 2181 (1959). Further examples of catalytic cycloadditions, leading to four-membered rings *via* vinyl cations have been reported in the interim, *e.g.* the one-step synthesis of hexamethyl(Dewar-benzene) from 2-butyne: *W. Schäfer* and *H. Hellmann*, Angew. Chem. *79*, 566 (1967); Angew. Chem. internat. Edit. *6*, 518 (1967).

[15] These reaction steps have analogs in the chemistry of alkyl cations: a) Competition between the combination of an intermediate cation with a nucleophile on the one hand and the alkylation of an olefin on the other has been reported for the addition of hydrogen bromide to propene, which leads not only to 2-bromopropane but also to bromohexane: *F. R. Mayo* and *M. G. Savoy*, J. Amer. chem. Soc. *69*, 1348 (1947); b) There have been several recent reports of intramolecular cyclization reactions of unsaturated cationic intermediates bearing their positive center in a β position with respect to the double- or triple bond: *M. Hanack, I. Herterich*, and *V. Vött*, Tetrahedron Letters *1967*, 3871; *M. Hanack* and *I. Häffner*, *ibid.* *1964*, 2191.

On the basis of earlier reports, there was little likelihood of a cyclodimerization of methylacetylene with hydrogen bromide. This reaction had been very thoroughly investigated by *Kharasch* in connection with the discovery of the free-radical addition of hydrogen bromide. At that time only the simple Markownikoff adducts *(5)* and in particular *(6)* were found in the nucleophilic reaction [16].

However, re-examination of this reaction with the aid of modern analytical methods showed that methylacetylene is also partly cyclodimerized by hydrogen bromide; at −70 °C we obtained about 9% of *cis*- *(7)* and 32% of *trans*-1,3-dibromo-1,3-dimethylcyclobutane *(8)* in addition to *(5)* and *(6)* [17].

It is not yet certain whether the cyclodimerization of methylacetylene follows a path of its own (Scheme 2) or whether it proceeds *via* an acid-catalyzed isomerization to allene and subsequent cyclodimerization in accordance with Scheme 1. This question could probably be answered by the use of deuterium bromide as the addend. If the two reactions follow different routes each methyl group of the 1,3-dibromo-1,3-dimethylcyclobutane formed by cyclodimerization of allene and each methylene group of that formed by the cyclodimerization of methylacetylene should contain one deuterium atom



Scheme 2

Irrespective of these as yet unanswered questions concerning the reaction course, however, the cyclodimerization of methylacetylene provided a much better economic basis for the one-step synthesis of substituted reactive cyclobutane derivatives. Both allene and methylacetylene are still very expensive in the pure state, whereas stabilized mixtures (*i.e.* mixtures to which propane and propene have been added to reduce the explosion hazard) of allene and methylacetylene are available in large quantities as welding gas [18]. Enriched mixtures of these two substrates can probably be also obtained by work-up of the C_3 streams that occur in the thermal cracking of petroleum. Since in such mixtures the two isomers are often present in the ratio of their thermodynamic equilibrium, in which methylacetylene strongly predominates [19], it is advantageous for the overall yield that both substrates give roughly the same quantity of cyclodimerization product.

[16] *M. S. Kharasch, J. G. McNab*, and *M. C. McNab*, J. Amer. chem. Soc. *57*, 2463 (1935).

[17] *K. Griesbaum*, Angew. Chem. *76*, 782 (1964); Angew. Chem. internat. Edit. *3*, 697 (1964).

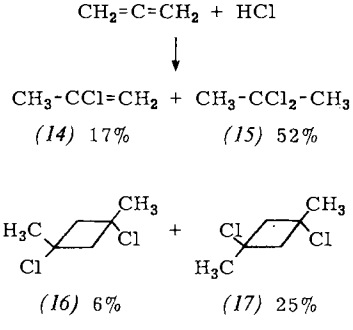
[18] Mixtures of this kind containing about 60% of allene and methylacetylene are marketed by the Dow Chemical Co. in the USA under the trade name MAPP Gas. See also *J. D. Hembree, R. W. Belfit, H. A. Reeves*, and *J. P. Baugham*, Welding *42*, 395 (1963).

[19] *J. F. Cordes* and *H. Günzler*, Chem. Ber. *92*, 1055 (1959).

3. Scope and Limitations of Electrophilic Cyclodimerizations *via* Vinyl Cations

Following the extension of the cyclodimerization to methylacetylene, we examined the question whether the reaction also proceeds with hydrogen chloride and hydrogen iodide.

The reaction of hydrogen chloride with allene at −78 °C had been reported to proceed at a significant rate only in the presence of catalysts, and to lead exclusively to the two Markownikoff adducts *(14)* and *(15)* in the presence of bismuth trichloride [20]. In contrast, we obtained a mixture of four components both in the presence of bismuth trichloride and in the much slower uncatalyzed reaction. These products were the two simple Markownikoff adducts 2-chloropropene *(14)* and 2,2-dichloropropane *(15)* and the two cyclodimerization products *cis*- *(16)* and *trans*-1,3-dichloro-1,3-dimethylcyclobutane *(17)* [21]. The extent to which cyclodimerization had occurred was again strongly dependent on the reaction temperature. Only about 2% of cyclodimerization products were obtained at room temperature, whereas up to 30% were formed at −70 °C. Since the low-temperature reaction with HCl, even in the presence of a catalyst, is much slower than the reaction of allene with HBr, the hydrochlorination is less suited for the preparation of cyclobutane derivatives than the hydrobromination.



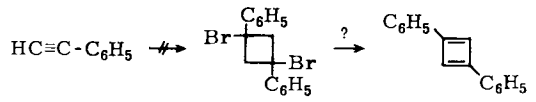
No cyclodimerization products were found in the reactions of hydrogen iodide with allene and with methylacetylene [21]. This is quite understandable, since the iodide ion is a better nucleophile than the bromide or chloride ions [22], and can thus direct the reaction exclusively in the direction of the simple Markownikoff adduct.

The reaction of phenylacetylene with hydrogen bromide appeared interesting in connection with the cyclobutadiene problem. On dehydrobromination of the expected 1,3-dibromo-1,3-diphenylcyclobutane *(18)* the double bonds should, apart from ring cleavage reactions, be introduced into the four-membered

[20] *T. L. Jacobs* and *R. N. Johnson*, J. Amer. chem. Soc. *82*, 6397 (1960).

[21] *K. Griesbaum, W. Nägele*, and *G. G. Wanless*, J. Amer. chem. Soc. *87*, 3151 (1965).

[22] *E. S. Gould*: Mechanism and Structure in Organic Chemistry, Holt & Co., New York 1959, p. 260; Mechanismus und Struktur in der organischen Chemie. Verlag Chemie, Weinheim 1964, 2nd Edit.



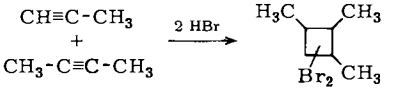
(18)

ring system, since no escape reactions giving exocyclic double bonds are possible.

However, the additions under the usual conditions for cyclodimerization gave only the normal Markownikoff adducts. It is not certain whether the cyclization is prevented in this case by steric factors or by the nature of the intermediate benzyl-vinyl cation. If, for example, the failure of cyclization were due to an enhanced stability of the vinyl cation owing to resonance stabilization, it should be possible to influence the reaction course by suitable *p*-substitution. It is also possible that on grounds of the geometry of the transition state, the cyclodimerization may depend on the occurrence of not strictly linear vinyl cations. For benzyl-vinyl cations a strictly linear structure has been postulated [8].

The higher homologs of allene can be used only to a limited extent, if at all, for such cyclodimerizations, since with increasing substitution by alkyl groups, alkyl cations are formed in preference to vinyl cations as intermediates, so that the higher allenes are protonated at the central carbon atom of the cumulative system [20]. Hence, apart from unsubstituted allene, the choice of substrates is limited to substituted acetylenes.

A possible extension of the preparative use of electrophilic cyclodimerizations was indicated during the investigation of the methylacetylene-hydrogen bromide reaction. Depending upon the source of methylacetylene the gas chromatogram of the crude product mixture contained a signal whose retention time was longer than that of the isomeric 1,3-dibromo-1,3-dimethylcyclobutanes. Investigation by combined gas chromatography and time-of-flight mass spectroscopy showed that the substance corresponding to the signal has the typical molecular-ion triplet (*m/e* = 254, 256, 258) and the fragment-ion doublet (P—Br: *m/e* = 177, 175) of a dibromide [23]. The mass spectrum also pointed to a trimethyl compound. Analysis of the batches of methylacetylene used for the experiments in question showed that they contained small quantities of 2-butyne. We therefore suspect that the by-product was one of the possible isomeric dibromotrimethylcyclobutanes, which may have been formed by co-cyclization of methylacetylene and 2-butyne.



The influence of catalysts on the cyclodimerization by acids has only received a cursory study thus far. Preliminary investigations have shown that boron trifluoride increases not only the rate of the hydrogen bromide-methylacetylene reaction but also the selectivity of the cyclodimerization. The results were, however, inconclusive because of partial resinification of the reaction product.

[23] *J. H. Beynon*: Mass Spectrometry and its Application to Organic Chemistry. Elsevier, Amsterdam 1960, p. 299.

[24] The reactions described in the following were carried out with a mixture of about 10% of *cis*- and 90% of *trans*-1,3-dibromo-1,3-dimethylcyclobutane as it was obtained from the cyclodimerization reaction.

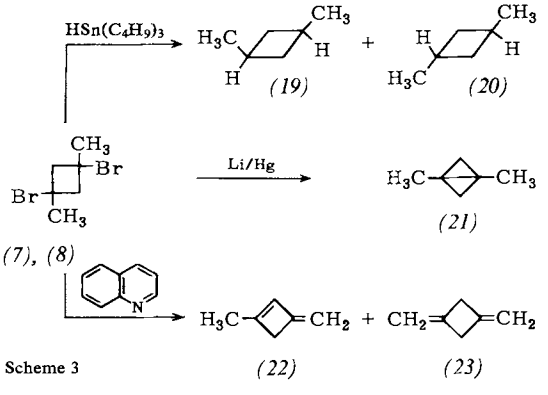
4. Chemistry of the 1,3-Dibromo-1,3-dimethylcyclobutanes[24]

Following the synthesis of the 1,3-dibromo-1,3-dimethylcyclobutanes *(7)* and *(8)*, we carried out a number of experiments mainly in order to support the structure assignments which were initially based purely on spectroscopic data, by conversion of these compounds into known cyclobutane derivatives (Scheme 3). During the course of this work it became evident that 1,3-dihalocyclobutanes, with their tertiary halogen substituents, are fairly reactive and should have a variety of uses.

When the dibromide was heated with an excess of tributyltin hydride, a mixture of *cis*- *(19)* [25] and *trans*-1,3-dimethylcyclobutane *(20)* [25] was obtained in 58% yield. During this reaction, the *cis-trans* ratio changed from 10 : 90 in the starting bromide to 30 : 70 in the reduction product. This is understandable if (as is assumed for such reactions [26]) the reaction proceeds *via* free-radical intermediates.

When the dibromide is stirred at room temperature with a suspension of 2% of lithium amalgam in dioxane, the bicyclic dehalogenation product 1,3-dimethylbicyclo[1.1.0]-butane *(21)* is formed with a selectivity of $> 85\%$ [27, 28].

Dehydrobromination of the dibromide with quinoline [29] at approximately 200 °C gave a mixture of the two dienes 1-methyl-3-methylenecyclobutene *(22)* [25, 30] and 1,3-dimethylenecyclobutane *(23)* [25] (ratio 80 : 20, respectively) in a yield of about 50%.



Scheme 3

These preliminary results demonstrate that cyclodimerizations leading to reactive cyclobutane derivatives are not only of mechanistic interest, but may also open up new paths for the synthesis of compounds that have hitherto only been obtainable either *via* roundabout routes [25] or in considerably smaller yields [28] and with greater effort.

Received: January 23, 1969 [A 726 IE]
German version: Angew. Chem. *81*, 966 (1969)
Translated by Express Translation Service, London

[25] First prepared by *F. F. Caserio, S. H. Parker, R. Piccolini,* and *J. D. Roberts*, J. Amer. chem. Soc. *80*, 5507 (1958); See also *J. Coburn jr.*, Dissertation, Yale University 1963.

[26] *H. G. Kuivila, L. W. Menapace,* and *C. R. Warner*, J. Amer. chem. Soc. *84*, 3584 (1962).

[27] *K. Griesbaum* and *P. E. Butler*, Angew. Chem. *79*, 467 (1967); Angew. Chem. internat. Edit. *6*, 444 (1967).

[28] First prepared by *W. von E. Doering* and *J. F. Coburn jr.*, Tetrahedron Letters 1965, 991.

[29] *K. Griesbaum*, unpublished experiments.

[30] The NMR spectrum of this conjugated diene is an interesting example of an eight-spin system in which five non-equivalent protons are coupled with one another. The signals of these protons have been assigned by spin decoupling experiments: *P. E. Butler* and *K. Griesbaum*, J. org. Chemistry *33*, 1956 (1968).

Organogermyl, Organostannyl, and Organoplumbyl Phosphines, Arsines, Stibines, and Bismuthines

By H. Schumann[*]

The preparation, properties, and reactions of the compounds named in the title are described, with particular reference to the possible participation of $(p\rightarrow d)_\pi$ components in the bonding between the group IVB and the group VB elements.

1. Introduction

A problem that is still of great interest in the field of covalent inorganic compounds is the nature of the bonding between silicon and oxygen. It is not yet generally accepted that the unexpected stability of this bond is due to decisive contributions from $(p\rightarrow d)_\pi$ double-bond components. A deeper insight into the nature of the bond should, however, be obtainable by comparison of the physical and chemical properties of such covalent silicon compounds with the properties of similar covalent compounds of the silicon homologs germanium, tin, and lead. The investigations should concentrate on the one hand on tin as one of the bonding partners and on the other on the homologous elements of oxygen and nitrogen. We have already reviewed the most important organometallic compounds containing bonds between germanium, tin, or lead and sulfur, selenium, or tellurium [1]. Covalent compounds of the group IV elements mentioned with phosphorus, arsenic, antimony, and bismuth are reported in the present article. These compounds were unknown until a few years ago.

2. Organogermyl, Organostannyl, and Organoplumbyl Phosphines

2.1. Synthesis

Only two phosphines with organometallic substituents were known in 1962. These were triethylstannyldiphenylphosphine, which was prepared in 1959 by *Kuchen* and *Buchwald* [2], and tris(trimethylstannyl)-phosphine, which was described in 1960 by *Bruker et al.* [3].

In analogy with the reactions of sulfur, selenium, and tellurium with tetraorganostannanes [4–7], organostannyl phosphines of various degrees of polymerization were obtained from tetraphenylstannane and phosphorus in a sealed tube above 220 °C [8–10]. Triphenylphosphine and alloy-like tin phosphides were also formed.

Diphenyltin and triphenylphosphine are formed first between 220 and 230 °C, and combine to form the addition complex diphenyltin-triphenylphosphine *(1a)*. Though this complex cannot be isolated, its existence can be demonstrated by the formation of the stable oxidation products diphenyltin oxide and triphenylphosphine oxide [11]. When the temperature is raised, the complex *(1a)* rearranges into the stable isomer triphenylstannyldiphenylphosphine *(2a)*, which in turn is dephenylated by excess phosphorus. At 230 to 250 °C, for example, cyclic trimeric diphenylstannylphenylphosphine is formed. Between 250 and 280 °C and with an excess of phosphorus, low molecular weight compounds of this type undergo cleavage of further P–C and Sn–C bonds to form highly polymeric organostannyl phosphines; however, these can be isolated only in the form of their oxidation products (Table 1). Above 280 °C, all the Sn–C bonds are broken; the end products of the degradation of phosphorus by tetraphenylstannane are triphenylphosphine and tin metal.

$$3\,(C_6H_5)_4Sn + 1/2\,P_4 \rightarrow 3\,(C_6H_5)_2Sn + 2\,(C_6H_5)_3P$$

$$(C_6H_5)_2Sn + P(C_6H_5)_3 \rightarrow (C_6H_5)_2Sn\leftarrow{:}P(C_6H_5)_3 \quad (1a)$$

$$\rightarrow (C_6H_5)_3Sn{-}P(C_6H_5)_2 \quad (2a)$$

$$3\,(C_6H_5)_4Sn + P_4 \rightarrow 3\,Sn + 4\,(C_6H_5)_3P$$

Whereas this reaction is not suitable for the specific synthesis of definite organometal phosphines, the reactions of organometal halides with phosphine or

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[1] *H. Schumann* and *M. Schmidt*, Angew. Chem. *77*, 1049 (1965); Angew. Chem. internat. Edit. *4*, 1007 (1965).

[2] *W. Kuchen* and *H. Buchwald*, Chem. Ber. *92*, 227 (1959).

[3] *A. B. Bruker, L. D. Balshova*, and *L. Z. Soborovskii*, Doklady Akad. Nauk SSSR *135*, 843 (1960).

[4] *M. Schmidt, H. J. Dersin*, and *H. Schumann*, Chem. Ber. *95*, 1428 (1962).

[5] *M. Schmidt* and *H. Schumann*, Chem. Ber. *96*, 462 (1963).

[6] *M. Schmidt* and *H. Schumann*, Chem. Ber. *96*, 780 (1963).

[7] *M. Schmidt* and *H. Schumann*, Z. Naturforsch. *19b*, 74 (1964).

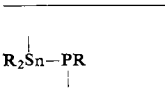
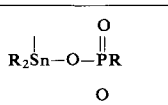
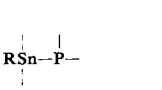
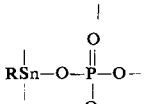
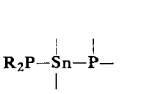
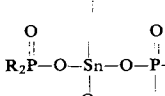
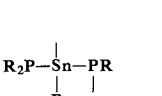
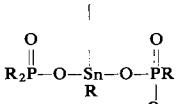
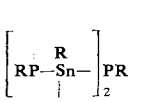
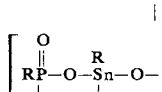
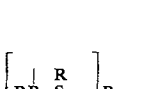
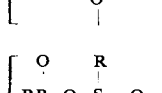
[8] *H. Schumann, H. Köpf*, and *M. Schmidt*, Angew. Chem. *75*, 672 (1963); Angew. Chem. internat. Edit. *2*, 546 (1963).

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Table 1. Oxidation products isolated as secondary products of the reaction of $Sn(C_6H_5)_4$ with P_x (between 250 and 280 °C) ($R = C_6H_5$).

Structural units of: Organostannylphosphine	Structural units of: Organotin phosphonate or phosphate	Degradation products
		R_2SnO $RP(O)(OH)_2$
		$RSn(O)OH$ H_3PO_4
		SnO_2 $R_2P(O)OH$ H_3PO_4
		$RSn(O)OH$ $R_2P(O)OH$ $RP(O)(OH)_2$
		$RSn(O)OH$ $RP(O)(OH)_2$
		$RSn(O)OH$ $RP(O)(OH)_2$ H_3PO_4

organophosphines (in the presence of triethylamine as a hydrogen halide acceptor) has been found to be very specific. Owing to the instability of the products, rigorous exclusion of moisture and oxygen is necessary. Thus triorganogermanium, triorganotin, or triorganolead halides react with diorganophosphines to give products of the type *(2)* [12–16a], while with monoorganophosphines [12, 16–17a] and with phosphine [12, 16, 16a, 18, 19] they form compounds such as *(3)* and *(4)*.

$$R_3MX + R'_2PH \xrightarrow[-[(C_2H_5)_3NH]X]{+(C_2H_5)_3N} R_3M{-}PR'_2 \quad (2)$$

$$2\,R_3MX + R'PH_2 \xrightarrow[-2[(C_2H_5)_3NH]X]{+2(C_2H_5)_3N} (R_3M)_2PR' \quad (3)$$

$$3\,R_3MX + PH_3 \xrightarrow[-3[(C_2H_5)_3NH]X]{+3(C_2H_5)_3N} (R_3M)_3P \quad (4)$$

When diorganometal dihalides are used, the reaction with diorganophosphines yields monomeric compounds of the type *(5)* [12–14], and the reaction with monoorganophosphines yields oligomers of the type $(R_2M{-}PR')_n$ [21]. Cyclic trimers of this type can be isolated in yields of up to 85% with suitable experimental conditions [20]. On the other hand, bis(chlorodiphenylgermyl)phenylphosphine *(3a)* is formed almost quantitatively from diphenylgermanium dichloride and phenylphosphine. With dipotassium phenylphosphide in monoglyme/ether, the two ring systems *(3b)* and *(3c)* are formed in a ratio of 3 : 1: monopotassium phenylphosphide leads almost exclusively to *(3b)*. The same mixture of *(3b)* and *(3c)* is also formed on reaction of *(3a)* with $K_2PC_6H_5$ or $KHPC_6H_5$ [21].

$$2\,R_2GeCl_2 + RPH_2 \xrightarrow[-2[(C_2H_5)_3NH]Cl]{+2(C_2H_5)_3N} R_2Ge(Cl){-}P(R){-}GeR_2(Cl) \quad (3a)$$

$$5\,R_2GeCl_2 + 5\,K_2PR \xrightarrow[-10\,KCl]{} \text{(3b)} + \text{(3c)}$$

$$2\,R_2GeCl_2 + 2\,KHPR \xrightarrow[-2\,KCl,\,-2\,HCl]{} \text{(3b)}$$

$R = C_6H_5$

The reactions of diorganometal dihalides with phosphine itself also give polymeric organometal phosphines, but in this case containing the structural units $R_2M\langle$ and $\rangle P$ [21].

In the special case of the reaction of diphenyltin dichloride with phosphine, small quantities of a benzene-soluble compound *(6)* were isolated as well as high polymers; an adamantane skeleton has to be proposed for this compound [21].

$$R_2MX_2 + 2\,R'_2PH \xrightarrow[-2[(C_2H_5)_3NH]X]{+2(C_2H_5)_3N} R_2M(PR'_2)_2 \quad (5)$$

$$3\,R_2MX_2 + 3\,R'PH_2 \xrightarrow[-6\,[(C_2H_5)_3NH]X]{+6\,(C_2H_5)_3N} \text{(6)}$$

$$6\,R_2SnCl_2 + 4\,PH_3 \xrightarrow[-12\,[(C_2H_5)_3NH]Cl]{+12\,(C_2H_5)_3N} \text{(6)}$$

$R = CH_3, C_4H_9, C_6H_5$, $R' = C_6H_5$

(6)

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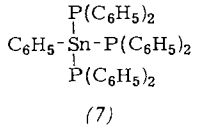
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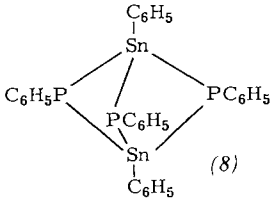
[20] *H. Schumann* and *H. Benda*, Angew. Chem. *80*, 845 (1968); Angew. Chem. internat. Edit. *7*, 812 (1968).

[21] *H. Schumann* and *H. Benda*, unpublished.

Phenyltin trichloride reacts with diphenylphosphine to form monomeric tris(diphenylphosphino)phenylstannane *(7)* [12] and with phenylphosphine to give a phenylstannylphosphine *(8)* (yield 5%) having the composition $(C_6H_5Sn)_2(PC_6H_5)_3$, together with high polymers of unknown structure. The IR and ^{31}P-NMR spectra [21] of *(8)* indicate a bipyramidal structure with three phosphorus atoms in equatorial positions and two tin atoms in axial positions.

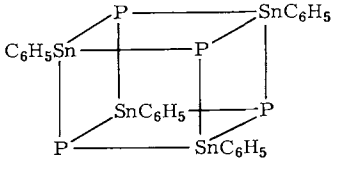


(7)

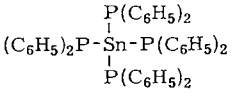


(8)

Methyltin and butyltin trichlorides give only highly polymeric reaction products with phosphine. On the other hand, small quantities of a tetrameric phenylstannylphosphine *(9)* having a cubane structure can be isolated from the polymer mixture obtained from phenyltin trichloride and phosphine [22]. Finally, tin tetrachloride reacts with diphenylphosphine to give tetrakis(diphenylphosphino)stannane *(10)* [12].



(9)



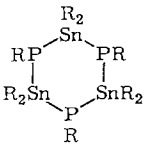
(10)

In addition to this versatile method, other syntheses for phosphines with organometallic constituents have also been developed in recent years. Examples of such syntheses are the reactions of organo-germanium or organotin halides with alkali metal organophosphides [2,3,8,12–14,17a,19,21,23–25] and of triphenylstannyllithium and phenylchlorophosphines [8,23,26,27]:

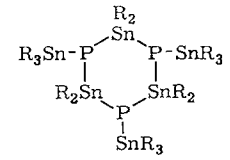
$$R_{4-n}MX_n + n\ LiPR'_2 \rightarrow R_{4-n}M(PR'_2)_n + n\ LiX, \quad M = Ge, Sn$$

$$n\ R_3SnLi + R'_{3-n}PCl_n \rightarrow (R_3Sn)_nPR'_{3-n} + n\ LiCl, \quad R = C_6H_5$$

Care must however be taken in the last reaction to ensure that the phosphorus chloride in question is present in excess right to the end of the reaction. Otherwise the initially formed monomeric reaction products are attacked by the strongly nucleophilic triphenylstannanide ion in a manner that has not yet been fully clarified, with formation of polymeric cyclic phenylstannylphosphines such as *(11)* and *(12)* [23].



(11) R = C_6H_5



(12)

Reactions of this type have also allowed the preparation of a trigonal bipyramidal phenylgermylphosphine of the type *(8)* and a heptameric phenylgermylphosphine $(C_6H_5GeP)_7$ from phenylgermanium tribromide and $K_2P(C_6H_5)$ or Na_3P respectively [21].

Organophosphines also react with organotin oxides [28, 29] and with organogermylamines [13,14,17a,19,30,31, 34] and organostannylamines [32,33] with liberation of water or amine and formation of corresponding metal phosphines.

Phosphines in which the phosphorus atoms carry different organometallic residues are also obtainable [16a,35]. Thus bis(triphenylstannyl)phenylphosphine is split by butyllithium in benzene solution with formation of butyltriphenylstannane and lithium phenyltriphenylstannylphosphide *(13)*. This product, which cannot be isolated, reacts with triphenylgermanium bromide and triphenyllead chloride to form the compounds *(14)* or *(15)* with mixed substituents Lithium bis(triphenylstannyl)phosphide, which is obtained in the same way as *(13)* from tris(triphenylstannyl)phosphine and butyllithium, reacts similarly.

$$[(C_6H_5)_3Sn]_2PC_6H_5 + LiC_4H_9 \rightarrow (C_6H_5)_3SnC_4H_9 + \underset{(13)}{(C_6H_5)_3Sn(C_6H_5)P\text{-}Li}$$

$$(13) + (C_6H_5)_3MX \rightarrow (C_6H_5)_3Sn(C_6H_5)P\text{-}M(C_6H_5)_3 + LiX$$

(14a), M = Ge; *(14b)*, M = Pb; X = Cl, Br

$$[(C_6H_5)_3Sn]_2PLi + (C_6H_5)_3MX \rightarrow [(C_6H_5)_3Sn]_2P\text{-}M(C_6H_5)_3 + LiX$$

(15a), M = Ge; *(15b)*, M = Pb; X = Cl, Br

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2.2. Physical Properties

Apart from the alkylgermyl and alkylstannyl derivatives which are liquid under normal conditions, all the known phosphines of this type are colorless to light yellow crystalline solids (Table 2). They dissolve readily, and without decomposing, in aromatic hydrocarbons and in some ethers, such as tetrahydrofuran. Aliphatic hydrocarbons such as pentane, or methylcyclohexane are excellently suited for recrystallization.

Table 2. Organogermyl, organostannyl, and organoplumbyl phosphines.

Compound	M.p. (°C)	B.p. (°C/torr)	Ref.
$(CH_3)_3GeP(C_6H_5)_2$		185–187/12	[30]
$(C_2H_5)_3GeP(C_2H_5)_2$		120/15	[31]
$(C_2H_5)_3GeP(C_6H_5)_2$		146/10^{-3}	[13, 14]
$(C_6H_5)_3GeP(C_6H_5)_2$	159–161		[1, 16a]
$[(CH_3)_3Ge]_2PCH_3$		53/1	[36]
$[(CH_3)_3Ge]_2PC_6H_5$		107/2	[17a]
$(CH_3)_3GePHC_6H_5$		60/2	[17a]
$[(C_6H_5)_3Ge]_2PC_6H_5$	110		[16, 16a]
$[(CH_3)_3Ge]_3P$		62–63/0.1	[16a, 19]
$[(C_6H_5)_3Ge]_3P$	128		[16, 16a]
$[Cl(C_6H_5)_2Ge]_2PC_6H_5$	118–120		[21]
$[(C_6H_5)_2GePC_6H_5]_3$	112–114		[21]
$[(C_6H_5)_2GePC_6H_5]_2$	40–42		[21]
$(C_6H_5Ge)_2(PC_6H_5)_3$	126 (decomp.)		[21]
$(C_6H_5GeP)_7$	140–142		[21]
$(CH_3)_3SnP(CH_3)_2$		10 (decomp.)	[37]
$(CH_3)_3SnP(t\text{-}C_4H_9)_2$		73/0.1	[102]
$(C_2H_5)_3SnP(C_2H_5)_2$		70/0.3	[24]
$(C_2H_5)_3SnP(C_2H_5)(C_6H_5)$		99–100/0.2	[24]
$(CH_3)_3SnP(C_6H_5)_2$		141–142/0.7	[24, 32, 33]
$(C_3H_7)_3SnP(C_2H_5)(C_6H_5)$		125–126/0.3	[24]
$(C_2H_5)_3SnP(C_6H_5)_2$		170/0.7	[2, 24, 33]
$(C_4H_9)_3SnP(C_4H_9)_2$		122–124/0.15	[29]
$(C_3H_7)_3SnP(C_6H_5)_2$		176–177/0.6	[24]
$(C_4H_9)_3SnP(C_6H_5)_2$	60	192/0.6	[8,12,24,28]
$(C_6H_5)_3SnP(C_6H_5)_2$ *(2a)*	127–130		[8, 12, 16a, 23, 24]
$[(CH_3)_3Sn]_2PCH_3$		89–90/3	[25–27]
$[(CH_3)_3Sn]_2PC_6H_5$ *(17)*	37–38	131–135/10^{-2}	[17]
$[(C_2H_5)_3Sn]_2PCH_3$		143–145/3	[25, 26]
$[(C_2H_5)_3Sn]_2PC_6H_5$		150–151/0.3	[24]
$[(C_4H_9)_3Sn]_2PC_6H_5$		178–181/10^{-2}	[28]
$[(C_6H_5)_3Sn]_2PC_6H_5$	180		[16, 16a]
$[(CH_3)_3Sn]_3P$		136–137/3	[3, 16a]
$[(C_6H_5)_3Sn]_3P$	201		[16, 16a,23]
$(CH_3)_2Sn[P(C_6H_5)_2]_2$	110–114		[12]
$(C_4H_9)_2Sn[P(C_6H_5)_2]_2$	98–102		[12]
$(C_6H_5)_2Sn[PC_6H_5)_2]_2$	78–80		[12, 24]
$(C_2H_5)_3SnP(CH_3)(SC_2H_5)$		86–88/2	[38]
$C_6H_5Sn[P(C_6H_5)_2]_3$ *(7)*	115–117		[12]
$Sn[P(C_6H_5)_2]_4$ *(10)*	106–107		[12]
$[(CH_3)_2SnPC_6H_5]_3$ *(16)*	130		[20]
$[(C_4H_9)_2SnPC_6H_5]_3$		Oil	[20]
$[(C_6H_5)_2SnPC_6H_5]_3$ *(11)*	161–163		[20]
$[(C_6H_5)_2SnPSn(C_6H_5)_3]_3$ *(12)*	98–102		[23]
$(C_6H_5Sn)_4P_4$ *(9)*	160		[22]
$[(C_6H_5)_2Sn]_6P_4$ *(6)*			[21]
$(C_6H_5Sn)_2(PC_6H_5)_3$ *(8)*	133–135		[21]
$[(C_6H_5)_3Sn][(C_6H_5)_3Ge]PC_6H_5$ *(14a)*	115–118		[16a, 35]
$[(C_6H_5)_3Sn][(C_6H_5)_3Pb]PC_6H_5$ *(14b)*	110 (decomp.)		[16a, 35]
$[(C_6H_5)_3Sn]_2PGe(C_6H_5)_3$ *(15a)*	160		[16a, 35]
$[(C_6H_5)_3Sn]_2PPb(C_6H_5)_3$ *(15b)*	171–172 (decomp.)		[16a, 35]
$(C_6H_5)_3PbP(C_6H_5)_2$	100 (decomp.)		[15, 16a]
$[(CH_3)_3Pb]_3P$	48–49		[16a, 18]
$[(C_6H_5)_3Pb]_3P$	110 (decomp.)		[16a, 18]
$(C_6H_5)_2Pb[P(C_6H_5)_2]_2$	10 (decomp.)		[15]
$[(C_6H_5)_3Pb]_2PC_6H_5$	110 (decomp.)		[16a]

The thermal stability of these compounds varies considerably. Thus organogermyl and organostannyl phosphines generally decompose only above 200 °C in an uncontrollable manner, whereas organoplumbyl phosphines decompose at very low temperatures with deposition of lead. Trimeric dimethylstannylphenylphosphine *(16)* is also thermally unstable, and decomposes above 130 °C to give bis(trimethylstannyl)-phenylphosphine *(17)*, cyclopenta(phenylphosphane) *(18)*, and tin [20].

$$\underset{(16)}{[(CH_3)_2Sn\text{–}PC_6H_5]_3} \xrightarrow{\Delta} \underset{(17)}{[(CH_3)_3Sn]_2PC_6H_5} + \underset{(18)}{(C_6H_5P)_5} + Sn$$

The vibration spectra of the organometal phosphines mentioned (Table 3) should contain, in addition to the vibrations of the methyl groups and the substituent-dependent and substituent-independent vibrations of the phenyl rings, a skeletal vibration ν M–P for compounds of symmetry C_s and three skeletal vibrations ν_{as} M–P–M, ν_s M–P–M, and δ M–P–M for compounds of symmetry C_{2v} as IR- and Raman-active vibrations. Four-particle molecules of the type M_3P with a planar arrangement of the atoms, corresponding to the symmetry D_{3h}, should give four skeletal vibrations, *i.e.* one symmetrical and one antisymmetrical stretching vibration, and two bands in the long-wave region of predominantly deformation character. The symmetrical stretching vibration is IR-inactive. With a trigonal pyramidal arrangement (symmetry C_{3v}), the nature and number of the vibrations remain the same, but the symmetrical stretching vibration is also IR-active. The fact that all four skeletal vibrations do in fact occur both in the IR and in the Raman spectra of the tris(triorganoelement)-substituted phosphines thus clearly shows the pyramidal structure of these molecules and indicates the absence of strong $(p\rightarrow d)_\pi$ multiple bond components [16a, 39–41].

The long-wave shifts of the frequencies ν M–P, ν_{as} and ν_s M_2P or M_3P, and δ M_2P or δ M_3P on replacement of M = Ge by Sn and Pb are due to the increase in the mass of the triorganoelement groups in the same direction. The differences $\nu_{as} - \nu_s$ (M–P–M) increase from 24 cm^{-1} for $[(C_6H_5)_3Ge]_2PC_6H_5$ to 41 cm^{-1} for the analogous tin compound, and 35 cm^{-1} for the corresponding lead derivative. This indicates an increase in the angle at the phosphorus due to the increase in the bulk of the triphenylelement unit.

The chemical shifts of the singlets that are found in every case as expected in the ^{31}P-NMR spectra (Table 4) [40,41] have surprisingly high positive values, which are exceeded only by the value for white phosphorus (δ = 462 ± 2 ppm [40]). It is also found that the δ values vary in the series $[(C_6H_5)_3Sn]_3P$,

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Table 3. IR and Raman frequencies of organogermyl, organostannyl, and organoplumbyl phosphines.

Compound C_{3v}	$\nu_s M_3P$ IR	Raman	$\nu_{as} M_3P$ IR	Raman	$\delta_s M_3P$ IR	Raman	$\delta_{as} M_3P$ IR	Raman
	(cm^{-1})		(cm^{-1})		(cm^{-1})		(cm^{-1})	
$[(CH_3)_3Ge]_3P$	320 m	320 (3) p	397 s	399 (2)	88 m	84 (2)	153 m	156 (7)
$[(C_6H_5)_3Ge]_3P$	308 s	311 (1)	375 s	366 (0)	88 m	85 (2)	168 m	171 (1)
$[(CH_3)_3Sn]_3P$	284 s	284 (4) p	351 s	359 (2)	66 m	62 (1)	125 m	123 (3)
$[(C_6H_5)_3Sn]_3P$	296 s	294 (1) p	347 s	350 (3)	88 w	88 (2)	123 w	?
$[(CH_3)_3Pb]_3P$	286 m		313 s		?		?	
$[(C_6H_5)_3Pb]_3P$	283 s		307 s					
Compound C_{2v}	$\nu_s M_2P$ IR	Raman	$\nu_{as} M_2P$ IR	Raman	δM_2P IR	Raman		
	(cm^{-1})		(cm^{-1})		(cm^{-1})			
$[(C_6H_5)_3Ge]_2PC_6H_5$	368 s		392 s		170 m			
$[(C_6H_5)_3Sn]_2PC_6H_5$	327 s	326 (3)	368 s	369 (2)	168 m	167 (3)		
$[(C_6H_5)_3Pb]_2PC_6H_5$	284 s		319 s		?			
Compound C_s	νMP IR	Raman						
	(cm^{-1})							
$(C_6H_5)_3GeP(C_6H_5)_2$	378 m							
$(C_6H_5)_3SnP(C_6H_5)_2$	351 m	356 (5)						
$(C_6H_5)_3PbP(C_6H_5)_2$	305 m							

Table 4. ^{31}P-NMR spectra of organogermyl and organostannyl phosphines (85% H_3PO_4 as external standard).

Compound	δ (ppm)
$[(CH_3)_3Ge]_3P$	+228
$[(CH_3)_3Sn]_3P$	+330
$[(C_6H_5)_3Sn]_3P$	+323
$[(C_6H_5)_3Sn]_2PC_6H_5$	+163
$(C_6H_5)_3SnP(C_6H_5)_2$	+ 56
$P(C_6H_5)_3$	+ 8

$[(C_6H_5)_3Sn]_2PC_6H_5$, $(C_6H_5)_3SnP(C_6H_5)_2$, $P(C_6H_5)_3$ in a manner that indicates the absence of $(p\rightarrow d)_\pi$ bond components between phosphorus and tin. As expected, however, the variation of the δ values in such series of compounds is determined, not by one variable, but by several parameters that act with or against one another. The ^{31}P-$^{117,119}Sn$ coupling constants, which are absolutely essential for a conclusive discussion of the situation, are not yet known. Pure $p_\sigma(P)-(sp^3)_\sigma(Si)$ bonds are assumed for similar organosilylphosphines on the basis of detailed ^{31}P-NMR spectroscopic measurements [42].

2.3. Chemical Properties and Reactions

2.3.1. Oxidation

The sensitivity of organogermyl, organostannyl, and organoplumbyl phosphines toward oxygen [43] depends mainly on the number and nature of the organic residues used to block the unwanted valences of the metal. Alkyl compounds are more sensitive than the corresponding phenyl derivatives toward oxygen. The attack of oxygen is slowest on tetrakis(diphenylphosphino)stannane *(10)* and tris(triphenylstannyl)phosphine, whereas all the other organometal phosphine derivatives investigated can be safely handled only in oxygen-free atmospheres. The oxidation, either on simple exposure to air or (always quantitatively) with hydrogen peroxide in ethanol, proceeds in accordance with the general equation

$$\gtrdot M-\ddot{P}\lessdot + O_2 \rightarrow \gtrdot M-O-\overset{O}{\overset{\|}{P}}\lessdot$$

with the formation of organometal phosphinates. The possible intermediates phosphine oxide *(20)* or phosphinite *(19)* have never been isolated in this reaction.

Even when *C,N*-diphenylnitrone, 1,2-dihydroisoquinoline *N*-oxide, or benzonitrile oxide is used as a specific oxidizing agent, triphenylstannyldiphenylphosphine for example is entirely oxidized to the final stage, *i.e.* to the phosphinate.

Attempted independent syntheses of one of the two intermediates of this oxidation in particular were unsuccessful in the case of triphenylstannyl diphenylphosphinite *(19a)*, which is extremely sensitive to oxygen, whereas triphenylstannyldiphenylphosphine oxide *(20a)* escapes isolation by immediate rearrangement into the isomeric phosphinite [43].

$$(C_6H_5)_3SnOLi + (C_6H_5)_2PCl \xrightarrow{-LiCl} (C_6H_5)_3Sn-O-\ddot{P}(C_6H_5)_2 \quad (19a)$$

$$(C_6H_5)_3SnLi + (C_6H_5)_2P(O)Cl \xrightarrow{-LiCl} (C_6H_5)_3Sn-P(O)(C_6H_5)_2 \quad (20a)$$

$$(C_6H_5)_3Sn-O-\ddot{P}(C_6H_5)_2 + 1/2\,O_2 \rightarrow (C_6H_5)_3Sn-O-P(O)(C_6H_5)_2$$

(19a), m.p. 120 °C — *(21a)*, m.p. 360 °C

Thus all the compounds described in the literature as organostannylphosphine oxides are in fact probably the corresponding phosphinates *(21)* as has already been stated by a number of authors [44–49].

[42] *E. Fluck, H. Bürger,* and *U. Goetze,* Z. Naturforsch. *22b,* 912 (1967).

[43] *H. Schumann, P. Jutzi, A. Roth, P. Schwabe,* and *E. Schauer,* J. organometallic Chem. *10,* 71 (1967).

[44] *B. A. Arbusov* and *N. P. Grechkin,* J. gen. Chem. (USSR) (English transl. of Ž. obšč. Chim.) *17,* 2166 (1947).

[45] *B. A. Arbusov* and *N. P. Grechkin,* J. gen. Chem. (USSR) (English transl. of Ž. obšč. Chim.) *20,* 107 (1950).

[46] *B. A. Arbusov* and *A. N. Pudovik,* J. gen. Chem. (USSR) (English transl. of Ž. obšč. Chim.) *17,* 2158 (1947).

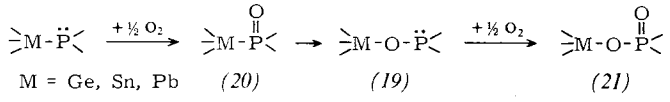
[47] *H. Schindelbauer* and *D. Hammer,* Mh. Chem. *94,* 644 (1963).

[48] *Y. Nagae* and *K. Wakamori,* Jap. Pat. 4575 (66) (March 25, 1963); Chem. Abstr. *65,* 2298h (1966).

[49] *B. A. Arbusov* and *N. P. Grechkin,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1956,* 440.

These results and the fact that organotin phosphinites *(19)* remove oxygen even from organostannanols to form organotin phosphinates [28] suggest the following oxidation course:

The organometal phosphines first add one oxygen atom to form the phosphine oxides. The strengthening of the metal-phosphorus bond is lost with the blockage of the originally free electron pair on the phosphorus. This bond is accordingly broken, and the phosphine oxide gives a phosphinite in a reverse Arbusov rearrangement. The subsequent addition of a second oxygen atom to the now restored lone pair of the electrons on the phosphorus leads to the formation of phosphinates. Since the second oxygen is added more



M = Ge, Sn, Pb *(20)* *(19)* *(21)*

rapidly than the first, only the phosphinates are obtained as stable end products in every case. Triphenylstannyldiphenylphosphine reacts similarly with elementary sulfur to give *(21b)*, whereas bis(triphenylstannyl)phenylphosphine and tris(triphenylstannyl)phosphine give, not the expected thiophosphates but only their decomposition products, *i.e.* bis(triphenylstannyl) sulfide and polymeric phenylphosphorus sulfides or P_2S_5 [43].

$$4\,(C_6H_5)_3Sn{-}P(C_6H_5)_2 + S_8 \rightarrow 4\,(C_6H_5)Sn{-}S{-}P(S)(C_6H_5)_2$$
(21b), m.p. 128–130 °C

2.3.2. Hydrolysis

Perphenylated organogermyl, organostannyl, and organoplumbyl phosphines are not hydrolyzed in the absence of air, probably because of insufficient wetting by water [1]. In alkyl-substituted compounds the metal-phosphorus bond is broken with formation of phosphines and germoxanes, stannanols, or plumbanols [1]. All known organometal-substituted phosphines are decomposed in this way by alcoholic sodium hydroxide solutions. The structure of the phosphine can be readily deduced from the degradation products (Table 1).

2.3.3. Polar Insertion Reactions

The metal-phosphorus bond of organogermyl and organostannyl phosphines can be broken by 1,2-dipolar reagents [50, 51, 31]. For example carbon disulfide is inserted between germanium and phosphorus in triethylgermyldiethylphosphine and between tin and phosphorus in triphenylstannyldiphenylphosphine to form triethylgermyl diethylphosphinodithioformate *(22a)* and triphenylstannyl diphenylphosphinodithioformate *(22b)* respectively.

$$(C_2H_5)_3Ge{-}P(C_2H_5)_2 + CS_2 \rightarrow (C_2H_5)_3Ge{-}S{-}C(S)P(C_2H_5)_2$$
(22a)

$$(C_6H_5)_3Sn{-}P(C_6H_5)_2 + CS_2 \rightarrow (C_6H_5)_3Sn{-}S{-}C(S)P(C_6H_5)_2$$
(22b)

COS, Cl_2CS, $(NH_2)_2CS$, C_6H_5NCO, and C_6H_5NCS also react as 1,2-dipoles to give the compounds shown in Table 5. Cleavage with CO_2, on the other hand, has been observed only in analogous organosilyl phosphines [52].

Table 5. Reaction products from organogermyl and organostannyl phosphines with 1,2-dipolar reagents.

	Reaction product	M.p. (°C)	Ref.
$(C_2H_5)_3GeP(C_2H_5)_2$			
+ CS_2	$(C_2H_5)_3Ge{-}SC(S){-}P(C_2H_5)_2$ *(22a)*	[a]	[31]
+ C_6H_5NCO	$(C_2H_5)_3Ge{-}N(C_6H_5)C(O){-}P(C_2H_5)_2$	[b]	[31]
+ C_6H_5NCS	$(C_2H_5)_3Ge{-}N(C_6H_5)C(S){-}P(C_2H_5)_2$	[c]	[31]
$(C_6H_5)_3SnP(C_6H_5)_2$			
+ CS_2	$(C_6H_5)_3Sn{-}SC(S){-}P(C_6H_5)_2$ *(22b)*	68	[50, 51]
+ COS	$(C_6H_5)_3Sn{-}OC(S){-}P(C_6H_5)_2$	97	[50, 51]
+ $CSCl_2$	$(C_6H_5)_3Sn{-}SC(Cl_2){-}P(C_6H_5)_2$	93	[50, 51]
+ $CS(NH_2)_2$	$(C_6H_5)_3Sn{-}SC[(NH_2)_2]{-}P(C_6H_5)_2$	115	[50, 51]
+ C_6H_5NCO	$(C_6H_5)_3Sn{-}N(C_6H_5)C(O){-}P(C_6H_5)_2$	58 (decomp. pt.)	[50, 51]
+ C_6H_5NCS	$(C_6H_5)_3Sn{-}N(C_6H_5)C(S){-}P(C_6H_5)_2$	87	[50, 51]
$Sn[P(C_6H_5)_2]_4$			
+ CS_2	$Sn[SC(S){-}P(C_6H_5)_2]_4$	55	[50]
+ C_6H_5NCO	$Sn[N(C_6H_5)C(O){-}P(C_6H_5)_2]_4$	50	[50]

[a] B.p. 98 °C/0.1 torr. [b] B.p. 83 °C/0.1 torr. [c] B.p. 92 °C/0.2 torr.

In analogy with the insertions in Si–N [53–56] and Sn–N compounds [32, 57], these reactions presumably also proceed by a polar four-center mechanism *via (23)*.

[50] *H. Schumann, P. Jutzi*, and *M. Schmidt*, Angew. Chem. *77*, 812 (1965); Angew. Chem. internat. Edit. *4*, 787 (1965).

[51] *H. Schumann* and *P. Jutzi*, Chem. Ber. *101*, 24 (1968).

[52] *E. W. Abel* and *I. H. Sabherwal*, J. chem. Soc. (London) *(A) 1968*, 1105.

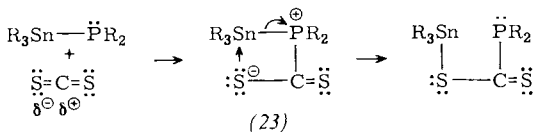
[53] *H. Breederveld*, Recueil. Trav. chim. Pays-Bas *79*, 1126 (1960); *81*, 276 (1962).

[54] *G. Oertel, H. Malz*, and *H. Holtschmidt*, Chem. Ber. *97*, 891 (1964).

[55] *W. Fink*, Chem. Ber. *97*, 1424, 1433 (1964).

[56] *W. W. Limburg* and *H. W. Post*, Recueil. Trav. chim. Pays-Bas *81*, 430 (1962).

[57] *T. A. George, K. Jones*, and *M. F. Lappert*, J. chem. Soc. (London) *1965*, 2157.

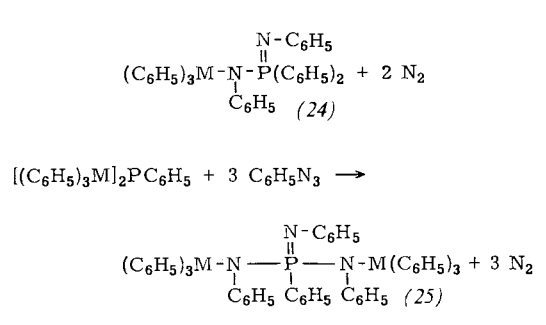


(23)

$Sn[P(C_6H_5)_2]_4$ also reacts, though very slowly, with CS_2 and phenyl isocyanate with cleavage of all four tin-phosphorus bonds; $[(C_6H_5)_3Sn]_3P$, on the other hand, does not undergo this cleavage. The difference in the behavior of these two stannyl phosphines again points to the participation of the lone pair of electrons on the phosphorus in the tin-phosphorus bond.

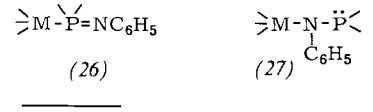
Whereas there are four lone pairs of electrons available on the phosphorus atoms of $Sn[P(C_6H_5)_2]_4$ to strengthen the bonds to a single tin atom, so that full use is not made of them, the lone pair of the single phosphorus atom in $[(C_6H_5)_3Sn]_3P$ is completely "exhausted" by participation in three tin-phosphorus bonds. Thus the electrophilic attack by 1,2-dipolar reagents is successful in the first case but not in the second.

This reaction principle does not extend to 1,3-dipolar reagents. Thus, whereas organostannyl phosphines are merely oxidized by nitrones and nitrile oxides [43] and do not react with nitrilimines and diazomethane, organic azides such as phenyl azide break the bonds between phosphorus and the group IVA elements mentioned to form novel iminophosphoranes such as *(24)* and *(25)* [17].



(24a), M = Sn, decomp. pt. 170 °C
(24b), M = Pb, m.p. 173–178 °C
(25a), M = Sn, m.p. 160 °C
(25b), M = Pb, decomp. pt. 40 °C

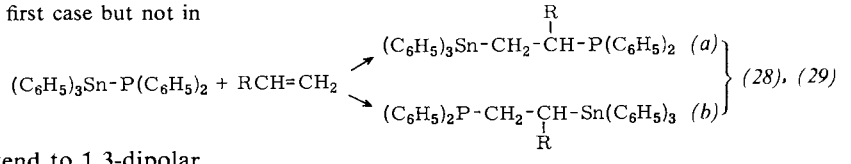
The reactions may be assumed to proceed by initial formation of an iminophosphorane of the type *(26)*, which is unstable (with *tert*-butyl residues on the phosphorus and a trimethylsilyl group on the nitrogen, *N,P*-organometal-substituted iminophosphoranes of this type have now been isolated [58]), and rearranges into an aminophosphine of the type *(27)* which takes up a further phenylimine residue to form the stable end product. The fact that reactions of this type proceed rapidly with mono-, slowly with bis-, and immeasurably slowly with tris-organometal-substituted phosphines again points to participation of the lone pair of P electrons in the M–P bond.



(26) *(27)*

2.3.4. Addition to Olefinic Double Bonds

Triphenylstannyldiphenylphosphine reacts with allyl chloride and with styrene to form chloromethyltriphenylstannylethyldiphenylphosphine *(28)* and phenyltriphenylstannylethyldiphenylphosphine *(29)* respectively [59]; the products in both cases are in two isomeric forms, which have not been separated.

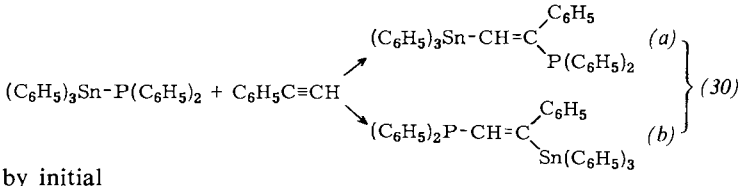


(28), *(29)*

(28a, b), R = $ClCH_2$, m.p. 39 °C
(29a, b), R = C_6H_5, m.p. 59 °C

The reaction with phenylacetylene stops at the stage of the phenyltriphenylstannylethylenediphenylphosphine *(30)* in the forms *(a)* and *(b)*, even when a large excess of triphenylstannyldiphenylphosphine is present [59].

By analogy with hydrostannation [60], this reaction may be assumed to proceed by a free-radical mechanism. This is supported both by the considerable increase in the yield on addition of catalytic amounts of azodiisobutyronitrile and by the simultaneous formation of different isomers. In the reaction of triethylgermyldiethylphosphine with phenylacetylene, two *cis* and two *trans* isomers could be detected by ^{1}H-NMR spectroscopy [31]. Acrylonitrile adds triethylgermyldiethylphosphine [31] and trimethylstannyldiphenylphosphine [61] exclusively to the olefinic double bond, while vinylogous carbonyl compounds such as mesityl oxide, acrolein, or cinnamaldehyde insert their carbonyl function between the tin and the phosphorus in a polar reaction with trimethylstannyldiphenylphosphine to give compounds of the type *(31)*, with no attack on the olefinic double bond [61].



(30)

(30a, b), m.p. 45 °C

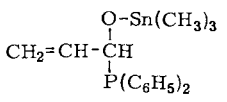
[58] *O. J. Scherer* and *G. Schieder*, Angew. Chem. *80*, 83 (1968); Angew. Chem. internat. Edit. *7*, 75 (1968).

[59] *H. Schumann*, *P. Jutzi*, and *M. Schmidt*, Angew. Chem. *77*, 912 (1965); Angew. Chem. internat. Edit. *4*, 869 (1965).

[60] *W. P. Neumann*, Liebigs Ann. Chem. *659*, 17 (1962).

[61] *H. Schumann* and *A. Yaghmai*, unpublished.

$(CH_3)_3Sn\text{-}P(C_6H_5)_2 + CH_2{=}CH\text{-}CHO \rightarrow$



(31a), m.p. 90–95° C

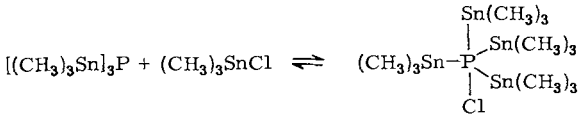
2.3.5. Phosphonium Salt Formation

Organogermyl, organostannyl, and organoplumbyl phosphines, unlike organosilyl phosphines [62], do not form stable phosphonium salts. Organogermyl phosphines [13,14], and organostannyl phosphines [12] react with Lewis acids only at very low temperatures to give addition products, which quantitatively decompose on warming, with cleavage of the Ge–P or Sn–P bond.

$$(CH_3)_3Sn\text{–}P(C_6H_5)_2 + 2\ CH_3I \rightarrow (CH_3)_3SnI + [(C_6H_5)_2\overset{\oplus}{P}(CH_3)_2]I^{\ominus}$$

Tris(trimethylstannyl)phosphine and trimethyltin chloride also fail to give stable tetrakis(trimethylstannyl)phosphonium chloride [63].

As has been shown by NMR spectroscopy, exchange merely occurs with the trimethylstannyl groups on the phosphorus atom. A 1 : 1 mixture of tris(trimethylstannyl)phosphine and trimethyltin chloride gives only one singlet signal for all the trimethylstannyl protons in the ^{1}H-NMR spectrum, even at −60 °C, whereas the original doublet signal of the stannyl phosphine is no longer found. Since cryoscopic molecular weight determinations and IR spectra clearly show that the two components are present together in such mixtures, the ^{1}H-NMR spectrum must be interpreted as resulting from a very rapid exchange of the $(CH_3)_3Sn$ groups *via* an extremely short-lived pentacoordinate state of the phosphorus.



Similar exchange reactions, though in some cases with formation of new end products, occur between tris(trimethylsilyl)-, tris(trimethylgermyl)-, tris(trimethylstannyl)-, or tris(trimethylplumbyl)phosphine and trimethylchlorosilane, trimethylgermanium chloride, trimethyltin chloride, trimethyllead chloride, trimethylstannyldimethylamine, and bis(trimethylstannyl) sulfide.

$$[(CH_3)_3M]_3P + 3\ (CH_3)_3M'Cl \rightleftarrows [(CH_3)_3M']_3P + 3\ (CH_3)_3MCl$$

M and M′ = Si, Ge, Sn, Pb.

With M = Si and M′ = Ge, Sn, or Pb because of the high tendency of $(CH_3)_3SiCl$ to be formed, and with M = Ge or Sn and M′ = Pb because of the fast thermal decomposition of the $[(CH_3)_3Pb]_3P$ present in equilibrium, this exchange proceeds quantitatively in the direction of the upper arrow; for M = Ge and M′ = Sn and for M = Sn and M′ = Ge, on the other hand, all four possible reaction products can be detected together.

2.3.6. Synthesis of Oligomeric Phenylphosphines

The reaction of organostannyl phosphines with phenylphosphorus or phenylarsenic chlorides leads to stable products containing two, three, or four directly linked phosphorus atoms and compounds in which a phosphorus atom is linked to one, two, or three arsenic atoms [64]. Thus the reaction of tris(trimethylstannyl) phosphine with diphenylphosphorus or diphenylarsenic chloride leads to elimination of trimethyltin chloride and formation of tris(diphenylphosphino)-phosphine or tris(diphenylarsino)phosphine:

$$[(CH_3)_3Sn]_3P + 3\ (C_6H_5)_2ElCl \rightarrow [(C_6H_5)_2El]_3P + 3\ (CH_3)_3SnCl$$

El = P, As

Similarly, diphenylphosphorus and diphenylarsenic chlorides react with bis(trimethylstannyl)phenylphosphine to give the compounds *(32a)* and *(32b)* respectively.

$$[(CH_3)_3Sn]_2PC_6H_5 + 2\ (C_6H_5)_2ElCl \rightarrow [(C_6H_5)_2El]_2PC_6H_5 + 2\ (CH_3)_3SnCl$$

(32a), El = P; *(32b)*, El = As

Compounds of this type, of which bis(diphenylphosphino)phenylphosphine [65] and tris(diphenylphosphino)arsine [66] have also been obtained by other routes, are colorless when pure, crystalline, and soluble in ether, cyclohexane, and aromatic hydrocarbons. Their structure has been verified by IR, Raman, and ^{31}P-NMR spectra (Table 6). Their sensitivity to oxygen

Table 6. Oligomeric phenylphosphines and phenylarsines.

Compound	M.p. (°C)	IR (cm^{-1})	Raman (cm^{-1})	δ (ppm)
$[(C_6H_5)_2P]_3P$	118–120	$\nu_{as}PP_3$ 486, ν_sPP_3 427	$\nu_{as}PP_3$ 481, ν_sPP_3 426	+16.9; +27.0
$[(C_6H_5)_2P]_3As$	120–123	$\nu_{as}AsP_3$ 357, ν_sAsP_3 280		+15.2
$[(C_6H_5)_2As]_3P$	169–172	$\nu_{as}PAs_3$ 311, ν_sPAs_3 274	ν_sPAs_3 294	+59.1
$[(C_6H_5)_2As]_3As$	143–147	$\nu_{as}AsAs_3$ 285, ν_sAsAs_3 262		
$[(C_6H_5)_2P]_2PC_6H_5$	70 (decomp.)			
$[(C_6H_5)_2P]_2AsC_6H_5$	125–129	$\nu_{as}AsP_2$ 311, ν_sAsP_2 293	ν_sAsP_2 297	+15.3
$[(C_6H_5)_2As]_2PC_6H_5$	155–158	$\nu_{as}PAs_2$ 354, ν_sPAs_2 282	$\nu_{as}PAs_2$ 320, ν_sPAs_2 275	−36.1
$[(C_6H_5)_2As]_2AsC_6H_5$	185–190	$\nu_{as}AsAs_2$ 293, ν_sAsAs_2 262		
$(C_6H_5)_2PAs(C_6H_5)_2$	115–117	νPAs 353	νPAs 375	

[62] *G. Fritz*, Angew. Chem. *78*, 80 (1966); Angew. Chem. internat. Edit. *5*, 53 (1966).

[63] *H. Schumann* and *O. Stelzer*, unpublished.

[64] *H. Schumann*, *A. Roth*, and *O. Stelzer*, Angew. Chem. *80*, 240 (1968); Angew. Chem. internat. Edit. *7*, 218 (1968).

[65] *E. Wiberg*, *M. van Ghemen*, and *G. Müller-Schiedmayer*, Angew. Chem. *75*, 814 (1963); Angew. Chem. internat. Edit. *2*, 646 (1963).

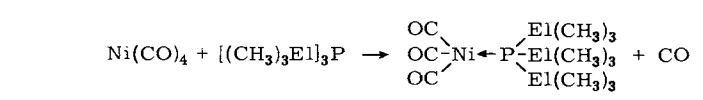
[66] *T. A. George* and *M. F. Lappert*, Chem. Commun. *1966*, 463.

decreases as the number of phenyl groups bound to the central P atom increases. $[(C_6H_5)_2P]_3P$ decomposes very rapidly into triphenylphosphine, tetraphenyldiphosphane, and $(C_6H_5P)_n$.

2.3.7. Transition Metal Complexes

It can be concluded from the chemical and physical properties already mentioned that the lone pair of electrons on the phosphorus in organometal-substituted phosphines makes a certain contribution to the phosphorus-metal bond in the sense of a $(p\rightarrow d)_\pi$ interaction. The phosphines discussed should therefore exhibit little or no tendency to occur in transition metal complexes as σ donors.

By reaction of tetracarbonylnickel with tris(trimethylsilyl)-, tris(trimethylgermyl)-, tris(trimethylstannyl)-, and tris(trimethylplumbyl)phosphines and with tris(*tert*-butyl)phosphine in tetrahydrofuran at room temperature, however, it is possible to synthesize nickel(0) complexes such as *(33)*, in which tertiary organometal-substituted phosphines with tetracoordinate phosphorus are present for the first time as ligands together with carbon monoxide [67,67a].



El = C, Si, Ge, Sn, Pb *(33)*

The complexes are formed quantitatively as colorless crystals, which unlike the starting phosphines, are surprisingly stable to atmospheric oxygen but are often thermally very unstable.

The considerable increase in the coupling constant $J_{^1H-C-El-^{31}P}$ that is always found on transition from the free phosphines (C = 9.80 Hz, Si = 4.62 Hz, Ge = 4.00 Hz, Sn = 1.95 Hz, Pb = 0 Hz) to the complexes (Table 7) confirms the increase in the s character of P–El bonds on transition from the substantially p^3-hybridized P atom in the free phosphines to the sp^3 state in the complexes. The slight shift of the ν_{as} PEl_3 band observed on comparison of the IR spectra of the free phosphines and of the complexes show that the element-phosphorus bonds are only slightly weakened by the complex formation. The stability of the complexes to oxygen supports the hypotheses that on oxidation of organometal-substituted phosphines, the attack of the oxygen takes place on the "lone" pair of electrons on the phosphorus, which is blocked in the complexes by coordination with nickel and is thus no longer available for electrophilic attack.

These phosphines containing tris(trimethylelement) groups also react with hexacarbonylchromium [67a,68],

Table 7. Transition metal complexes with organometal-substituted phosphine ligands.

Compound	$J_{^1HCM^{31}P}$ (Hz)	νCO (cm^{-1})	νPM_3 (cm^{-1})	Decomp. pt. (°C)	Ref.
$[(CH_3)_3Si]_3PNi(CO)_3$	5.2	2074, 1995	363	30	[67]
$[(CH_3)_3Ge]_3PNi(CO)_3$	4.65	2070, 1996	362	100	[67]
$[(CH_3)_3Sn]_3PNi(CO)_3$	3.35	2057, 1968	345	90	[67]
$[(CH_3)_3Pb]_3PNi(CO)_3$	2.9	2049, 1960	321	85	[67]
$[(CH_3)_3Sn]_2PC_6H_5Ni(CO)_3$	3.4	2037, 1965		50	[103]
$(CH_3)_3SnP(C_6H_5)_2Ni(CO)_3$	3.5	2049, 1976		60	[103]
$Sn[P(C_6H_5)_2]_4[Ni(CO)_2]_2$		2062, 2000		160	[70]
$[(CH_3)_3SnP(C_6H_5)_2]_2Ni(CO)_2$		1993, 1927			[71]
$(CH_3)_2Sn[P(C_6H_5)_2]_2Ni(CO)_2$		2001, 1947			[71]
$[(CH_3)_3Si]_3PCo(CO)_2NO$ *(35a)*	5.5	2024, 1965, 1742 (νNO)	413, 389	100	[68]
$[(CH_3)_3Ge]_3PCo(CO)_2NO$ *(35b)*	5.3	2016, 1960, 1739 (νNO)	392, 376	132	[68]
$[(CH_3)_3Sn]_3PCo(CO)_2NO$ *(35c)*	3.6	2008, 1938, 1718 (νNO)	352, 345	190	[68]
$Sn[P(C_6H_5)_2]_4[Co(CO)_2NO]_4$		2020, 1960, 1740 (νNO)			[70]
$Sn[P(C_6H_5)_2]_4[Co(CO)(NO)]_2$		1964, 1948, 1732, (νNO) 1717 (νNO)		305	[70]
$[(CH_3)_3Si]_3PFe(CO)_4$ *(36a)*	5.25	2020, 1946, 1908, 1873	447	110	[69]
$[(CH_3)_3Ge]_3PFe(CO)_4$ *(36b)*	5.45	2024, 1946, 1908, 1880	434	120	[69]
$[(CH_3)_3Sn]_3PFe(CO)_4$ *(36c)*	3.6	2032, 1957, 1923, 1887	425	142	[69]
$Sn[P(C_6H_5)_2]_4[Fe(CO)(NO)_2]_4$		1990, 1710 (νNO) 1760 (νNO)			[70]
$Sn[P(C_6H_5)_2]_4[Fe(NO)_2]_2$		1763 (νNO) 1740 (νNO)		312	[70]
$[(CH_3)_3Si]_3PCr(CO)_5$ *(34a)*	4.85	2058, 1934, 1901	424	100	[68]
$[(CH_3)_3Ge]_3PCr(CO)_5$ *(34b)*	4.7	2057, 1934, 1904	389	150	[68]
$[(CH_3)_3Sn]_3PCr(CO)_5$ *(34c)*	3.3	2053, 1927, 1898	347	190	[68]
$(CH_3)_3SiP(C_6H_5)_2Cr(CO)_5$		2049, 2004, 1972, 1942, 1919, 1890		80	[103]
$[(CH_3)_3Si]_2PC_6H_5Cr(CO)_5$	4.5	2049, 1996, 1972, 1965, 1927, 1887		70	[103]
$[(CH_3)_3Sn]_2PC_6H_5Cr(CO)_5$	3.3	2050, 1991, 1982, 1930, 1923, 1900		120	[103]
$Sn[P(C_6H_5)_2]_4[Cr(CO)_4]_2$		2017, 1936, 1913, 1905		170	[70]
$[(CH_3)_3Sn]_3PMo(CO)_5$ *(34d)*	3.2	2045, 1953, 1916, 1890	347	180	[103]
$(CH_3)_3SnP(t\text{-}C_4H_9)_2Mo(CO)_5$	13.8 [a], 2.0 [b]	2058, 2008, 1965, 1910, 1890		98	[103]
$Sn[P(C_6H_5)_2]_4[Mo(CO)_4]_2$		2033, 1968, 1968, 1925		160	[70]
$[(CH_3)_3Sn]_3PW(CO)_5$ *(34e)*	3.3	2045, 1905, 1880	350	180	[103]
$Sn[P(C_6H_5)_2]_4[W(CO)_4]_2$		2032, 2001, 1954, 1890		220	[70]
$[(CH_3)_3Si]_3PMn(CO)_2(C_5H_5)$ *(37a)*	4.6	1923, 1848	444	120	[103]
$[(CH_3)_3Ge]_3PMn(CO)_2(C_5H_5)$ *(37b)*	4.2	1923, 1852	401	100	[103]
$[(CH_3)_3Sn]_3PMn(CO)_2(C_5H_5)$ *(37c)*	2.8	1919, 1852	355	140	[103]

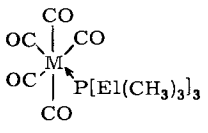
[a] $J_{^1HCC^{31}P}$; [b] $J_{^1HCSn^{31}P}$.

[67] *H. Schumann* and *O. Stelzer*, Angew. Chem. *79*, 692 (1967); Angew. Chem. internat. Edit. *6*, 701 (1967).

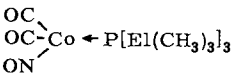
[67a] *H. Schumann*, *O. Stelzer*, and *U. Niederreuther*, J. organometallic Chem. *16*, P 64 (1969).

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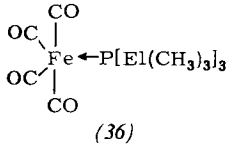
hexacarbonylmolybdenum, and hexacarbonyltungsten [67a, 103], tricarbonylnitrosylcobalt [67a, 68], pentacarbonyliron or enneacarbonyldiiron [67a, 69], and tricarbonylcyclopentadienylmanganese [67a, 103] on UV irradiation, with displacement of carbon monoxide to give transition metal complexes of the types *(34)* to *(37)*.



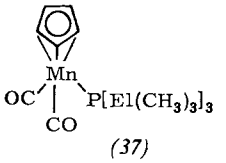
(34)



(35)



(36)



(37)

M = Cr, Mo, W; El = C, Si, Ge, Sn, Pb

Complexes in which phosphines with organometal groups are present as polydent ligands have also been reported [70, 71].

3. Organogermyl-, Organostannyl-, and Organoplumbylarsines

3.1. Synthesis

The first organometallic compounds containing covalent bonds between arsenic and an element of group IVB, apart from a mention in a patent [72], were obtained in 1964 by *Jones* and *Lappert* [32, 33] and by *Schumann* and *Schmidt* [73].

$$(CH_3)_3Sn{-}N(CH_3)_2 + (C_6H_5)_2AsH \rightarrow (CH_3)_3Sn{-}As(C_6H_5)_2 + (CH_3)_2NH$$

$$3\,(C_6H_5)_3SnLi + AsCl_3 \rightarrow [(C_6H_5)_3Sn]_3As + 3\,LiCl$$

A large number of organostannyl arsines and some organogermyl and organoplumbyl arsines were prepared slightly later by *Campell, Fowles*, and *Nixon* [74] and by *Schumann et al.* [75–77]. Organogermanium, organotin, and organolead halides, as well as tin tetrachloride, react with sodium diphenylarsenide in liquid ammonia to form organometal-substituted diphenylarsines in which one to four diphenylarsine residues are bonded to the element in question.

$$R_{4-n}SnCl_n + n\,NaAs(C_6H_5)_2 \rightarrow R_{4-n}Sn[As(C_6H_5)_2]_n + n\,NaCl$$

R = C_2H_5, C_3H_7, C_4H_9, C_6H_5; n = 1, 2, 3, 4

$$(C_6H_5)_3MCl + NaAs(C_6H_5)_2 \rightarrow (C_6H_5)_3MAs(C_6H_5)_2 + NaCl$$

M = Ge, Pb)

Another series of compounds, in which one to three triphenylstannyl residues are bonded to arsenic, can be prepared by the reaction of triphenylstannyllithium with phenylarsenic chlorides or arsenic trichloride in tetrahydrofuran [75].

$$n\,(C_6H_5)_3SnLi + Cl_nAs(C_6H_5)_{3-n} \rightarrow n\,LiCl + [(C_6H_5)_3Sn]_nAs(C_6H_5)_{3-n}$$

n = 1, 2, 3

The yields of organostannyl arsine are generally low, since side reactions such as condensation and transmetalation cannot be eliminated despite adherence to special experimental conditions. Organostannyl arsines can on the other hand be obtained without by-products by reaction of organotin halides with organoarsines or AsH_3 in benzene in the presence of triethylamine as a hydrogen chloride acceptor [76].

$$n\,R_3SnCl + R'_{3-n}AsH_n \xrightarrow[-n[(C_2H_5)_3NH]Cl]{+n(C_2H_5)_3N} (R_3Sn)_nAsR'_{3-n}$$

R, R' = CH_3, C_6H_5; n = 1, 2, 3

The analogous tris(triorganogermyl)- and tris(triorganoplumbyl)-arsines can be synthesized in the same way [18] or by reaction of trimethylgermyldimethylamine with AsH_3 [19].

$(C_6H_5)_2Sn[As(C_6H_5)_2]_2$, $C_6H_5Sn[As(C_6H_5)_2]_3$, and $Sn[As(C_6H_5)_2]_4$ can also be prepared by reaction of the corresponding tin halides with $KAs(C_6H_5)_2$ in

Table 8. Organogermyl-, organostannyl-, and organoplumbylarsines.

Compound	M.p. (°C)	B.p. (°C/torr)	Ref.
$(CH_3)_3GeAs(CH_3)_2$		85–87/99–101	[104]
$(C_6H_5)_3GeAs(C_6H_5)_2$	114		[77]
$[(CH_3)_3Ge]_3As$		67–68/0.1	[19]
$(CH_3)_3SnAs(CH_3)_2$		170–172/760	[76, 78, 104]
$(CH_3)_3SnAs(C_6H_5)_2$		150–152/1	[32, 33, 76]
$(C_2H_5)_3SnAs(C_6H_5)_2$		140–143/0.15	[74]
$(C_3H_7)_3SnAs(C_6H_5)_2$		159–161/0.2	[74]
$(C_4H_9)_3SnAs(C_6H_5)_2$		163–164/0.09	[74]
$(C_6H_5)_3SnAs(CH_3)_2$	90 (decomp.)		[76]
$(C_6H_5)_3SnAs(C_6H_5)_2$	132–135		[75, 76]
$[(CH_3)_3Sn]_2AsCH_3$		105–108/1	[76]
$[(CH_3)_3Sn]_2AsC_6H_5$		145–148/10^{-3}	[76]
$[(C_6H_5)_3Sn]_2AsC_6H_5$	133–135		[75, 76]
$[(CH_3)_3Sn]_3As$		99–100/1	[76]
$[(C_6H_5)_3Sn]_3As$	205–208		[73, 75, 76]
$(C_6H_5)_2Sn[As(C_6H_5)_2]_2$	130–133 (decomp.)		[75, 76]
$C_6H_5Sn[As(C_6H_5)_2]_3$	84–86		[75, 76]
$Sn[As(C_6H_5)_2]_4$	130–133		[75, 76]
$(C_6H_5)_3PbAs(C_6H_5)_2$	115 (decomp.)		[77]
$[(CH_3)_3Pb]_3As$	43–45		[18]
$[(C_6H_5)_3Pb]_3As$	158		[18]

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liquid ammonia [76]. Methylstannyl and methylarsine derivatives of this type cannot be synthesized by this method; they undergo dismutation with methyl shift to give $Sn[As(C_6H_5)_2]_4$ and $(CH_3)_3Sn-As(C_6H_5)_2$ or $Sn(CH_3)_4$ and $(CH_3)_2As-As(CH_3)_2$. The organogermyl-, organostannyl-, and organoplumbylarsines known at present are listed in Table 8.

3.2. Physical Properties

The organogermyl-, organostannyl-, and organoplumbylarsines largely correspond to the homologous phosphorus compounds in their physical properties. Thus alkylgermyl- and alkylstannylarsines are colorless liquids that can be distilled without decomposing under reduced pressure, while the corresponding phenyl compounds and the organoplumbylarsines are colorless to light yellow solids. They dissolve readily and without decomposition in organic solvents such as tetrahydrofuran, diethyl ether, or aromatic hydrocarbons. Their thermal stability is generally higher than that of their phosphorus analogs. The IR (Table 9) and the (so far only incompletely measured) Raman spectra again indicate the pyramidal structure of the compounds. Some of the ^{1}H-NMR spectra of some organometal-substituted arsines have been recorded [19, 76, 78, 104], but no theoretical information has been deduced from the results.

Table 9. IR and Raman frequencies of organometal arsines.

Compound		IR (cm^{-1})	Ref.
$(CH_3)_3GeAs(CH_3)_2$	C_s	νGeAs 267	[104]
$[(CH_3)_3Ge]_3As$	C_{3v}	$\nu_{as}AsGe_3$ 275, ν_sAsGe_3 256	[19]
$[(CH_3)_3Sn]_3As$	C_{3v}	$\nu_{as}AsSn_3$ 233, ν_sAsSn_3 211 [a]	[76]
$[(C_6H_5)_3Sn]_3As$	C_{3v}	$\nu_{as}AsSn_3$ 244, ν_sAsSn_3 211	[76]
$[(CH_3)_3Sn]_2AsCH_3$	C_{2v}	$\nu_{as}AsSn_2$ 234, ν_sAsSn_2 217	[76]
$[(CH_3)_3Sn]_2AsC_6H_5$	C_{2v}	$\nu_{as}AsSn_2$ 237, ν_sAsSn_2 190	[76]
$[(C_6H_5)_3Sn]_2AsC_6H_5$	C_{2v}	$\nu_{as}AsSn_2$ 236, ν_sAsSn_2 213	[76]
$(CH_3)_3SnAs(CH_3)_2$	C_s	νAsSn 203 [76], 226 [104]	[76, 104]
$(CH_3)_3SnAs(C_6H_5)_2$	C_s	νAsSn 188	[76]
$(C_6H_5)_3SnAs(CH_3)_2$	C_s	νAsSn 180	[76]
$(C_6H_5)_3SnAs(C_6H_5)_2$	C_s	νAsSn 199	[76]
$(C_6H_5)_2Sn[As(C_6H_5)_2]_2$	C_{2v}	$\nu_{as}SnAs_2$ 261, ν_sSnAs_2 228	[76]
$C_6H_5Sn[As(C_6H_5)_2]_3$	C_{3v}	$\nu_{as}SnAs_3$ 262, ν_sSnAs_3 228	[76]
$Sn[As(C_6H_5)_2]_4$	T_d	ν_dSnAs_4 260, 228	[76]
$[(CH_3)_3Pb]_3As$	C_{3v}	$\nu_{as}AsPb_3$ 208, ν_sAsPb_3 182	[18]
$[(C_6H_5)_3Pb]_3As$	C_{3v}	$\nu_{as}AsPb_3$ 207, ν_sAsPb_3 175	[18]

[a] Raman frequencies: $\nu_{as}AsSn_3$ 223, ν_sAsSn_3 209 cm^{-1} [39].

3.3. Chemical Properties and Reactions

Arsines containing organometal groups are sensitive to oxygen. They are oxidized in air at various rates to give isolable metal arsinates of the type *(38)* [78a] (Table 10).

$$\gtrless M-\ddot{A}s\lessgtr + O_2 \longrightarrow \gtrless M-O-\overset{O}{\overset{\|}{A}}s\lessgtr \qquad M = Ge, Sn, Pb$$

(38)

Table 10. Organometal arsinates.

Compound	M.p. (°C)	Ref.
$(C_6H_5)_3Ge-O-As(O)(C_6H_5)_2$	178	[77]
$(CH_3)_3Sn-O-As(O)(CH_3)_2$	157–158 (decomp.)	[78a]
$(CH_3)_3Sn-O-As(O)(C_6H_5)_2$	192–195	[78a]
$(C_2H_5)_3Sn-O-As(O)(C_6H_5)_2$	166–167	[74]
$(C_3H_7)_3Sn-O-As(O)(C_6H_5)_2$	204–205	[74]
$(C_4H_9)_3Sn-O-As(O)(C_6H_5)_2$	196–198	[74]
$(C_6H_5)_3Sn-O-As(O)(CH_3)_2$	181–183 (decomp.)	[78a]
$(C_6H_5)_3Sn-O-As(O)(C_6H_5)_2$ *(38a)*	323–324	[74, 75, 78a]
$(C_6H_5)_2Sn[OAs(O)(C_6H_5)_2]_2$ *(38b)*	330	[75]
$C_6H_5Sn[OAs(O)(C_6H_5)_2]_3$ *(38c)*	180 (decomp.)	[75]
$(C_6H_5)_3Pb-O-As(O)(C_6H_5)_2$	280 (decomp.)	[77]

Compounds of this type have been prepared independently from organotin halides and diphenylarsinic acid in the presence of triethylamine as a proof of their structure [74, 75].

$$(C_6H_5)_{4-n}SnCl_n + n\ HO-As(O)(C_6H_5)_2 \xrightarrow[-n[(C_2H_5)_3NH]Cl]{+n(C_2H_5)_3N} (C_6H_5)_{4-n}Sn[O-As(O)(C_6H_5)_2]_n \quad (38)$$

$n = 1, 2, 3$

The products of the type *(38)*, which are found to be identical, are colorless crystals of which only the dimeric [74] alkylstannyl derivatives dissolve in organic solvents. Oxygen-free water does not attack organostannylarsines, as is shown by the synthesis of a compound of this type in water [104]. Hydrogen peroxide breaks the Sn–As bond of methylstannylarsine derivatives [78a], the nature of the cleavage product providing evidence of the constitution of the starting arsine. Polar reagents such as methyl iodide split the Sn–As bond more slowly than the Sn–P bond to form organotin iodides and tetraorganoarsonium iodides [74, 78a].

Triphenylstannyldiphenylarsine and bis(triphenylstannyl)phenylarsine react with phenyl azide to form the new organotin-substituted aminoiminoarsines *(39)* and *(40)* respectively [78b].

Tris(triphenylstannyl)arsine, on the other hand, is not attacked by phenyl azide even in boiling benzene.

$$(C_6H_5)_3SnAs(C_6H_5)_2 + 2\ C_6H_5N_3 \longrightarrow (C_6H_5)_3Sn-\overset{\overset{NC_6H_5}{\|}}{N}-As(C_6H_5)_2 + 2\ N_2$$

$$\quad\quad\quad

The high formation tendency of trimethyltin chloride allows the use of organostannylarsines for the synthesis of interesting oligomeric phenylarsines, in which up to four arsenic atoms are linked to one another [64] (Table 6). Thus tris(trimethylstannyl)arsine reacts with diphenylphosphorus or diphenylarsenic chloride to form tris(diphenylphosphino)arsine or tris(diphenylarsino)arsine. Bis(diphenylphosphino)phenylarsine and bis(diphenylarsino)phenylarsine can be prepared similarly from diphenylphosphorus or diphenylarsenic chloride and bis(trimethylstannyl)phenylarsine. Diphenylphosphinodiphenylarsine *(41)* can be synthesized from trimethylstannyldiphenylarsine and diphenylphosphorus chloride.

$$[(CH_3)_3Sn]_nAs(C_6H_5)_{3-n} + n\,(C_6H_5)_2ElCl \rightarrow [(C_6H_5)_2El]_nAs(C_6H_5)_{3-n} + n\,(CH_3)_3SnCl$$

El = P, As; n = 3, 2

$$(CH_3)_3SnAs(C_6H_5)_2 + (C_6H_5)_2PCl \rightarrow (C_6H_5)_2PAs(C_6H_5)_2 + (CH_3)_3SnCl \quad (41)$$

With diphenylantimony or diphenylbismuth chlorides and with methylphosphorus or methylarsenic chloride the separation of trimethyltin chloride has also been observed, but the oligomeric phenylarsinostibines or phenylarsionobismuthines and oligomeric methylphosphinoarsines or methylarsinoarsines could not be isolated, presumably because of their low stability.

A number of recent investigations [71,79] show that organometal-substituted arsines can be bonded to transition metals as complex ligands.

4. Organogermyl-, Organostannyl-, and Organoplumbylstibines

4.1. Synthesis

Organogermyl-, organostannyl-, and organoplumbylstibines, as expected, are very similar to the analogous arsenic compounds. Useful synthetic routes were again offered by the reactions of organometal halides with $NaSb(C_6H_5)_2$ [74,77,80], Li_3Sb [81,82], or SbH_3 [18] in liquid ammonia or benzene, or the reaction of triphenylstannyllithium with $(C_6H_5)_2SbCl$, $C_6H_5SbCl_2$, or $SbCl_3$ in tetrahydrofuran [73,80].

The last of these reactions gives the desired compounds only in unsatisfactory yields, since transmetalation and condensation occur at the same time.

Stibines of the type $(R_3M)_3Sb$ (M = Si, Ge, Sn) are obtained in a very elegant manner from triethylstibine and triethyl- or triphenylsilane, -germane, or -stannane with elimination of ethane. Stibines of the type *(42)* can also be obtained by displacement reactions [83–85].

$$3\,R_3MH + (C_2H_5)_3Sb \rightarrow (R_3M)_3Sb + 3\,C_2H_6$$

M = Si, Ge, Sn; R = C_2H_5, C_6H_5

$$[(C_2H_5)_3M]_3Sb + 3\,(C_2H_5)_3M'H \rightarrow [(C_2H_5)_3M']_3Sb + 3\,(C_2H_5)_3MH \quad (42)$$

M = Si, M′ = Ge, Sn; M = Ge, M′ = Sn

Finally, trimethylstannyldibutylstibine is formed as a by-product in the presumably free-radial hydrostannation of ethynyldibutylstibine with trimethylstannane [86].

$$(C_4H_9)_2Sb{-}C{\equiv}CH + (CH_3)_3SnH \rightarrow (C_4H_9)_2Sb{-}Sn(CH_3)_3 + C_2H_2$$

4.2. Physical and Chemical Properties

Organometal-substituted stibines (Table 11) are colorless liquids or crystalline solids that dissolve readily and in the monomeric state in aromatic hydrocarbons or tetrahydrofuran. They can be recrystallized from aliphatic hydrocarbons in the absence of oxygen. Oxygen-free water does not attack phenylstannylstibines, presumably because of their non-wettability. On the other hand all these compounds are sensitive to oxygen. As in the oxidation of the analogous phosphorus and arsenic compounds, two oxygen atoms are initially taken up per metal-antimony bond, but in this case the oxidation does not lead to definite products [74,80], since antimony-carbon bonds are evidently also oxidatively broken in this case. Small quantities of $AlBr_3$ catalyze the thermal decomposition

$$R_3MCl + NaSb(C_6H_5)_2 \rightarrow R_3MSb(C_6H_5)_2 + NaCl$$

M = Sn; R = C_2H_5, C_3H_7, C_4H_9, C_6H_5
M = Ge or Pb; R = C_6H_5

$$(C_6H_5)_{4-n}SnCl_n + n\,NaSb(C_6H_5)_2 \rightarrow (C_6H_5)_{4-n}Sn[Sb(C_6H_5)_2]_n + n\,NaCl$$

n = 1, 2, 3

$$3\,(CH_3)_3MCl + Li_3Sb \rightarrow [(CH_3)_3M]_3Sb + 3\,LiCl$$

M = Ge, Sn

$$3\,R_3MCl + SbH_3 \xrightarrow[-3[(C_2H_5)_3NH]Cl]{+3(C_2H_5)_3N} (R_3M)_3Sb$$

M = Ge, Pb; R = CH_3, C_6H_5

$$n\,(C_6H_5)_3SnLi + (C_6H_5)_{3-n}SbCl_n \rightarrow [(C_6H_5)_3Sn]_nSb(C_6H_5)_{3-n} + n\,LiCl$$

n = 1, 2, 3

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Table 11. Organogermyl-, organostannyl-, and organoplumbylstibines.

Compound	M.p. (°C)	B.p. (°C/torr)	Ref.
$(C_6H_5)_3GeSb(C_6H_5)_2$	120		[77]
$[(CH_3)_3Ge]_3Sb$	11–13		[19, 81, 82]
$[(C_2H_5)_3Ge]_3Sb$		157–161/1	[84, 85]
$(CH_3)_3SnSb(C_4H_9)_2$		126/0.5	[86]
$(C_2H_5)_3SnSb(C_6H_5)_2$		144–146/0.18	[74]
$(C_3H_7)_3SnSb(C_6H_5)_2$		168–170/0.13	[74]
$(C_4H_9)_3SnSb(C_6H_5)_2$		179–180/0.15	[74]
$(C_6H_5)_3SnSb(C_6H_5)_2$	116		[80]
$[(C_6H_5)_3Sn]_2SbC_6H_5$	120 (decomp.)		[80]
$[(CH_3)_3Sn]_3Sb$	39		[81, 82]
$[(C_2H_5)_3Sn]_3Sb$		174–177/1.5	[84, 85]
$[(C_6H_5)_3Sn]_3Sb$	214–215		[73, 80]
$(C_6H_5)_2Sn[Sb(C_6H_5)_2]_2$	150		[80]
$C_6H_5Sn[Sb(C_6H_5)_2]_3$	90		[80]
$Sn[Sb(C_6H_5)_2]_4$	75		[80]
$(C_6H_5)_3PbSb(C_6H_5)_2$	115 (decomp.)		[77]
$[(C_6H_5)_3Pb]_3Sb$	150 (decomp.)		[18]

of $[(C_2H_5)_3Sn]_3Sb$ to form $Sn(C_2H_5)_4$, Sn, and Sb. The cleavage of organostannylstibines with methyl iodide [74], benzoyl peroxide [84], and organohalides [84] has also been investigated.

5. Organogermyl-, Organostannyl-, and Organoplumbylbismuthines

In contrast with the organometal compounds of phosphorus, arsenic, and antimony, which have now grown considerably in number, the number of organogermanium-bismuth and organotin-bismuth compounds (Table 12) is very small. No compounds containing covalent lead-bismuth bonds are known as yet. Apart

Table 12. Organogermyl- and organostannylbismuthines.

Compound	M.p. (°C)	B.p. (°C/torr)	Ref.
$[(CH_3)_3Ge]_3Bi$		114–116/0.1	[88]
$[(C_2H_5)_3Ge]_3Bi$		167–168/2.5	[84, 85, 87]
$[(C_2H_5)_3Sn]_3Bi$	160–170 (decomp.)		[84, 85, 87]
$[(C_6H_5)_3Sn]_3Bi$	138–142 (decomp.)		[73, 83]

from a passing reference to the use of triethylstannyldiphenylbismuthine as an antioxidant in lubricants [72], *Schumann* and *Schmidt* [73] were the first to report the successful synthesis of small quantities of tris(triphenylstannyl)bismuthine from triphenylstannyllithium and bismuth chloride in tetrahydrofuran. *Creemers* [83] increased the yield to more than 75% by reaction of triethylbismuthine with triphenylstannane.

$$3\,(C_6H_5)_3SnLi + BiCl_3 \rightarrow [(C_6H_5)_3Sn]_3Bi + 3\,LiCl$$

$$3\,(C_6H_5)_3SnH + Bi(C_2H_5)_3 \rightarrow [(C_6H_5)_3Sn]_3Bi + 3\,C_2H_6$$

Tris(triethylgermyl)bismuthine and tris(triethylstannyl)bismuthine [84,85,87], as well as the extremely sensitive tris(trimethylgermyl)bismuthine [88], have also been synthesized.

$$3\,(C_2H_5)_3MH + Bi(C_2H_5)_3 \rightarrow [(C_2H_5)_3M]_3Bi + 3\,C_2H_6$$

M = Si, Ge, Sn

$$3\,(C_2H_5)_3SnH + [(C_2H_5)_3Ge]_3Bi \rightarrow [(C_2H_5)_3Sn]_3Bi + 3\,(C_2H_5)_3GeH$$

$$3\,(CH_3)_3GeCl + Na_3Bi \xrightarrow[\text{in } NH_3]{} [(CH_3)_3Ge]_3Bi + 3\,NaCl$$

The compounds with M = Ge or Sn, whose chemical properties have not yet been extensively studied, decompose at about 100 °C into hexaorganodigermanes or hexaorganodistannanes and bismuth. In the presence of catalytic amounts of $AlCl_3$, they decompose at even lower temperatures into tetraethylgermane or tetraethylstannane, germanium or tin, and bismuth. All the substances are sensitive to oxygen.

6. Comparisons

The starting point for the consideration of bonding in covalent compounds between elements of groups IVB and VB was the comparison of silicon-nitrogen compounds [89] with analogous silicon-oxygen compounds. In investigations of this nature, strong $(p\rightarrow d)_\pi$ double-bond components were discussed for both the Si–O and the Si–N bonds. The evidence presented to support the hypothesis of such strengthening of the Si–N bond was above all the planar structure of the trisilylamine [90], on which strong doubt has now been cast [91].

The possibility of $(p\rightarrow d)_\pi$ bond strengthening has also been investigated for the homologs of the silicon-nitrogen compounds. Thus $(p\rightarrow d)_\pi$ double-bond components were postulated not only for organostannylamines [92–94] but also for trisilylphosphine, for which a planar structure was thought to have been found [95]. Views on this point have also been reversed since then [96]. Other investigations [42,62] refute such a hypothesis. Thus trimethylsilyldiethylphosphine reacts with ethyl iodide to give a stable phosphonium salt, which melts without decomposition at 122 °C [97]. HI [97], $(BH_3)_2$, BF_3, BCl_3, and BBr_3 [98] also add as Lewis acids to the lone pair of electrons on the

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phosphorus in silylphosphines or monogermylphosphines [105].

Similar contradictions can be found for organogermyl-, organostannyl-, and organoplumbylphosphines. The course of the oxidation and the unsuccessful attempts at specific syntheses of organostannylphosphine oxides or organostannylphosphonium salts lead one to attribute the stability of the tin-phosphorus bond to a necessary $(p\rightarrow d)_\pi$ contribution, since the Sn–P bond is broken as soon as the lone pair of electrons on the phosphorus is engaged. The 1,2-dipolar additions of carbon disulfide and phenyl isocyanate also support this hypothesis, since $Sn[P(C_6H_5)_2]_4$ is accessible to these reactions, whereas no electrophilic attack of these 1,2-dipoles on $[(C_6H_5)_3Sn]_3P$ is observed.

This interpretation of the covalent bond appears to be opposed by the vibration spectra, which can be interpreted only in terms of a pyramidal structure of the compounds, though it should be pointed out that it is by no means certain that $(p\rightarrow d)_\pi$ double-bond components must be associated with a planar structure of the molecule [99,100]. The reactions of the tris(trimethylmetal)-substituted phosphines with carbonyl compounds of the transition metals also show very clearly that it is possible to use the lone pair of electrons on the phosphorus for coordinate bonding without breaking the original $P-M^{IV}$ bonds.

As regards the stability of compounds of elements of groups IVB and VB, the investigations carried out so far show clearly that the most stable molecules are obtained with approximately equal covalent radii of the bonding partners [84,85,87,101].

In the light of our present knowledge, the hypothesis of the participation of the lone pair of electrons of phosphorus, arsenic, antimony, and bismuth in the bond with silicon, germanium, tin, or lead seems quite feasible. The final decision should be left to detailed physicochemical studies and structure analyses.

The author is grateful to Dipl.-Chem. Ulrike Arbenz, Dr. H. Benda, Dr. P. Jutzi, Dr. H. Köpf, U. Niederreuther, Fräulein Thea Östermann, Dr. A. Roth, L. Rösch, Fräulein Elke Schauer, Dr. P. Schwabe, Dr. O. Stelzer, and Dipl.-Chem. A. Yaghmai for their assistance in his own work in this field. Thanks are also due to Prof. Dr. M. Schmidt for valuable discussions, to Badische Anilin- und Soda-Fabrik, Farbenfabriken Bayer, Farbwerke Hoechst, Werk Gendorf, and the Union Minière du Haut Katanga for the free supply of valuable starting materials, and to the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft for financial support.

Received: December 18, 1968 [A 732 IE]
German version: Angew. Chem. *81*, 970 (1969)
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Crystal Structure Analysis by Neutron Diffraction II[**]

By G. Will[*]

This second part of the article "Crystal Structure Analysis by Neutron Diffraction" deals with the diffraction of neutrons by magnetically ordered crystals. Neutron diffraction is at present the only reliable method for the determination of the magnitude, direction, and spatial distribution of magnetic moments in crystalline substances. Since the magnetic moments are essentially due to the unpaired electrons, the distribution of these electrons in the crystal can be measured in this way.

1. Introduction

An important application of neutron diffraction is the determination of magnetic spin structures in crystals in the magnetically ordered state. The neutron, or rather its magnetic moment, acts as a probe, by means of which the spatial electron spin distribution in the crystal can be measured in atomic dimensions. Neutron diffraction is at present the only method that allows the reliable determination of the magnetic environmental relations between the individual atoms or ions and of the long-range order of the spin. The investigation of magnetism and the use of constantly improving magnetic materials has now become so important that the chemist engaged in the preparation and analysis of such compounds must also be familiar with the magnetic properties and their investigation.

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[**] Part II: Neutron Diffraction and Magnetic Structures. – Part I: Neutron Diffraction at Atomic Nuclei [1].

2. Physical Principles

The neutron has a magnetic moment of $\mu_n = -1.91319$ nuclear magnetons (μ_N), and can therefore enter into magnetic dipole-dipole interaction with the magnetic moments of the atoms. The interaction with the magnetic moments of shell electrons that are situated in incomplete shells, and which therefore produce a resultant magnetic moment, is particularly important. The interaction with the magnetic moments of the atomic nuclei, on the other hand, is weaker by a factor of about 2000, and can be detected only under certain conditions; this interaction can be disregarded in the present connection.

The elastic scattering of the thermal neutrons by crystals consists essentially of two components having approximately equal orders of magnitude (scattering lengths between 10^{-12} and 10^{-13} cm):

1. nuclear scattering due to interactions between the neutron and the atomic nuclei [1];

2. magnetic scattering due to a classical dipole interaction between the magnetic moment of the neutron and the magnetic moments of the shell electrons.

The observed intensity of a diffracted neutron beam from a crystal is made up additively from these two components.

$$I = I_{\text{nucl}} + I_{\text{magn}} \tag{1}$$

Since the intensities in general are proportional to the squares of the crystallographic structure factors, we can write

$$|F|^2 = |F|^2_{\text{nucl}} + q^2 \cdot |F|^2_{\text{magn}} \tag{2}$$

$\mathbf{q}$ = magnetic interaction vector (see eq. (6)), F = crystallographic structure factor.

$$F_{\text{nucl}} = \sum_j b_j \cdot e^{2\pi i(hx_j + ky_j + lz_j)} \tag{3a}$$

$$F_{\text{magn}} = \sum_j p_j \cdot e^{2\pi i(hx_j + ky_j + lz_j)} \tag{3b}$$

The structure factor in X-ray diffraction, for comparison, is

$$F_{\text{x-ray}} = \sum_j f_j^R \cdot e^{2\pi i(hx_j + ky_j + lz_j)} \tag{3c}$$

where f_i^R are the *X-ray atomic scattering factors*, which describe the spatial distribution of *all* the electrons around the atomic nuclei. The nuclear scattering amplitudes, which are independent of the scattering angle, are represented by b_j; p_j are the angle-dependent magnetic scattering amplitudes.

The magnetic scattering of neutrons was discussed by *Halpern* and *Johnson* [2], and later in an extended form by *Trammell* [3] and *Blume* [4]. According to these authors the magnetic scattering amplitude p_j is given by

$$p_j = p_j(\boldsymbol{k}) = -\frac{e^2\mu_n}{mc^2} \cdot S_j \cdot f_j(\boldsymbol{k}) \tag{4a}$$

$$= 0.539 \cdot 10^{-12} \cdot S_j \cdot f(\boldsymbol{k}) \text{ cm}.$$

e,m = charge and mass of the electron

μ_n = magnetic moment of the neutron (in μ_N)

S_j = spin quantum number of the atom j

$f_j(\boldsymbol{k})$ = corresponding *magnetic form factor*

$$\boldsymbol{k} = \frac{4\pi \sin\Theta}{\lambda} \cdot \boldsymbol{\epsilon}$$

$\boldsymbol{\epsilon}$ = scattering vector (unit vector)

2Θ = scattering angle (Θ = Bragg angle)

Where the orbital moment cannot be neglected, eq. (4a) becomes

$$p_j(\boldsymbol{k}) = -\frac{e^2\mu_n}{mc^2} \cdot \frac{1}{2}\left[L_j^J \cdot f_j^L(\boldsymbol{k}) + 2\,S_j^J \cdot f_j^S(\boldsymbol{k})\right] \tag{4b}$$

with L^J and S^J, the projections of these quantum numbers on the vector $\mathbf{J}$.

$f_j(\boldsymbol{k})$ are now *magnetic form factors*, which describe the spatial distribution of the *unpaired electrons*. When the orbital moments are not negligible, separate form factors f^L and f^S must be used for the orbital and spin moments; this is so *e.g.* for lanthanides.

The magnetic scattering of neutrons is particularly interesting when the spins, in other words the individual magnetic moments, undergo a transition into an ordered state, *i.e.* when collective magnetism arises. Neutron diffraction is at present the only method by which the long-range order of the magnetic moments and their relative and absolute orientation can be determined. The neutron diffraction experiments provide information about:

1. the existence of collective magnetism;

2. the transition temperature (Curie or Néel temperature, T_C or T_N);

3. the nature of the magnetism: paramagnetism, ferromagnetism, antiferromagnetism, or ferrimagnetism;

4. the size of the magnetic unit cell;

5. the distribution of the magnetic atoms (or ions) in the sublattice and their relative orientation;

6. the absolute orientation of the moments with respect to the crystal axes;

7. the magnitude of the magnetic moments of the individual atoms or ions;

8. the magnitude and direction of the internal fields (by application of an external magnetic field);

9. the temperature dependence of the magnetization;

10. the local distribution of the magnetic moment density in the crystal, *i.e.* in the case of 3d electrons, the local distribution of the 3d electron density (covalency effects).

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3. Examples of Applications

3.1. Antiferromagnetic Structure of MnO

The method and the derivation of the results is best illustrated with the aid of examples. MnO was the first substance whose antiferromagnetic structure was established by neutron diffraction [5]. This experiment provided evidence of the very existence of antiferromagnetic order. The same magnetic order as in MnO has also been found in NiO [6] and in EuTe [7]. Though FeO [6] and CoO [6,8] assume an order with the same spin-sign sequence as MnO, the moments have a different orientation in relation to the crystal axes (Table 1).

Table 1. Magnetic properties of 3d metal oxides and Eu-chalcogenides.

	MnO	FeO	CoO	NiO
T_N (°K)	122	198	291	523
Symmetry below T_N	rhombohedral $\alpha < 60°$	rhombohedral $\alpha > 60°$	tetragonal $c/a < 1$	rhombohedral $\alpha < 60°$
Direction of magnetic moment	(111)	[111]	[$\bar{1}\bar{1}$7]	(111)

	EuO	EuS	EuSe	EuTe
Magnetic order	ferro	ferro	antiferro	antiferro
T_C resp. T_N (°K)	77	16.5	4.6 [a]	7.8

[a] According to *G. Busch, P. Junod, R. G. Morris,* and *J. Muheim,* Helv. physica Acta *37*, 637 (1964). Considerable uncertainty still exists concerning the magnetic behavior and even the transition temperatures. Thus *Busch et al.* found a second transition at 3.8 °K, which could be confirmed by recent neutron diffraction experiments.

Magnetic order manifests itself in the appearance of coherent scattering. Collective magnetism can therefore be recognized immediately if two neutron diffraction diagrams are recorded, one above and one below the Curie or Néel temperature, the difference diagram, representing the magnetic scattering, then being found by subtraction.

$$I_{magn} = I^{T<T_N}_{magn+nucl} - I^{T>T_N}_{nucl} \qquad (5)$$

Figure 1 shows a recent neutron diffraction diagram of MnO recorded by the author, and Figure 2 shows the antiferromagnetic structure derived from this diagram. MnO crystallizes in a face-centered cubic cell with the NaCl structure. The space group extinction rules for the nuclear scattering are therefore

h,k,l = even: $F = b_{Mn} + b_O = -3.7 + 5.77 = 2.07f$

h,k,l = odd: $F = b_{Mn} - b_O = -3.7 - 5.77 = -9.47f$

The nuclear scattering lengths are $b_{Mn} = -3.7\,f$ and $b_O = 5.77\,f$ ($1\,f = 1$ fermi $= 10^{-13}$ cm; cf. also [11]). When MnO powder is cooled in a cryostat, new reflections that point to magnetic order of the spins are observed below $T_N = 122$ °K. These new reflections can be indexed as $h/2$, $k/2$, $l/2$ where all the indices h, k, l are odd. Integer Miller indices are obtained by multiplication by 2; this means that to describe the magnetic arrangement of the spins in the crystal, the unit cell dimensions must be doubled in all three directions. The dimensions of the magnetic unit cell are thus double the dimensions of the chemical unit cell (see Fig. 1):

$$a_{magn} = 2 \cdot a_{nucl}$$
$$b_{magn} = 2 \cdot b_{nucl}$$
$$c_{magn} = 2 \cdot c_{nucl}$$

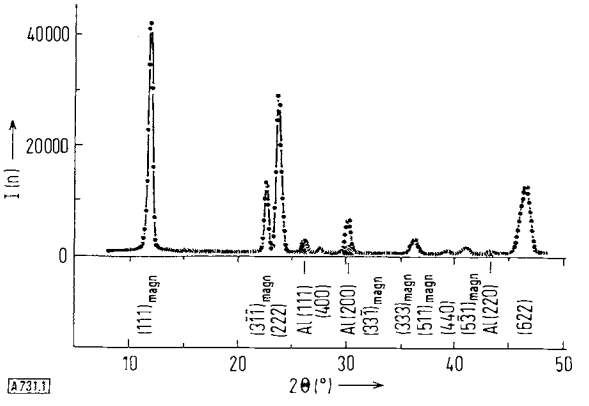


Fig. 1. Neutron-diffraction diagram of antiferromagnetically ordered MnO recorded at 4.2 °K. Owing to the doubling of the unit cell in the magnetically ordered state, all the reflections of the magnetic scattering have odd indices; all the nuclear scattering reflections have even indices. The reflections (222) and (622) (= h, k, l odd × 2) are strong, and the reflections (400) and (440) (h, k, l even × 2) are weak, corresponding to the intensity conditions for a face-centered cubic lattice (NaCl structure) and considering the negative sign of the nuclear scattering length of manganese.

The magnetic phase transition is associated with a crystallographic phase transition. Below 122 °K, in the antiferromagnetic range, MnO crystallizes with a rhombohedral unit cell, though the angle α differs only very slightly from 90°. At 4.2 °K, $a_{nucl} = b = c = 4.415$ Å and $\alpha = 90.6°$.

The magnetic order can now be deduced from the size of the magnetic unit cell together with the observed extinction rules for the magnetic reflections (MnO: h, k, l even not observed). For MnO, this gives an antiparallel orientation of the spins along the three crystal axes: ↑↓↑↓↑↓. Since only the relative orientation is expressed, the situation can be described by a sign sequence: $+-+-+-\ldots$. This gives the antiferromagnetic structure as shown in Figure 2. It consists of ferromagnetic (111) planes in which all the spins are parallel, with an antiferromagnetic sequence of such (111) planes normal to the plane in the [111] direction.

The absolute orientation and the magnitude of the magnetic moments can be determined from the intensities of the individual reflections. The quantity q^2 from eq. (2) is used for this purpose.

q is known as the magnetic interaction vector, and represents a relation between the direction of the

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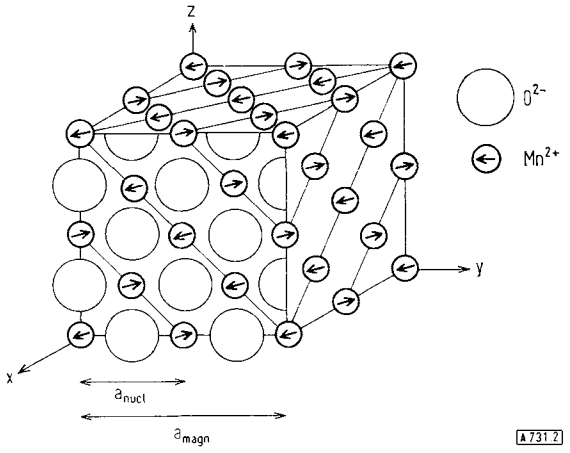


Fig. 2. Antiferromagnetic structure MnO. The spins lie in the (111) planes, and all the spins are parallel within the same (111) plane. The same magnetic structure is also found in NiO and EuTe.

magnetic moments, described by a unit vector $\boldsymbol{\varkappa}$, and the orientation of the reflecting crystal plane *h k l*, described by the scattering vector $\boldsymbol{\epsilon}$ (unit vector), which is normal to the plane *hkl* (cf. Fig. 3).

$$\mathbf{q} = \boldsymbol{\epsilon}(\boldsymbol{\epsilon} \cdot \boldsymbol{\varkappa}) - \boldsymbol{\varkappa} \tag{6}$$

Multiplication gives

$$q^2 = 1 - (\boldsymbol{\epsilon} \cdot \boldsymbol{\varkappa})^2 = \sin^2\alpha \tag{7}$$

where α is the angle between $\boldsymbol{\epsilon}$ and $\boldsymbol{\varkappa}$.

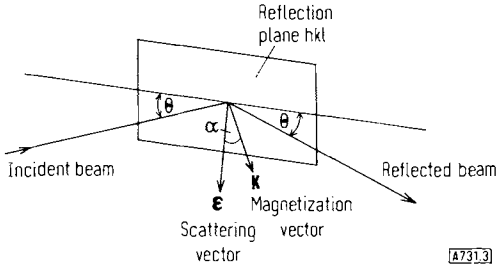


Fig. 3. Vector relation between incident neutron beam, diffracted beam, orientation of the reflecting plane, and the magnetization direction. The scattering intensity is proportional to $\sin^2\alpha$, *i.e.* the intensity has a maximum when the magnetic moments lie in the reflecting plane *hkl*.

Since the orientation of the various crystallites in a powder is random, limits are placed on the determination of the angle α from powder measurements. Thus it can be shown that for cubic crystal symmetry, $\langle q^2 \rangle$ = constant = $^2/_3$, and is thus independent of the orientation. In a cubic crystal therefore, the orientation of the spins in relation to the crystal axes cannot be determined from powder measurements. In crystals with rhombohedral, tetragonal, or hexagonal symmetry, the orientation of the spins can be given in relation to the unique axis of the crystal system, *i.e.* in relation to [111] in rhombohedral crystals and in relation to the *c* axis in tetragonal or hexagonal crystals.

For MnO, and also for EuTe, the measured intensity *ratios* show that the magnetic moments lie in the (111) planes as shown in Figure 2. Within the (111) plane the orientation cannot be determined from powder data.

The magnitude of the magnetic moment at the individual ions can be calculated from the absolute intensities using eq. (4a) or (4b). The determination of the absolute scale is rather easy in neutron diffraction studies, since the always-present nuclear scattering reflections can be used as an internal standard.

3.2. Investigations on Europium Chalcogenides

The special importance of the chalcogenides EuO, EuS, EuSe and EuTe is that they allow the direct study of the magnetic exchange forces as a function of the interionic distance in a series of simple compounds. They are of general interest because they represent the first ferromagnetic insulators that have been found which are optically transparent in the visible part of the spectrum. The compounds crystallize in the simple, parameter-free NaCl structure, which is particularly convenient for theoretical considerations. The magnetic properties of these compounds are shown in Table 1, and Figure 4 shows the exchange interactions as a function of the lattice constants. Since the Eu–Eu distances are directly reflected in the lattice constants, it is possible to combine the lattice constants and the magnetic behavior and estimate from them the exchange interactions. The strong ferromagnetic interaction J_1 between the nearest-neighbor Eu ions in EuO and EuS is responsible for the ferromagnetic behavior of both compounds. In EuTe, the antiferromagnetic interaction J_2 between next-nearest neighbors is distinctly greater than J_1; EuTe therefore behaves antiferromagnetically. Our neutron diffraction studies [7] have shown an antiferromagnetic order of the second kind in EuTe, which means that the compound has the same spin configurations as MnO (Fig. 2).

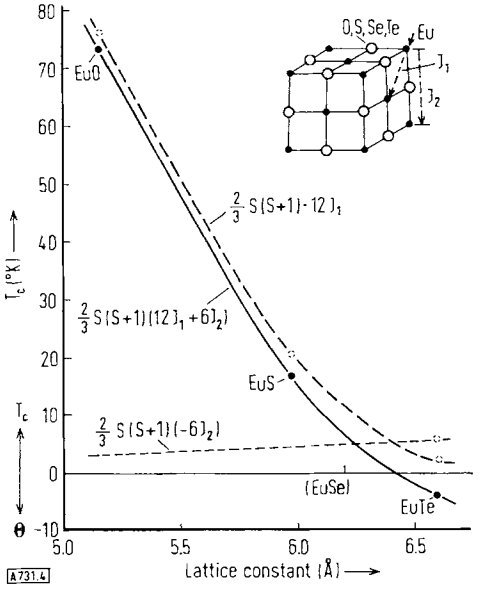


Fig. 4. Plot of the magnetic interactions J_1 and J_2 in europium chalcogenides as a function of the lattice constants.

The results for the magnetic properties of EuSe are contradictory. The magnetic structure may be influenced by small quantities of impurities or Eu^{3+} ions. A neutron diffraction study by *Pickart* and *Al-*

perin [9] showed that the sample used by these authors had a complicated antiferromagnetic structure, but that this structure could be changed into a ferromagnetic order by even a small external magnetic field of about 1700 Oe. EuSe was therefore not taken into account for the dependence of the exchange forces J_1 and J_2 in Figure 4.

3.2.1. Sublattice Magnetization and Exchange Interactions

In a face-centered cubic lattice, each ion has twelve nearest neighbors (nn) at a distance $\sqrt{2}/2\,a_0$ along the face diagonals [110] and six next-nearest neighbors (nnn) at a distance a_0 along the axes [100]. In the order of the second kind, as the antiferromagnetic order observed in MnO is called, each Mn^{2+} ion has six parallel and six antiparallel nearest neighbors and six antiparallel next-nearest neighbors (Table 2).

Table 2. Neighborhood relations in face-centered cubic lattices.

Neighbors	ferro-magnetic	antiferromagnetic	
		1st kind	2nd kind
nn	12 p	4 p, 8 ap	6 p, 6 ap
nnn	6 p	6 p	6 ap

When the magnetic order and the transition temperatures have been determined they can be used together with *Weiss*'s molecular field theory to derive the Heisenberg exchange interactions. *Heisenberg*'s view of ferromagnetism is based on the idea that the exchange interactions between two atoms i and j are responsible for the orientation of the magnetic moments. The magnetic exchange energy is described by a Hamiltonian operator $\mathfrak{H}$.

$$\mathfrak{H} = -2 \sum_{i>j} \cdot J_{i,j}\, \mathbf{S}_i \cdot \mathbf{S}_j \qquad (8)$$

$\mathbf{S}_i$ and $\mathbf{S}_j$ are spin operators $J_{i,j}$ is the exchange integral between the atoms i and j. Since the theory of exchange interactions is based on *ad-hoc* assumptions and the exchange integrals themselves cannot be calculated J must be determined experimentally if one wishes to understand the magnetic behavior of the substances. However, other interactions such as magnetic dipole-dipole coupling or the effects of anisotropy energies must generally be taken into account in addition to the exchange interactions. Measurements on simple structures such as the parameter-free structures of the NaCl type are therefore of great interest for the theory of magnetism. The series MnO, FeO, CoO, NiO and EuO, EuS, EuSe, EuTe have been extensively investigated; the oxides of the 3d transition metals are all antiferromagnetic, while a transition from ferromagnetism to antiferromagnetism is observed in the europium chalcogenides (cf. Table 1).

The exchange parameters J can be derived from the experimental data by means of relations from *Weiss*'s molecular field theory [10]. The following relations are valid:

$$\Theta = T_C = {}^2/_3\, S(S+1)\,[\,12J_1 + 6J_2] \qquad (9a)$$
$$T_{N_1} = {}^2/_3\, S(S+1)\,[-\,4J_1 + 6J_2] \qquad (9b)$$
$$T_{N_2} = {}^2/_3\, S(S+1)\,[\;\;0 - 6J_2] \qquad (9c)$$
$$T_{N_3} = {}^2/_3\, S(S+1)\,[-\,4J_1 + 2J_2] \qquad (9d)$$

T_C is the ferromagnetic Curie temperature; for antiferromagnetic crystals, Θ is the paramagnetic or asymptotic Curie-Weiss temperature, which follows from the Curie-Weiss law. For EuTe it was found that $\Theta = -7.5\,^\circ K$, and this together with the experimentally found Néel point $T_{N_2} = 7.8\,^\circ K$ [7] gives eq. 9a and 9b (order of the second kind):

$$J_2 = -(0.12 \pm 0.01)\,^\circ K; \quad J_1 = (0.025 \pm 0.025)\,^\circ K$$

(Energies are obtained by multiplication by $k = 1.38 \times 10^{-16}$ erg $^\circ K^{-1}$).

EuTe thus has a negative nnn exchange interaction, which is responsible for the antiferromagnetic orientation of the spins, and which is about five times as great as the positive direct nn exchange interaction.

Important information about the sublattice magnetization is obtained from the temperature behavior of the magnetic scattering. Figure 5a shows the temperature dependence of the magnetic scattering for the (111) reflection of EuTe. It is found from this that $T_N = 7.8\,^\circ K$. For comparison with the temperature dependence of magnetization as given by *Brillouin*, the observed intensity I_{rel} is normalized to I/I_0 and plotted against the normalized temperatures T/T_N. These normalized values are shown in Figure 5b; it can be seen that the experimental values do not agree with the theoretical Brillouin curve for a system having spin 7/2.

Both Mn^{2+} ($3d^5$) in MnO and Eu^{2+} ($4f^7$) in EuTe are in pure S states. There are therefore no orbital moment components to be taken into account. The dipole interactions are also negligibly small in these crystals, and the magnetic anisotropy energy is large only within the (111) planes while it is small perpendicular to these planes, *i.e.* in the direction of the antiferromagnetic coupling. The relations are therefore simple and the deviation of the experimental points from the Brillouin curve is surprising at first.

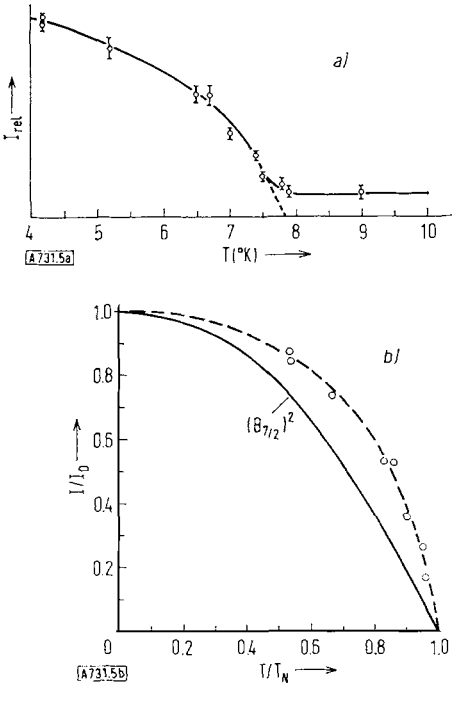


Fig. 5. Temperature dependence of the (strongest) magnetic reflection (111) in EuTe.

(a) Dependence of the intensity on temperature: The (111) reflection disappears at $T_N = 7.8\,^\circ K$; EuTe is in a paramagnetic state above this temperature.

(b) Intensity and temperature normalized to I_0 and $T_N \cdot I = f(T)$ thus becomes universal, and should follow the Brillouin function for spin S = 7/2 (continuous curve). The observed dependence, on the other hand, corresponds to a curve (broken) that was calculated by insertion of a biquadratic term of about 1% into the Hamiltonian exchange function.

[9] *S. J. Pickart* and *H. A. Alperin*, J. Physics Chem. Solids *29*, 414 (1968).

[10] *J. S. Smart*, Physic. Rev. *86*, 968 (1952).

To explain the discrepancy, *Rodbell, Jacobs, Owen,* and *Harris*[11] introduced a biquadratic contribution into the normally linear exchange interaction.

$$\mathfrak{H} = -2 \sum_{i>j} \{ J (\mathbf{S}_i \cdot \mathbf{S}_j) - j (\mathbf{S}_i \cdot \mathbf{S}_j)^2 \} \qquad (10)$$

If this biquadratic term is taken into account in the calculation of the Brillouin function, a very satisfactory agreement with the experimental point (broken curve in Fig. 5b) is obtained. Similar deviations of the experimental points from the Brillouin curve were found for MnO and NiO, and a biquadratic exchange term could also be detected for these crystals.

The biquadratic component amounts to about 1 % of J, and is therefore very small (in EuTe, j was found to be ≈ 0.001 °K). It is only rarely of such importance as in MnO and EuTe, and is generally overshadowed by the much larger exchange contributions of the dipole interaction and the magnetic anisotropy. It would therefore be wrong to try to explain every deviation from a Brillouin function by a biquadratic component of the exchange interaction.

3.3. Ferrimagnetic Structure of Ferrites

Reference was made in the first part of this article to the important role of neutron diffraction in the investigation of ferrites having the general composition $[X^{2+}(Y^{3+})_2(O^{2-})_4]$[1]. Since X and Y are normally adjacent elements in the periodic system they can be difficult or even impossible (*e. g.* in the case of $MnFe_2O_4$) to distinguish by X-rays. The neutron scattering powers of elements of adjacent atomic numbers on the other hand are generally quite distinct; neutron diffraction thus permits a definite identification of the ions.

X and Y in the ferrites are usually 3d transition elements. The analysis of the magnetic scattering of neutrons below the ordering temperature T_N also gives the ionization states of the ions and their distribution over the lattice sites. A classical example is the investigation of magnetite $Fe_3O_4 = [Fe^{2+}(Fe^{3+})_2(O^{2-})_4]$. Fe^{2+} and Fe^{3+} differ in their spin quantum numbers, S=2 and S=5/2 respectively, and consequently also have different magnetic scattering powers, p = 1·09 and $1{\cdot}36\times10^{-12}$ cm respectively. Neutron scattering at room temperature[12] gave an inverse spinel structure for magnetite with Fe^{3+} in the tetrahedral (or A) sites while the octahedral (or B) sites are uniformly occupied by Fe^{2+} and Fe^{3+}. The neutron diffraction data also show that the moments of the ions in the A and B sites are antiparallel to one another, so that the resultant magnetic moment corresponds to the moment of one Fe^{2+} ion per Fe_3O_4 formula unit. Fe_3O_4 is an example of ferrimagnetism postulated by *Néel*[13]. The magnetic structure is shown in Figure 6; the magnetic unit cell has the same dimensions as the chemical unit cell.

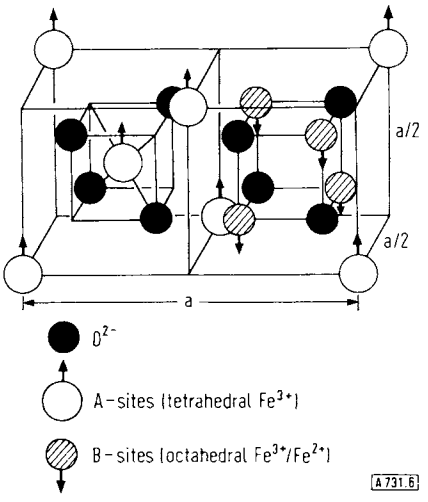


Fig. 6. Magnetic structure of magnetite at room temperature $[Fe^{2+}(Fe^{3+})_2(O^{2-})_4]$. Magnetite crystallizes with the spinel structure. One quarter of the unit cell is shown.

Magnetite exhibits a second magnetic phase transition, which was elucidated by an elegant experiment. Below 110–120 °K (the exact temperature depends on impurities in the crystals) the crystals exhibit a sudden change in electric conductivity and in magnetization. To explain this, *Verwey et al.*[14] postulated a crystallographic phase transition from the cubic spinel structure to an orthorhombic structure, combined with ordering of the Fe^{2+}/Fe^{3+} ions on the octahedral sites.

Hamilton[15] was able to confirm this hypothesis by neutron diffraction with a synthetic Fe_3O_4 single crystal. In this crystal, ordering of the iron ions on the octahedral sites (now in an orthorhombic unit cell) takes place at 119 °K. The Fe^{3+} ions form simple chains parallel to the a axis, while the Fe^{2+} ions are arranged perpendicular to these in chains parallel to the b axis. The orthorhombic a and b axes correspond to the cubic [110] face diagonals (Fig. 7). All the magnetic moments in the structure below 119 °K are parallel or antiparallel to the orthorhombic c (= cubic) axis. The experimental detection of this order is based

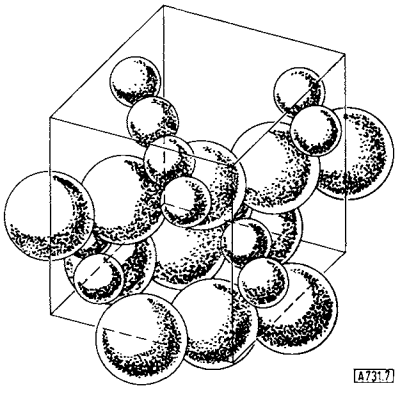


Fig. 7. Distribution of Fe^{2+} ions (large spheres) and Fe^{3+} ions (small spheres) in magnetite on the octahedral sites below the second magnetic transition at 119 °K. The ions, which are randomly distributed above this temperature (Fig. 6), now form mutually perpendicular ordered chains.

[11] *D. S. Rodbell, I. S. Jacobs, J. Owen,* and *E. A. Harris,* Physic. Rev. Letters *11*, 10 (1963).

[12] *C. G. Shull, E. O. Wollan,* and *W. C. Koehler,* Physic. Rev. *84*, 912 (1951).

[13] *L. Néel,* Ann. Physik *3*, 137 (1948).

[14] *E. J. W. Verwey, P. W. Haayman,* and *J. Roneijn,* J. chem. Physics *15*, 181 (1947).

[15] *W. Hamilton,* Physic. Rev. *110*, 1050 (1958).

on the appearance of the (002) reflection on neutron diffraction; this reflection is proportional to the difference in the scattering powers $p(Fe^{3+})-p(Fe^{2+})$, and is forbidden for the cubic random distribution.

3.4. Magnetic Behavior of Solid Solutions in the Ternary System Fe_2O_3–Cr_2O_3–Al_2O_3

The sesquioxides α-Fe_2O_3, Cr_2O_3, Ti_2O_3, V_2O_3 and Al_2O_3 all crystallize hexagonally in the corundum structure, but only the crystals of α-Fe_2O_3 and Cr_2O_3 exhibit magnetic long-range order of the spins; no long-range order of the magnetic moments could be detected by neutron diffraction in Ti_2O_3 and V_2O_3, despite the observed anomalies in the temperature dependence of the magnetic susceptibility.

the sign sequence (+−+−). (When Fe_2O_3 is cooled below about −23 °C, the spins flip from the (111) plane into the [111] direction. This phase transition has not however been found in any solid solutions; if it does exist it does so only in a very narrow range around pure Fe_2O_3.)

Since the oxides discussed here form solid solutions, information on the magnetic interactions, and hence on the conditions for the various magnetic structures, should be obtainable from the magnetic properties of the solid solutions. Thus *Cox et al.* [18] found that in the system Fe_2O_3–V_2O_3, the magnetic structure of α-Fe_2O_3 persists up to a V_2O_3 content of 60 %. A particularly interesting phase in the system Fe_2O_3–Ti_2O_3 is a solid solution having the the composition $FeTiO_3$, in which there is a completely ordered distribution of the Fe^{2+} and Ti^{4+} ions over the A and B sites [19].

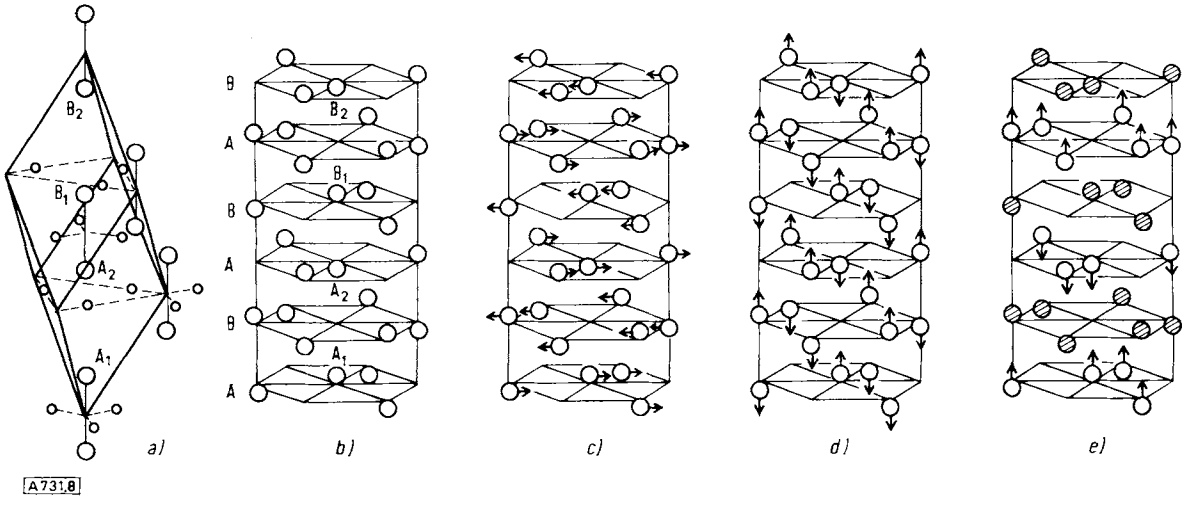


Fig. 8. Crystalline and magnetic structures of some sesquioxides.
a) Corundum structure — rhombohedral cell. Large circles = metal ions, small circles = oxygen ions.
b) Corundum structure — hexagonal representation. Only the metal ions, are shown.
c) Magnetic structure of α-Fe_2O_3 at 25 °C.
d) Magnetic structure of Cr_2O_3.
e) Magnetic structure of $FeTiO_3$. Open circles = Fe^{2+}, shaded circles = Ti^{4+}.

α-Fe_2O_3 and Cr_2O_3 have the same crystal structure, but quite different spin structures [16, 17] (Fig. 8). In Fe_2O_3, the spins lie in the hexagonal basal plane at 25 °C; the spins are parallel within a plane, and the planes are arranged in antiparallel sequence along the hexagonal *c*-axis. (In a rhombohedral description of the unit cell, we have ferromagnetic (111) planes in an antiferromagnetic sequence along [111].) The structures are described by the atomic positions A_1, A_2, B_1, and B_2. The spins in these positions in α-Fe_2O_3 then have the sign sequence (++−−).

In Cr_2O_3, on the other hand the spins are directed parallel to rhombohedral [111]; an antiferromagnetic arrangement exists within the individual (111) planes. In the rhombohedral [111] direction, the spins have

$FeTiO_3$ has an antiferromagnetic structure, in which ferromagnetic (111) planes form an antiparallel sequence in the [111] direction. These ferromagnetic planes are separated by layers of non-magnetic Ti^{4+} ions. The sign sequence can be given purely formally as (+−00); the spins themselves are oriented parallel and antiparallel to [111].

Complicated magnetic behavior is expected, and observed [20], in the solid solutions of the system Fe_2O_3–Cr_2O_3, since here we have interaction of two magnetic structures with opposite spin directions and different orders. A neutron diffraction study showed that the magnetic structure from 100 to 35 mole-% of Fe_2O_3 is that of α-Fe_2O_3, while at 10 to 0 mole-% of Fe_2O_3 it is that of Cr_2O_3. The transition temperature decreases with increasing Cr content: Fe_2O_3: T_N = 965 °K; Fe_2O_3–Cr_2O_3 (40:60 mole-%): T_N = 400 °K. Between 35 and 10 mole-% of Fe_2O_3, there is a helical structure described as an "umbrella structure", *i.e.* an arrangement in which the spins lie on cones, adjacent spins being turned through an angle α that is different

[16] *C. G. Shull, W. A. Strausser*, and *E. O. Wollan*, Physic. Rev. *83*, 333 (1951).

[17] *B. N. Brockhouse*, J. chem. Physics *21*, 961 (1953).

[18] *D. E. Cox, W. J. Takei, R. C. Miller*, and *G. Shirane*, J. Physics Chem. Solids *23*, 863 (1962).

[19] *G. Shirane, S. J. Pickart, R. Nathans*, and *Y. Ishikawa*, J. Physics Chem. Solids *10*, 35 (1959).

[20] *D. E. Cox, W. J. Takei*, and *G. Shirane*, J. Physics Chem. Solids *24*, 405 (1963).

by 180° in relation to one another. Both α and the apex angle of the cone vary with the Cr content. The orientation of the axis of the cone in the crystal also changes. The axis of the cone is initially (above 35 % Fe_2O_3) perpendicular to the *c* axis, *i.e.* parallel to the collinear moments in Fe_2O_3, the (half) apex angle of the cone being 19°. The apex angle increases to 77° at 20 % Fe_2O_3, and then decreases again. The orientation of the cone switches into the direction of the *c* axis at about 15 % Fe_2O_3; it then corresponds to the collinear moments in Cr_2O_3. The investigations were recently carried on by *Scharenberg* [21] and extended to include the presence of non-magnetic aluminum ions. Dilution of the magnetic lattice in this way yields valuable information concerning the range of the exchange forces and the stability of the magnetic structures. The results of these measurements can be seen in the magnetic phase diagram of Fe_2O_3–Cr_2O_3–Al_2O_3 (Fig. 9), from which the ranges of the various structure types are immediately recognizable.

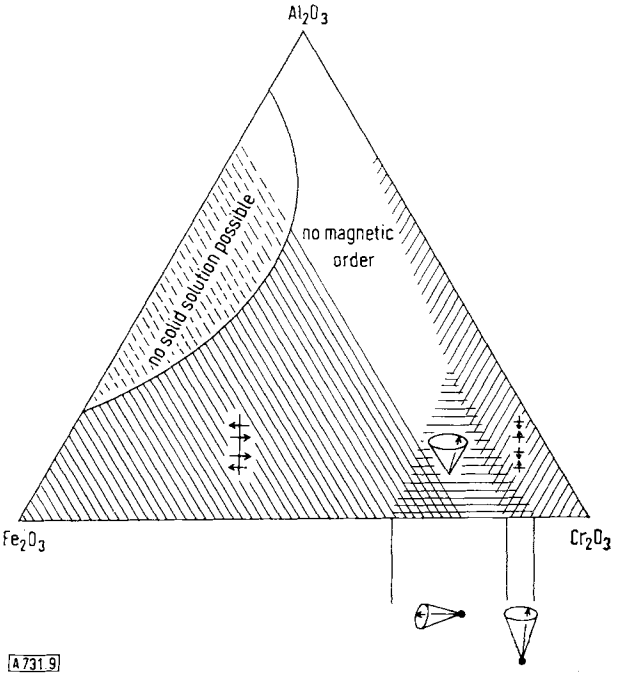


Fig. 9. Magnetic phase diagram of the ternary system Fe_2O_3–Cr_2O_3–Al_2O_3. In the regions with double shading, the crystals have two magnetic transitions: paramagnetic state $-T_{N_1}$ (magnetic collinear structure) $-T_{N_2}$ (magnetic spiral structure).

3.5. Determination of Covalent Bond Components in Antiferromagnetic Salts from Neutron Diffraction Data

In most antiferromagnetic salts of the 3d transition metals, *e.g.* $LaCrO_3$ or $KMnF_3$, the 3d metal ion is surrounded octahedrally by six ligands. The orbitals of the ligands are of s or p character, and give bonding and antibonding orbitals with the five d orbitals of the central ion. Only the antibonding orbitals are of interest for the consideration of the magnetic properties. The bonding orbitals have such low energy levels in the complexes discussed here that these levels are all doubly occupied by electrons. Only the higher antibonding orbitals are singly occupied, and are thus responsible for the magnetic behavior. We follow the procedure used by *Hubbard* and *Marshall* [22] and consider first a simple antiferromagnetic chain of p and d orbitals as shown in Figure 10.

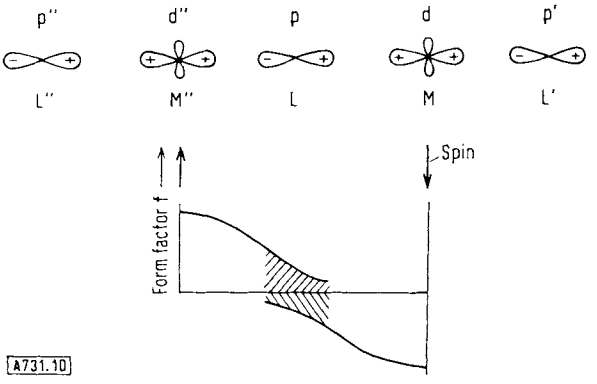


Fig. 10. Schematic diagram of the orbitals of an antiferromagnetic chain and the overlap of the form factors of 3d electrons. In the case of antiferromagnetic orientation of the spins, interference extinction occurs in the neutron diffraction in the region of the ligands.

L = ligand ion, M = metal ion. Owing to the antiferromagnetic order, the spins, and hence also the spin densities and the form factors, have opposite signs in M and M''.

The magnetically active orbital of M can no longer be described simply by d orbitals, but we have to take into account the admixture of p orbitals (covalency).

$$\psi_M(\mathbf{r}) = N \{ d(\mathbf{r}) - A \cdot p(\mathbf{r}) + A \cdot p'(\mathbf{r}) \} \qquad (11)$$

A are the admixture parameters and N is a normalization factor. S_σ is the overlap integral between p and d

$$1/N^2 = 1 - 4A \cdot S_\sigma + 2A^2 \qquad (12)$$

orbitals. This can be used to find the moment density $D(\mathbf{r})$ around M; if overlap between p and p' is neglected, we obtain for $D(\mathbf{r})$

$$\begin{aligned} D(\mathbf{r}) = {} & d^2(\mathbf{r}) \{ 1 + 4A \cdot S_\sigma - 2A^2 \} \\ & - 2A \{ d(\mathbf{r}) \cdot p(\mathbf{r}) - d(\mathbf{r}) \cdot p'(\mathbf{r}) \} \\ & + A^2 \{ p^2(\mathbf{r}) + p'^2(\mathbf{r}) \} \end{aligned} \qquad (13)$$

The first term containing $d^2(\mathbf{r})$ is confined to the magnetic ion M. The second term describes the overlap density between p and d orbitals, and is also confined to the immediate neighborhood of M. The third term, on the other hand, describes a density distribution, which lies exclusively at the position of the ligands; the distance from L to the neighboring metal ion M'' is the same as the distance from M. The analogous density due to the ion M'' at the position L is roughly equal to the contribution due to M, but is of opposite sign in antiferromagnetic substances. This means that $A^2p^2(\mathbf{r})$ and $A^2p'^2(\mathbf{r})$ cancel out with the analogous contributions from M and M''. It is

[21] *W. Scharenberg*, Dissertation, Universität Bonn 1968.

[22] *J. Hubbard* and *W. Marshall*, Proc. physic. Soc. *86*, 561 (1965).

clear therefore that in a neutron diffraction experiment on an antiferromagnetically ordered crystal, only the contributions of the first two terms in eq. (13) are observable in the Bragg maximum.

$$\mu(\mathbf{r})_{obs} = d^2(\mathbf{r}) \{ 1 + 4A \cdot S_\sigma - 2A^2 \} - 2A \{ d(\mathbf{r}) \cdot p(\mathbf{r}) - d(\mathbf{r}) \cdot p'(\mathbf{r}) \} \quad (14)$$

Thus whereas the integration of eq. (13) gives 1, integration of eq. (14) merely gives

$$\mu(\mathbf{r})_{obs} = \int \mu(\mathbf{r})\, d\mathbf{r} = 1 - 2A^2 \quad (15)$$

Calculation of the magnetic moments μ_{obs} (*e.g.* according to eq. (4)) from the measured diffraction intensity gives a value that is smaller by $2A^2$ than the true moment μ_0.

It is therefore possible, in principle at least, to determine the covalent part in antiferromagnetic complexes of this type from neutron diffraction data. The effects are naturally very small, and the measurements are therefore laborious and require a number of precautions to eliminate possible sources of error such as, for example, "$\lambda/2$ contamination" of the neutron beam (cf. [1]).

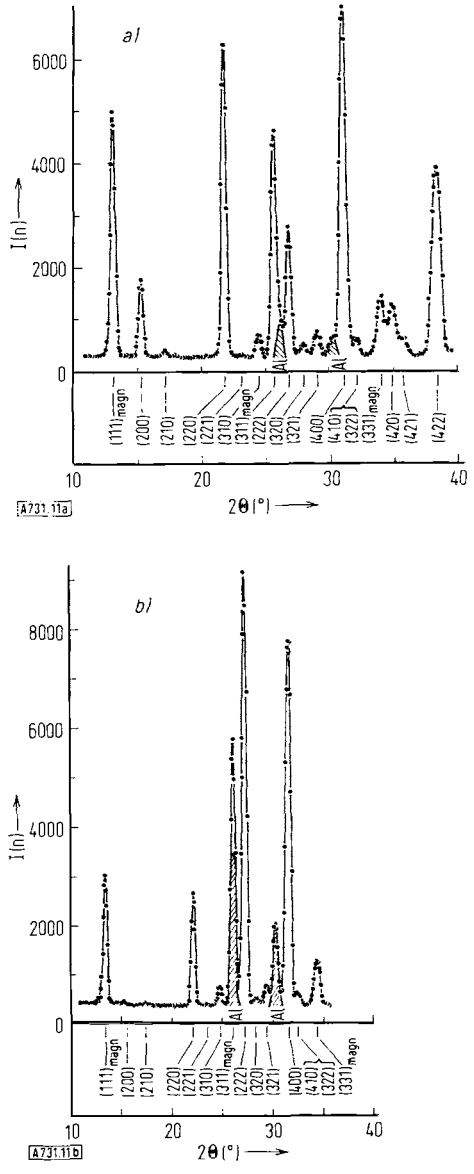


Fig. 11. Neutron diffraction diagram of a) $LaFeO_3$ and b) $LaCrO_3$, recorded at 4.2 °K in the antiferromagnetic state.

We have carried out neutron diffraction experiments of this type on $LaCrO_3$, $LaFeO_3$, and $LaMnO_3$ as well as on a series of fluorites having the composition KMF_3 (M = 3d transition elements), and have actually been able to detect this effect in $LaCrO_3$ and $LaFeO_3$ [23]. Figure 11 shows the neutron diffraction diagrams of $LaFeO_3$ and $LaCrO_3$.

On application to the three-dimensional crystal structure, considerations analogous to those used for equations (11) to (15) lead to the following relations (A = covalency coefficient) [22].

$$\mu_{obs}/\mu_0 = \begin{cases} 1 - 3(A_\sigma^2 + A_\delta^2) & Ni^{2+} \\ 1 - 4A_\pi^2 & Cr^{3+} \\ 1 - 1.2(A_\sigma^2 + 2A_\pi^2 + A_\delta^2) & \begin{cases} Mn^{2+} \\ Fe^{3+} \end{cases} \end{cases}$$

The evaluation of our measurements on powder specimens is concentrated mainly on the first magnetic reflection (111) at small scattering angles, where reliable theoretical assumptions regarding the form factor can be made. This means that the observed deviations in the values of the form factor can be entirely attributed to the covalency of the bond, and not *e.g.* to a possible asymmetric charge distribution. The measurements were hampered by a very small coherent nuclear scattering contribution to the magnetic scattering. This nuclear scattering component is the result of the distortion of the perovskite-like crystal structure from the ideal (cubic) perovskite structure; it must be determined separately by a crystal structure analysis [24]. However, this contribution can only increase the effect and cannot decrease it. $LaCrO_3$ and $LaFeO_3$ crystallize in a perovskite-like structure, in which each cation is octahedrally surrounded by antiparallel oriented neighbors. The magnetic structure of $LaMnO_3$ is different: each Mn^{3+} ion has two parallel and four antiparallel neighbors. The unfavorable ratio 2 : 4 of parallel to antiparallel neighbors decreases the effect; we feel, that for this reason, among others, we were unable to detect the covalency parameters in $LaMnO_3$.

Table 3 also shows the results of measurements on NiO [25], MnO [26], and MnF_2 [27]. Results of nuclear magnetic resonance measurements [28] are given for comparison.

The values for Fe^{3+} and Mn^{2+} both of which have the $3d^5$ configuration are particularly interesting. It is

[23] *R. Nathans, G. Will,* and *D. E. Cox,* Proc. int. Conf. Magnetism, Nottingham 1964, p. 327.

[24] *G. Will* and *D. E. Cox,* Acta crystallogr., in press.

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[28] *R. G. Shulman* and *S. Suzano,* Physic. Rev. *130*, 506 (1963); *R. G. Shulman* and *K. Knox,* Physic. Rev. Letters *4*, 603 (1960), *T. P. P. Hall, W. Hayes, R. W. H. Stevenson,* and *J. Wilkens;* J. chem. Physics *38*, 1977 (1963).

Table 3. Covalency parameters in some antiferromagnetic salts of 3d elements.

Ion	From NMR measurements		From neutron diffraction measurements	
	Compound	Covalency coefficients (%)	Compound	Covalency coefficients (%)
Ni^{2+}	$KNiF_3$	$A_\sigma^2 + A_S^2 = 4.32$	NiO	$A_\sigma^2 + A_S^2 = 6.0$
Cr^{3+}	K_2NaCrF_6	$A_\pi^2 = 4.7$	$LaCrO_3$	$A_\pi^2 = 4.6$
Fe^{3+}	Fe^{3+} in $KMgF_3$	$A_\sigma^2 - A_\pi^2 = 3.3$ $A_S^2 = 0.76$	$LaFeO_3$	$A_\sigma^2 + 2A_\pi^2 + A_S^2 = 10.0$
Mn^{2+}	$KMnF_3$	$A_\sigma^2 - A_\pi^2 = 0.18$ $A_S^2 = 0.52$	MnF_2 MnO	$A_\sigma^2 + 2A_\pi^2 + A_S^2 = 3.3$ 5.5
Mn^{3+}			$LaMnO_3$	no effect found

possible to determine A_σ^2 and A_π^2 (in %) individually by a combination of NMR and neutron diffraction data

Fe^{3+}: $A_\sigma^2 = 5.4$ $A_\pi^2 = 2.1$
Mn^{2+} in $MnF_2(MnO)$: $A_\sigma^2 = 1.2\ (1.8)$ $A_\pi^2 = 1.0\ (1.6)$

3.6. Determination of the Local 3d Spin Density Distribution in Crystals[29]

The magnetic form factor f can be deduced from the measured magnetic scattering with the aid of eq. (4). It is then possible by Fourier transformation of the diffraction data to calculate the spatial distribution of the magnetic moments in the crystal. The result is a diagram of the density distribution of the magnetic moments around the centers of the atoms similar to the electron density distribution obtained in X-ray structure analyses. If we confine our considerations to the 3d elements, where the crystal fields are strong compared with the spin-orbital coupling, so that the orbital moments are generally suppressed, then the magnetic moment density from the neutron diffraction data directly describes the spin density, and hence the density of the unpaired (outer) electrons, which are responsible for the chemical bonding.

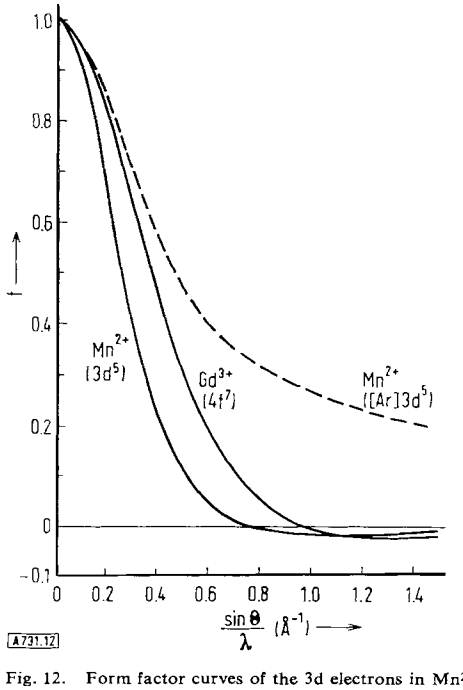


Fig. 12. Form factor curves of the 3d electrons in Mn^{2+} and of the 4f electrons in Gd^{3+} for the magnetic scattering of neutrons [the form factor curve of Mn^{2+} (with all electrons) for the diffraction of X rays is also given for comparison].

[29] For a review see *e.g. G. Will*, Z. angew. Physik *24*, 260 (1968).

Since the outer electrons are on average farther from the nucleus than the mean total electron density that determines the X-ray diffraction, the magnetic form factor, which is a shape factor in the present example of the 3d electrons, falls off much more rapidly than the X-ray form factor. This is illustrated in Figure 12 for Mn^{2+} (the magnetic form factor of Gd^{3+} is also shown for comparison). In the lanthanides the unpaired electrons (4f electrons) are on average denser at the nucleus; the fall-off of the form factor is therefore rather less. Mn^{2+} and Gd^{3+} are in an S state with electronic configurations $3d^5$ and $4f^7$ respectively, and the electron distribution is spherically symmetrical.

Whereas the electron distribution around the nucleus can be taken as spherically symmetrical on the whole in X-ray structure analysis, the distribution of the outer bonding electrons, which are "seen" by the neutrons, is generally not spherically symmetrical. Consequently, the "form factor curves" for neutron diffraction are not smooth curves; the experimental points are scattered more or less widely about an average curve. Figure 13 shows form factor values for

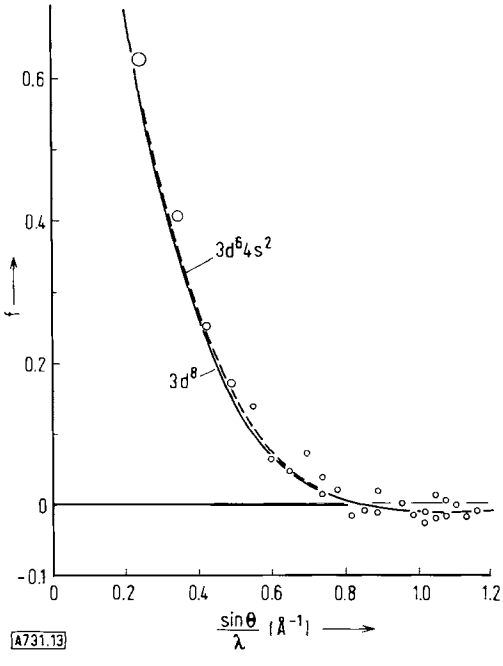


Fig. 13. Experimental magnetic form factor values (circles) found for elementary iron with polarized neutrons, compared with theoretical curves for various electronic configurations.

elementary iron in the ferromagnetic state measured with polarized neutrons, together with the theoretical spherically symmetrical electronic configurations for comparison. The deviations of the experimental points from the spherical symmetry curves are real (*e.g.* outside the error limits), and are a direct measure of the asymmetric distribution of the 3d electrons (the size of the circles corresponds approximately to the experimental accuracy).

The resolution in the density diagram is found to depend on the number of reflections measured, and is determined by the $\sin\Theta/\lambda$ range. A resolution of 1 Å corresponds roughly to $\sin\Theta/\lambda = 0.3$ to 0.4 $Å^{-1}$ (1 Å $\approx 0.66\ \lambda/2\sin\Theta$); to obtain a resolution of 0.25 Å, therefore, measurement up to $\sin\Theta/\lambda = 1.2\ Å^{-1}$ is necessary. The deviations of the electron density distribution from spherical symmetry are particularly evident in the region around 0.8 $Å^{-1}$; on the other hand, the magnetic form factors are very small between $\sin\Theta/\lambda = 0.8$ and 1.2 $Å^{-1}$ so that the determination of the 3d electron distribution necessitates the accurate measurement of very small quantities. It is interesting to note the change in the sign of the form factor curves from $+f$ to $-f$ at about $\sin\Theta/\lambda = 0.8\ Å^{-1}$ as a result of the limited spread of the 3d electrons (the maximum is situated about 0.35 to 0.40 Å from the center of the nucleus).

The usual technique of diffraction of unpolarized neutrons is generally inadequate for the reliable determination of the form factors and hence the 3d electron densities. Much more accurate measurements are possible with polarized neutrons.

The neutron has a spin of 1/2, and can occur in the energetically different spin states + 1/2 and −1/2. Both spin states normally occur with equal probability in a neutron beam (unpolarized neutrons). With a suitable experimental arrangement (Fig. 14), however, it is possible to obtain a neutron beam that contains only neutrons in a single spin state (polarized neutrons). A polarized neutron beam of this type is obtained *e.g.* by Bragg reflection from a "polarization monochromator" (nowadays nearly always a single crystal having the composition $Co_{0.92}Fe_{0.08}$ which is magnetized in an external field). Approximately 99 % of the neutrons in the resulting beam are in the same spin state. The direction of the spin vector is described by a unit vector $\pm\ \boldsymbol{\lambda}$, which is referred to the external magnetic field. The neutron beam can be converted from one spin state into the other by superposition of a low frequency field on the polarized beam ("flipper").

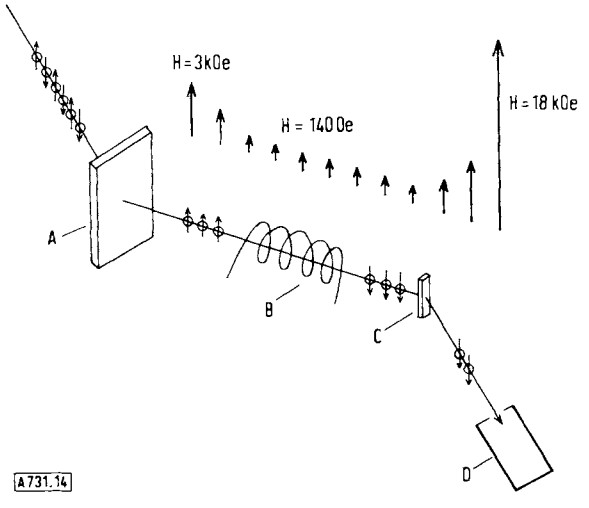


Fig. 14. Schematic representation of the experimental arrangement for measurements with polarized neutrons. A: Polarization monochromator ($Co_{0.92}Fe_{0.08}$); B: "flipper"; C: test crystal; D: counter.

The conditions for the polarization of the neutrons are obtained by insertion of eq. (3a) and (3b) in eq. (2). The structure factor F can then be expressed in the general form

$$F = \sum_j \{\ b_j + (\mathbf{q}_j \cdot \boldsymbol{\lambda})\, p_j\ \} \cdot e^{2\pi i (hx_j + ky_j + lz_j)} \qquad (16)$$

The vectors $+\boldsymbol{\lambda}$ and $-\boldsymbol{\lambda}$ are present in equal proportions in a beam of unpolarized neutrons; the scattered intensity is proportional to F^2 and therefore to $b^2 + p^2$; the cross term $(\mathbf{q}\boldsymbol{\lambda})$ thus becomes zero [eq. 2]. For polarized neutrons, on the other hand, we have *e.g.* $+\boldsymbol{\lambda} = 1$ and $-\boldsymbol{\lambda} = 0$. Eq. (16) now leads to a phase dependence of the nuclear scattering on the magnetic scattering. The resultant intensity is proportional to $(b + p)^2$:

polarized neutrons: $I \sim (b + p)^2$

unpolarized neutrons: $I \sim b^2 + p^2$

The requirement for the polarization monochromator is therefore simply $b = p$. In this case we have for an unpolarized neutron beam $I_{(+\lambda)} = (b + p)^2 = 2b^2$ and $I_{(-\lambda)} = (b - p)^2 = 0$.

To detect very small scattering contributions p, therefore, it would be necessary with unpolarized neutrons to measure a term p^2 whose square is small and a term b^2 whose square is large, whereas for polarized neutrons there is a linear relation between p and b. Another advantage of polarized neutrons lies in the measuring technique itself. For the accurate determination of p one need only determine accurately the ratio p:b; the method is therefore on a relative scale, and is thus independent of systematic errors (such as the determination of an absolute scale or of the temperature factor, which is known to cause a decrease in the scattering intensity with increasing scattering angle, similar to the decrease in the form factor itself.) In measurements with polarized neutrons, one simply determines the polarization ratio P by recording first I^+ with neutrons having $\boldsymbol{\lambda} = +1$, and then I^- with neutrons having $\boldsymbol{\lambda} = -1$.

$$P = \frac{I^+}{I^-} = \frac{(b + p)^2}{(b - p)^2} \qquad (17)$$

This leads to very accurate values of p, and hence of f.

The limits of the method can also be found very readily from eq. (17). To obtain a difference between I^+ and I^-, coherent overlap of neutron scattering and magnetic scattering must occur in the reflections. Investigations so far have been concentrated on ferromagnetic crystals, where this condition is always satisfied. This is not generally the case in antiferromagnetic crystals, and measurement with polarized neutrons is fundamentally impossible for *e.g.* MnO or NiO, where the neutron scattering reflections and the magnetic reflections are rigorously separated because the magnetic unit cell is twice as large as the chemical unit cell, and the crystallographic extinction rules separate the two sets of reflections exactly.

Detailed investigations have been carried out on the ferromagnetic elements iron [30], nickel [31], and hexagonal cobalt [32], as well as on Pd-0.01 Fe [33], Fe_3Al [34], and some Fe–Rh alloys [35]. A Fourier synthesis with the experimental data as amplitudes gives the electron density distribution of the unpaired electrons. If only the difference values of the experimental points from the spherically symmetrical average curve are used as amplitudes, the deviation of the electron distribution

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from spherical symmetry is obtained directly. Figure 15 shows the result of such a difference Fourier synthesis using the values for iron from Figure 13. An interesting feature of this spin density distribution is the extended negative areas, which represent a density distribution of spins of opposite sign, *i.e.* antiferromagnetic orientation. The negative polarization is assigned to the 4s conduction electrons that uniformly fill the entire crystal with the opposite spin direction.

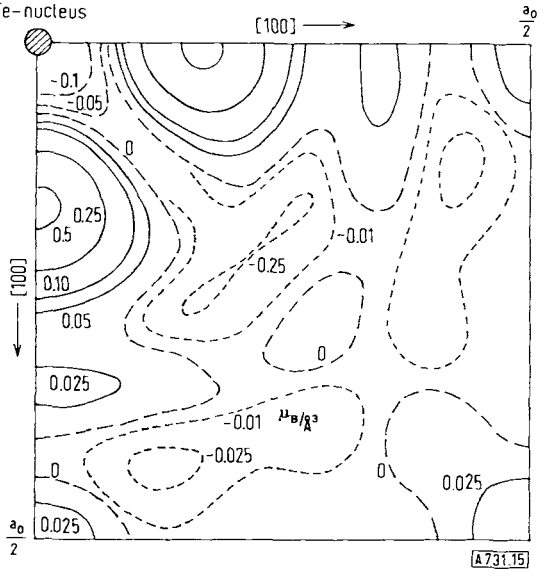


Fig. 15. Deviation of the spin density distribution from spherical symmetry in an iron crystal (difference Fourier diagram). The extended negative regions are due to the negatively polarized 4s electrons which form a uniform antiferromagnetic background in the otherwise ferromagnetic crystal (3d electrons). The maxima therefore essentially denote an additional 3d electron density; a distinct concentration of the 3d electrons along the crystal axes is evident. This distribution is characteristic of the e_g symmetry of the 3d electrons.

The e_g or t_{2g} character of the electron distribution can be deduced from the observed concentration of the electron density in certain directions in the crystal. Iron crystallizes in a body-centered cubic lattice. The five-fold degenerate 3d energy levels are split by the crystal field into two states with e_g symmetry and three states with t_{2g} symmetry. Owing to the octahedral symmetry of the environment of the iron atoms, the energies of the e_g levels are higher than those of the t_{2g} levels. The observed electron concentration along the cubic [100] axes (Fig. 15) thus points to e_g symmetry of the electron distribution. Careful numerical evaluation of the experimental data [30], in which a small component of the orbital moment and 4s electron contributions were taken into account, gave +2.39 μ_B for positive magnetization and −0.21 μ_B for negative magnetization. Assuming that Hund's rule is valid, therefore, there are 7.6 electrons in the 3d band and 0.4 electrons in the conduction band. The electronic configuration in ferromagnetic elementary iron should thus be $3d^{7.6}\ 4s^{0.4}$. Of the 7.6 electrons, 53% are in an e_g symmetry state (along the cube axes) and 47% in a t_{2g} symmetry state (along the cube diagonals).

Exactly the opposite situation is found in nickel, which crystallizes in a face-centered cubic lattice; 19% of the 3d electrons are in e_g levels and 81% in t_{2g} levels (the distribution for spherical symmetry is 40% e_g, 60% t_{2g}). The electron distribution obtained by analysis of the neutron diffraction data are: $3d_{spin} = 0.656\ \mu_B$, $3d_{orbital} = +0.055\ \mu_B$; for 4s conduction electrons, one finds $-0.105\ \mu_B$.

Table 4. Character of the electron distribution in some 3d elements and 3d–4d alloys.

Composition	3d configuration		
	e_g (%)	t_{2g} (%)	
Theoretical values for spherical symmetry (cubic)	40	60	
Fe (body-centered cubic)	53	47	
Ni (face-centered cubic)	19	81	
Co (doped with Fe) (body-centered cubic)	21	79	
V (body-centered cubic)	19	81	
$Fe_{0.52}Rh_{0.48}$ (ferromagnetic)	47	53	
$Fe_{0.5}Rh_{0.5}$ (antiferromagnetic)	48	52	
$Fe_{0.013}Pd_{0.987}$	28	72	
Fe_3Al : FeI	60	40	
FeII	48	52	
Theoretical values for spherical symmetry (hexagonal)	e_{2g} (%)	e_{1g} (%)	a_{1g} (%)
	40	40	20
Co (hexagonal)	39.4	41.6	19.0

3.7. The Magnetic Structure of Oxygen

Finally, brief mention should be made of a neutron diffraction study on solid oxygen, which showed an antiferromagnetic order [36]. Crystalline oxygen exists in three phases:

α-O_2 (0–24 °K); β-O_2 (24–44 °K); γ-O_2 (44–54 °K).

The γ phase has 8 molecules in a cubic unit cell. The β phase has one molecule in a rhombohedral cell, the molecule probably being oriented along the trigonal axis. The structure of the α phase is unknown. The symmetry is presumably monoclinic. Magnetic measurements on gaseous, liquid, and solid γ oxygen indicate two unpaired electrons in a $^3S_1$ state [37]; the susceptibility indicates an anti-ferromagnetic order at low temperatures. In the neutron diffraction experiments on solid β- and α-oxygen, the diagram of α-O_2 did in fact contain two additional lines at small scattering angles, which must be attributed to an antiferromagnetic order in α-O_2. Since the magnetically ordered spins are due to unpaired p-electrons which have a relatively large spread, the magnetic form factor falls off very rapidly, with the result that the detection of magnetic reflections become difficult ($f = 0.5$ for $\sin\Theta/\lambda = 0.2\ Å^{-1}$). No magnetic long-range order was observed for β-O_2. The magnetic and neutron diffraction data (maximum of the diffuse scattering at $\sin\Theta/\lambda = 0.1\ Å^{-1}$), however, indicate an antiferromagnetic short-range order in β-O_2.

Received: December 11, 1968 [A 731 IE]
German version: Angew. Chem. *81*, 984 (1969)
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Small Charged Heterocycles

By D. R. Crist and N. J. Leonard[*]

The synthesis and important reactions of stable aziridinium salts are described in this article. The more stable azetidinium salts, which undergo similar reactions, have also been studied. Polar and dipolar cycloadditions produce heterocycles by ring expansions that can be represented as ③$^{\oplus}$ + 2→⑤$^{\oplus}$, ③$^{\oplus}$ + 3→⑥$^{\oplus}$, *and* ④$^{\oplus}$ + 3→⑦$^{\oplus}$.

1. Introduction

Small rings are of interest not only for theoretical reasons but also because of new industrial and biological applications. This is particularly true of aziridine derivatives, which find use as alkylating agents [1], chemical mutagens [2], insect chemosterilants [3], models for pharmacological studies [4], and in polymerizations [5]. Moreover, stable aziridinium salts are now more readily available owing to new synthetic methods and suppression of decomposition reactions [6]. This review will be limited to the synthesis and reactions of isolable three- and four-membered heterocycles that bear a positive charge. This definition of scope excludes a) cations related to the cyclopropyl skeleton [7], b) acid-catalyzed reactions of ethylene oxides [8] and sulfides [9] that proceed through non-isolable cations, and c) α- and β-lactams [10, 11] that are uncharged in their stable forms.

Aziridinium and azetidinium salts are more stable than their oxygen or sulfur analogs because of the greater basicity of nitrogen. The driving force for most reactions of these salts is the release of the strain energy inherent in a small ring [12]. Both aziridinium and azetidinium systems give more stable ring-opened or ring-expanded products. In the presence of nucleophiles the initial reaction produces an amino group, which is itself a good nucleophile. This property leads to varied and useful reactions. Differences between the systems relate to ease of formation and stability: the aziridinium ion is formed more readily owing to an entropy effect but is also considerably more reactive.

2. Aziridinium Salts

2.1. Aziridinium Salts as Reactive Intermediates

In order to explain the biological effects, abnormal reactivity, and rearrangements of β-haloethylamines, aziridinium ions were frequently postulated and, in certain cases, could be isolated. For example, picrylsulfonate salts having biological activity similar to the starting material could be isolated from aged solutions of nitrogen mustards [13] and other β-haloethylamines [14]. The postulate of aziridinium ions such as *(1)* as the physiologically active component was consistent with kinetic studies [15].

In the presence of various nucleophiles, chloride ion formation occurs at a rate independent of the nature or concentra-

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[1] a) *J. S. Fruton, W. H. Stein,* and *M. Bergmann,* J. org. Chemistry *11,* 559 (1946); b) *J. S. Fruton, W. H. Stein, M. A. Stahmann,* and *C. Golumbic, ibid. 11,* 571 (1946); c) *C. Golumbic, J. S. Fruton,* and *M. Bergmann, ibid. 11,* 581 (1946); d) *E. Pfeil* and *U. Harder,* Angew. Chem. *79,* 188 (1967); Angew. Chem. internat. Edit. *6,* 178 (1967); e) *H. Stamm,* Chem. Ber. *99,* 2556 (1966).

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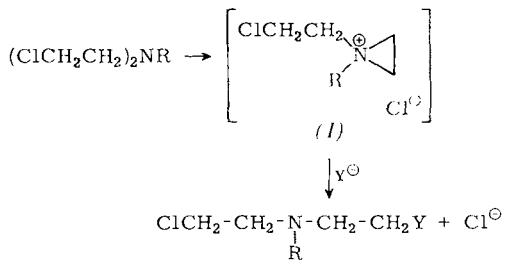
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[13] a) *C. Golumbic, J. S. Fruton,* and *M. Bergmann,* J. org. Chemistry *11,* 518 (1946); b) *J. S. Fruton* and *M. Bergmann, ibid. 11,* 543 (1946); c) *C. Golumbic, M. A. Stahmann,* and *M. Bergmann, ibid. 11,* 550 (1946).

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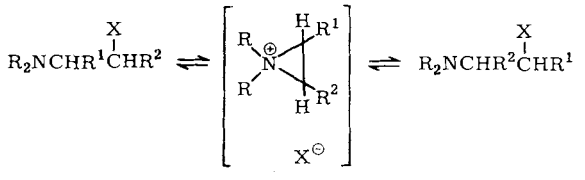
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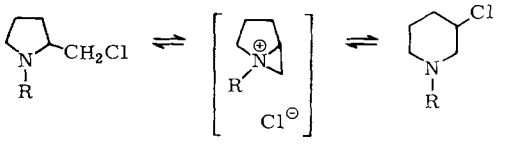
(1)

tion of the nucleophile. A complete kinetic analysis including all products is consistent with *(1)* as an essential intermediate, and NMR methods have enabled direct observation of an increasing aziridinium ion concentration and subsequent dimerization [16].

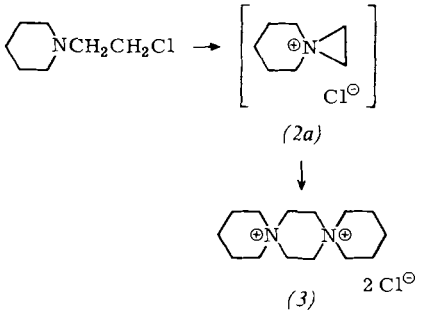
Early workers observed rearrangements of the following type [17].



The rearrangement occurs with α-bromo-β-(tertiary-amino) ketones ($R^2 = COC_6H_5$) [18] in a reaction recently observed [19] to be stereospecific. For cyclic amines, this rearrangement can cause ring expansions [20] or contractions [21].

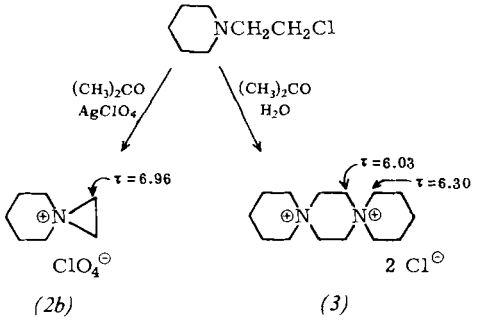


An early claim [22] to the isolation of *(2a)* as a salt appears erroneous [23], since the reaction conditions would have favored formation of piperazinium salt *(3)*.



(2a) *(3)*

Unambiguous proof that the isolated product was dimeric comes from the independent synthesis [24] of salts corresponding to both *(2b)* and *(3)* and the demonstration that the original reaction conditions gave a product consistent only with structure *(3)*.



(2b) *(3)*

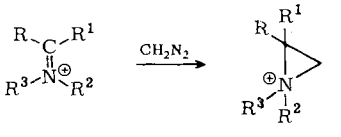
The upfield NMR shift of aziridinium ring protons relative to unstrained $-\overset{\oplus}{N}-CH_2-$ is similar to the upfield shift of cyclopropane protons and is diagnostic of an aziridinium ring. The first authentic isolated aziridinium salt is probably the picrylsulfonate reported by *Golumbic*, *Fruton*, and *Bergmann* [13a]; however, in this and later cases [25] low solubility hindered further study.

2.2. Synthesis of Stable Aziridinium Salts

The success of new synthetic methods for the isolation of aziridinium salts depends to a large extent on a judicious choice of solvent and nucleophiles involved. In the absence of adequate reactivity and spectral data or molecular weight determinations, the possibility that the product is dimeric should be recognized.

2.2.1. Reaction of Diazomethane with Iminium Salts

The most general preparation of stable aziridinium salts is by the reaction of diazomethane with an iminium perchlorate or tetrafluoroborate [*] in methanol/ether, acetonitrile, acetone, or, preferably, methylene chloride at 0 °C [26].



[16] a) *P. L. Levins* and *Z. B. Papanastassiou*, J. Amer. chem. Soc. *87*, 826 (1965); b) *G. R. Pettit*, *J. A. Settepani*, and *R. A Hill*, Canad. J. Chem. *43*, 1792 (1965).

[17] a) *J. F. Kerwin*, *G. E. Ullyot*, *R. C. Fuson*, and *C. L. Zirkle*, J. Amer. chem. Soc. *69*, 2961 (1947); b) *W. R. Brode* and *M. W. Hill*, *ibid. 69*, 724 (1947); c) *E. M. Schultz* and *J. M. Sprague*, *ibid. 70*, 48 (1948); d) *A. C. Cope et al.*, *ibid. 71*, 554 (1949); e) *S. D. Ross*, *ibid. 69*, 2982 (1947).

[18] *N. H. Cromwell* and *D. J. Cram*, J. Amer. chem. Soc. *65*, 301 (1943).

[19] *P. L. Southwick*, *A. K. Colter*, *R. J. Owellen*, and *Y.-C. Lee*, J. Amer. chem. Soc. *84*, 4299 (1962).

[20] *R. C. Fuson* and *C. L. Zirkle*, J. Amer. chem. Soc. *70*, 2760 (1948).

[21] *R. H. Reitsema*, J. Amer. chem. Soc. *71*, 2041 (1949).

[22] *W. Marckwald* and *O. Frobenius*, Ber. dtsch. chem. Ges. *34*, 3544 (1901).

[23] *H. Bestian* in *Houben-Weyl-Müller*: Methoden der Organischen Chemie. Georg Thieme Verlag, Stuttgart 1958, Vol. 11/2, p. 234.

[24] *N. J. Leonard* and *J. V. Paukstelis*, J. org. Chemistry *30*, 821 (1965).

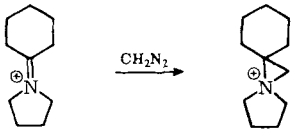
[25] a) *N. B. Chapman*, *J. W. James*, *J. D. P. Graham*, and *G. P. Lewis*, Chem. and Ind. *1952*, 805; b) *W. E. Hanby*, *G. S. Hartley*, *E. O. Powell*, and *H. N. Rydon*, J. chem. Soc. (London) *1947*, 519.

[*] Unless otherwise indicated, the aziridinium salts discussed here have tetrafluoroborate or perchlorate as the counter ion.

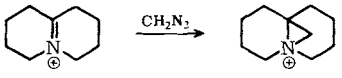
[26] *N. J. Leonard* and *K. Jann*, J. Amer. chem. Soc. *82*, 6418 (1960); *84*, 4806 (1962).

Numerous examples show that a wide range of *N*-alkyl and *C*-alkyl or -aryl substitution is allowed [27]. In a few cases, however, low product stability can lead to further reaction, such as thermal rearrangement of *N,N*-dibenzylaziridinium salts [28] or dimerization of the product when R = H, R^1 = aryl [29]. Other diazoalkanes also react with iminium salts to give products with a higher degree of substitution [26]. First discovered [26] with salt *(4)*, this preparative method has been extended [30] to bi- and tricyclic systems by similar reactions of the endocyclic iminium salts *(5)* and *(6)*.

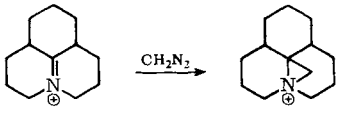
(4)



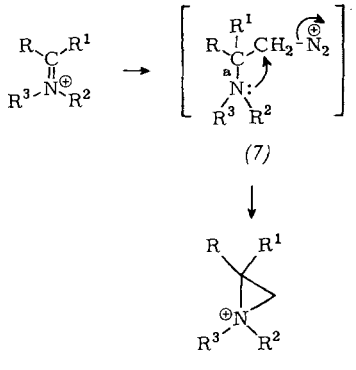
(5)



(6)



The mechanism of addition probably involves initial attack of diazomethane [31] at the highly electrophilic carbimino position [6] of the iminium salt. The timing of subsequent steps is uncertain, but the reaction can be considered in simplified form as a stepwise process analogous to diazomethane addition to ketones to give epoxides [32]. This is suggested by the preliminary finding that the reaction is not completely stereospecific.



(7)

Mixtures of *N*-ethyl-*N*-methylisobutylideneammonium tetrafluoroborate containing 65, 35, and 14% of the *cis* isomer (obtained by fractional crystallization), in reaction with diazomethane gave aziridinium salts containing 42, 25, and 21% *cis* isomer, respectively [33]. *N*-Ethylisobutylideneammonium tetrafluoroborate containing 100% *trans* isomer (presumed on a steric basis and consistent with NMR data) gave 13% of the *cis* product.

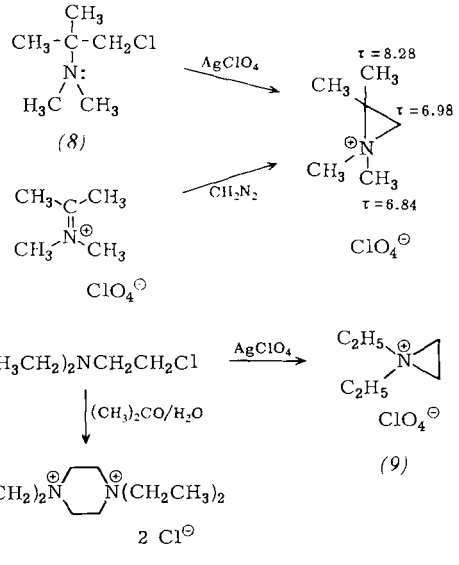
A reasonable explanation of these data is that the reaction intermediate involves diazonium or derived carbonium ions which can equilibrate by rotation about a bond [a in *(7)*]. Since the product distribution resembles that of the starting material, ring closure of the initial adduct *(7)* appears to be more rapid than rotation about bond a in the limited number of cases examined.

In those few cases where ring expansion has also been observed [34, 35], the intermediacy of *(7)* or the derived carbonium ion is indicated, and $C \rightarrow C^{\oplus}$ migration can apparently compete with $N \rightarrow C^{\oplus}$ ring closure.

Most starting iminium salts can be prepared from the enamines or, in a modified procedure, directly from the ketone and amine perchlorate in the presence of a trace of free amine [36].

2.2.2. Reaction of β-Haloethylamines with Silver Perchlorate

This method, conceptually like the original reactions in which aziridinium ions were postulated, differs in that the reaction is carried out in the absence of good nucleophiles and under conditions where halide loss is



(8)

(9)

[27] *N. J. Leonard, J. V. Paukstelis,* and *L. E. Brady,* J. org. Chem. *29,* 3383 (1964). Simple aziridinium salt formation has not been observed when R^1 was a halogeno, tertiary amino, or alkoxy group [29, 77]).

[28] *N. J. Leonard, P. C. Kelley, J. E. Mulvaney, B. Müller,* and *A. G. Cook,* to be published.

[29] *J. A. Klainer,* Ph. D. Thesis, University of Illinois, 1968.

[30] *N. J. Leonard, K. Jann, J. V. Paukstelis,* and *C. K. Steinhardt,* J. org. Chemistry *28,* 1499 (1963).

[31] a) *B. Eistert* in *W. Foerst*: Newer Methods of Preparative Organic Chemistry. Interscience, New York 1948, p. 513ff; b) *P. K. Kadaba,* Tetrahedron *23,* 2453 (1967); c) *N. J. Turro* and *W. B. Hammond,* J. Amer. chem. Soc. *88,* 3672 (1966); d) *F. Arndt, B. Eistert, R. Gompper,* and *W. Walter,* Chem. Ber. *94,* 2125 (1961).

[32] *C. D. Gutsche,* Org. Reactions *8,* 364 (1954).

[33] *K. Zahn,* Ph.D. Thesis, University of Illinois, 1967. (One explanation for the apparent discrepancy for the 14% *cis* iminium salt mixture is that the *cis* rotamer comprises about 20% of the equilibrium mixture of intermediates. The effect of partial equilibrium is to cause any distribution of starting material to approach this value.)

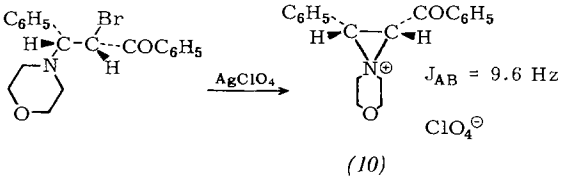
[34] *G. Opitz* and *A. Griesinger,* Liebigs Ann. Chem. *665,* 101 (1963).

[35] *P. C. Kelley,* Ph.D. Thesis, University of Illinois, 1965.

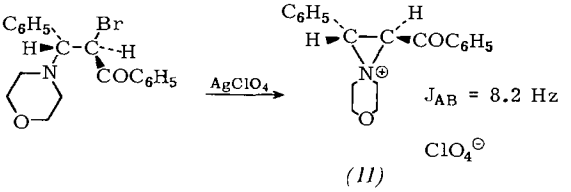
[36] a) *N. J. Leonard* and *J. V. Paukstelis,* J. org. Chemistry *28,* 3021 (1963) and references therein; b) *R. M. Scribner, ibid. 30,* 3203 (1965).

irreversible[24,37]. It also appears to be general, limited only by the availability of the starting amine. Treatment of the chloroamine *(8)* with silver perchlorate gives the same product as the diazomethane reaction with the iminium salt. The reactive intermediate *(9)* postulated in early kinetic studies[15c] was isolated in 94% yield by this method.

The product showed characteristic NMR absorption at τ 6.93 and was found to be monomeric, whereas the piperazinium salt, formed on standing in acetone-water, showed absorption at τ 6.03. In the rearrangement of α-bromo-β-(tertiary-amino) ketones, *threo* and *erythro* forms produced isomeric aziridinium intermediates which could be assigned structures *(10)* and *(11)*, respectively, by NMR[37]. From the assignment it could be concluded that these haloamines proceed stereospecifically to the aziridinium intermediate as suggested earlier[19].

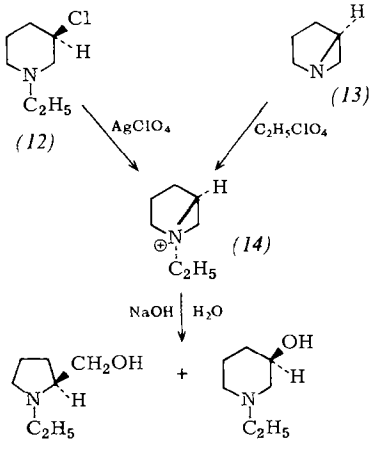


(10)



(11)

A similar stereospecific reaction sequence has been reported[38] for the chloromethylpyrrolidine-chloropiperidine system. Thus *(12)* reacts with silver perchlorate to give the same product as that obtained by alkylation of 1-azabicyclo[3.1.0]hexane *(13)*. Both the aziridinium salt *(14)* and the chloropiperidine give the same product mixture on alkaline hydrolysis. Moreover the entire process is stereospecific, since 95 ± 5% retention of configuration is observed in the conversion of *(12)* into the hydroxypiperidine, thereby ruling out a dissociated carbonium ion intermediate.

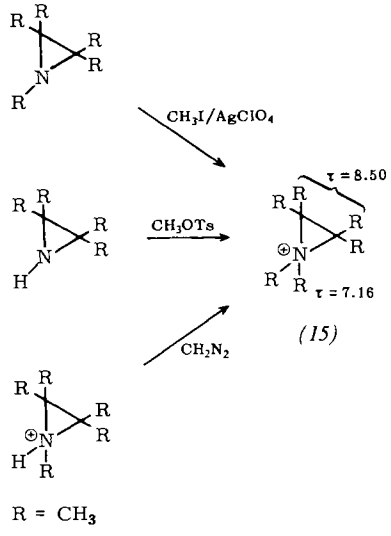


(12) *(13)* *(14)*

2.2.3. Quaternization

A promising method for quaternization[24] appears to be the use of alkyl halides in the presence of silver perchlorate[39]. Even the highly strained 1-ethyl-1-azoniabicyclo[3.1.0]hexane salt *(14)* prepared in this manner withstood ring opening when perchlorate was the only nucleophile present[38].

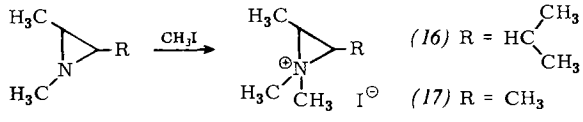
This procedure provides a route to hexamethylaziridinium salts *(15)*, which can also be obtained by alkylation with methyl tosylate or by the method of diazomethane insertion into an $N^{\ominus}$–H bond[40,41].



(15)

Some aziridinium salts have been synthesized by direct alkylation but the method seems to depend upon steric hindrance to subsequent reactions. This is indicated by the fact that the iodide *(16)* could be crystallized[42] while *(17)* decomposed on attempted crystallization[43].

Steric effects probably account for the unusual stability of the aziridinium iodides made in this manner from imines of cycloheptene[44], cyclooctene[45], cyclodecene[45], and cyclo-



(16) R = HC(CH3)2

(17) R = CH3

[37] *N. J. Leonard, R. Y. Ning*, and *R. L. Booth*, J. org. Chemistry *30*, 4357 (1965).

[38] *C. F. Hammer* and *S. R. Heller*, Chem. Commun. *1966*, 919. The stereochemistry shown in *(12)*, *(13)*, *(14)*, and the hydrolysis products were indicated by private communication from Prof. *Hammer*.

[39] a) *H. Bruton* and *P. F. G. Praill*, Chem. and Ind. *1951*, 939; b) *J. Radell, J. W. Connolly*, and *A. J. Reymond*, J. Amer. chem. Soc. *83*, 3958 (1961).

[40] a) *E. Müller, H. Huber-Emden*, and *W. Rundel*, Liebigs Ann. Chem. *623*, 34 (1959); b) *E. Müller, H. Kessler*, and *B. Zech*, Fortschr. chem. Forsch. *7*, 128 (1966).

[41] *N. J. Leonard* and *B. Müller*, unpublished work.

[42] *A. T. Bottini* and *R. L. VanEtten*, J. org. Chemistry *30*, 575 (1965).

[43] *G. K. Helmkamp, R. D. Clark*, and *J. R. Koskinen*, J. org. Chemistry *30*, 666 (1965).

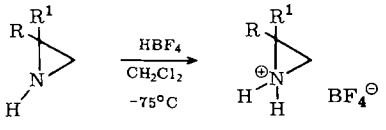
[44] *P. E. Fanta, R. Golden*, and *H.-J. Hsu*, J. chem. Engng. Data *9*, 246 (1964).

[45] *P. E. Fanta, L. J. Pandya, W. R. Groskopf*, and *H.-J. Su*, J. org. Chemistry *28*, 413 (1963).

dodecene[46]. In several of these cases, structures are known by X-ray analysis[46,47]. In general, the initial reaction of an aziridine with alkyl halides is followed by ring opening by the nucleophilic counter ion[22,48]. Furthermore, alkylation at elevated temperatures can lead to thermal rearrangement of the desired product, as shown by recent work[49] which disproved a patent claim for simple alkylation in refluxing benzyl chloride[50].

2.2.4. Protonation of Aziridines

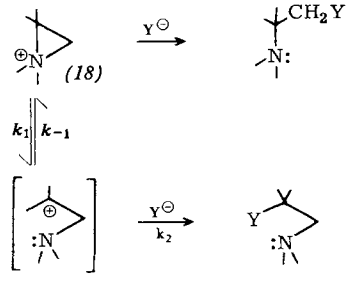
Certain aziridinium salts containing $^{\oplus}$N–H have been isolated, but such isolation seems to depend upon special circumstances such as product insolubility, low temperature isolation, steric hindrance to displacements, or non-nucleophilic counter ions. Thus hydrochlorides[51] and poly-nitro or-halogenophenolates[52] have been isolated by precipitation from the reaction medium at low temperature. Use of non-nucleophilic acids such as picric[53] and picrylsulfonic acids[51c] and 1,1-dinitroethane[54] enabled isolation of salts due to low solubility. A recent development of considerable synthetic potential in this area is the use of tetrafluoroboric acid[55].



This method avoids the usual difficulty attendant upon protonation: facile ring opening by nucleophile or solvent[56]. Competitive S_N1 and S_N2 reactions can occur, with the dominant process determined by the particular substrate and nucleophile[57]. A recent example of the opening of a steroidal aziridine to give exclusively a *trans* diaxial product has been reported[58].

2.3. Reactions of Stable Aziridinium Salts

The most important reactions of aziridinium salts, including solvolysis, nucleophilic attack, dipolar additions, and thermal rearrangements, are shown in Scheme 1. These reactions can be classified, to some extent arbitrarily, as direct displacements by nucleophiles or as reactions of aminocarbonium ions. Whether the second process is S_N1 depends on the

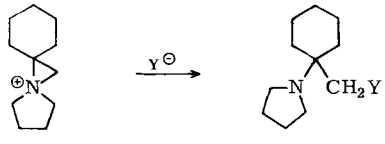


Scheme 1

relative rates of k_{-1} *vs* k_2 [$Y^{\ominus}$], and this point is under current investigation. However, for the purposes of this review reactions will be discussed in these terms on the basis of product analysis. In either case, as mentioned earlier, a reactive electrophile is converted into a good nucleophile (the $-NR_2$ group).

2.3.1. Direct Displacements

It has long been known that aziridinium ions react readily[13a] with thiosulfate to give Bunte salts[59], a reaction which can be used for quantitative analysis[60]. Good nucleophiles cause ring opening with attack at the less hindered carbon atom in the manner of S_N2 reactions[61].



Y = CN, OCH_3, N_3, OAc, C_6H_5O

A related process is the tendency of aziridines under cationic catalysis to dimerize or polymerize, depending upon the nature of the solvent, nucleophiles present, and aziridine substitution[62]. After formation of *(19)*, the reaction can take two courses: Reaction with an

[46] *L. M. Trefonas* and *J. Couvillion*, J. Amer. chem. Soc. *85*, 3184 (1963).

[47] a) *L. M. Trefonas* and *R. Towns*, J. heterocyclic Chem. *1*, 19 (1964); b) *L. M. Trefonas* and *R. Majeste*, Tetrahedron *19*, 929 (1963).

[48] *T. Taguchi* and *M. Eto*, J. Amer. chem. Soc. *80*, 4075 (1958).

[49] *N. J. Leonard, B. Müller, F. Toda*, and *P. C. Kelley*, unpublished work.

[50] a) *E. W. Gassenmeier* and *C. Schuster*, German Pat. 879695 (June 15, 1953) Badische Anilin- & Soda-Fabrik; Chem. Zbl. *1955*, 6342; b) *E. W. Gassenmeier* and *C. Schuster*, US Pat. 2694704 (Nov. 16, 1954); Chem. Abstr. *49*, 13296 (1955).

[51] *G. F. Hennion* and *P. E. Butler*, J. org. Chemistry *27*, 2088 (1962); b) *W. A. Skinner, A. P. Martinez, H. F. Gram, L. Goodman*, and *B. R. Baker*, *ibid. 26*, 148 (1961); c) *R. D. Clark* and *G. K. Helmkamp*, *ibid. 29*, 1316 (1964).

[52] a) *S. J. Kuhn*, US Pat. 3335130 (August 8, 1967); Chem. Abstr. *68*, 78114 (1968); b) *S. J. Kuhn*, US Pat. 3335132 (August 8, 1967); Chem. Abstr. *68*, 87131; additional reactions can occur with phenols [57d].

[53] *L. B. Clapp, E. A. Rick, W. B. Moniz*, and *V. B. Schatz*, J. Amer. chem. Soc. *77*, 5116 (1955).

[54] *J. S. Belew, C. E. Grabiel*, and *L. B. Clapp*, J. Amer. chem. Soc. *77*, 1110 (1955).

[55] *U. Harder, E. Pfeil*, and *K. F. Zenner*, Chem. Ber. *97*, 510 (1964).

[56] a) *A. Weissberger* and *H. Bach*, Ber. dtsch. chem. Ges. *65*, 631 (1932); b) *J. E. Earley, et al.*, J. Amer. chem. Soc. *80*, 3458 (1958).

[57] a) *V. B. Schatz* and *L. B. Clapp*, J. Amer. chem. Soc. *77*, 5113 (1955); b) *L. B. Clapp*, *ibid. 70*, 184 (1948); c) *G. Meguerian* and *L. B. Clapp*, *ibid. 73*, 2121 (1951); d) *L. B. Clapp*, *ibid. 73*, 2584 (1951); e) for reference to the hydrolysis of ethylidenimmonium ion, see *B. T. Baliga, A. K. Rantamaa*, and *E. Whalley*, J. physic. Chem. *69*, 1751 (1965).

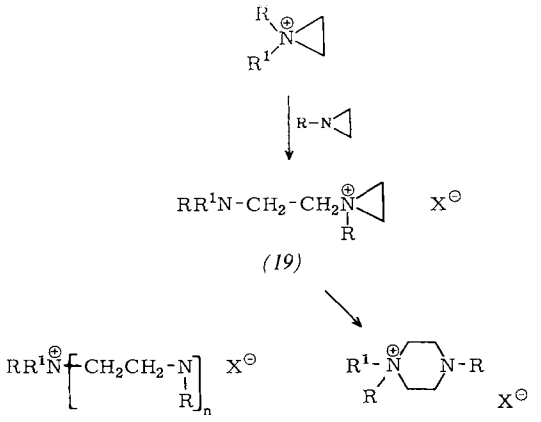
[58] *A. Hassner* and *C. Heathcock*, J. org. Chemistry *30*, 1748 (1965).

[59] *H. Distler*, Angew. Chem. *79*, 520 (1967); Angew. Chem. internat. Edit. *6*, 544 (1967).

[60] a) *F. C. Schaefer, J. T. Geoghegan*, and *D. W. Kaiser*, J. Amer. chem. Soc. *77*, 5918 (1955); b) *E. Allen* and *W. Seaman*, Analytic. Chem. *27*, 540 (1955).

[61] *N. J. Leonard, J. E. Mulvaney*, and *E. F. Kiefer*, unpublished work.

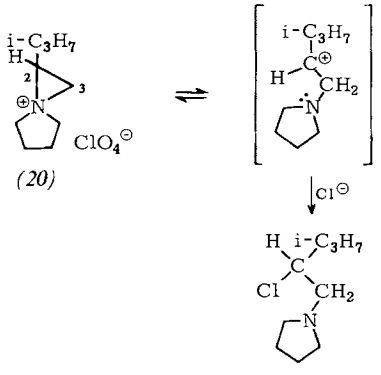
[62] *C. R. Dick*, J. org. Chemistry *32*, 72 (1967).

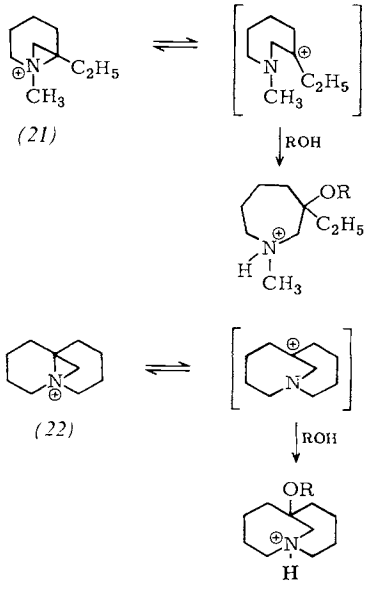


excess of aziridine leads to polymer, while reaction with $X^{\ominus}$ will cause ring opening and subsequent closure to dimer. By suitable choice of anion and solvent, quantitative yields of either polymer or dimer can be achieved.

2.3.2. Aminocarbonium Ion Reactions

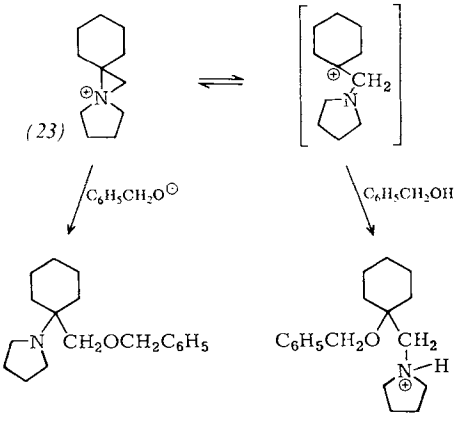
The tendency of an aziridinium salt to react as an aminocarbonium ion is shown by the reaction of *(20)* with chloride ion at C-2 [24]. A reasonable interpretation is that reaction proceeds through the more stable of two possible carbonium ions. In an S_N2-type process, nucleophilic attack would have occurred at the less hindered C-3. Solvolysis under neutral conditions also gives products derived from an aminocarbonium ion [26], in contrast to the direct displacement when alkoxide ions are present.



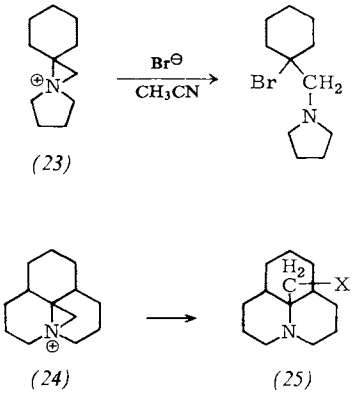


If the original aziridinium C–N$^{\oplus}$ bond is endocyclic, the reaction of such an aminocarbonium ion with solvent can bring about a ring expansion, as illustrated by the alcoholysis of *(21)* [30]. This reaction has been extended to bicyclic compounds such as *(22)* to effect double ring expansion.

As with typical S_N1 and S_N2 reactions, competition between the two mechanisms occurs, and changing reaction conditions or substrates can reverse the preferred pathway. For example, *(23)* undergoes an aminocarbonium ion reaction under neutral solvolysis conditions but an S_N2 reaction occurs with alkoxide [63].



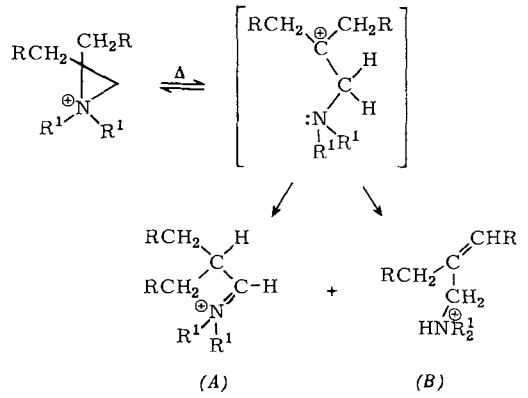
As an illustration of the case in which the same reaction conditions give either type of product, depending on the substrate [30], the perchlorate of *(23)* with lithium bromide in acetonitrile reacts as an aminocarbonium ion while *(24)* undergoes displacement to give *(25)* (X = Br). The more rigid carbon skeleton in the tetracyclic case probably resists the ring flattening and expansion necessary to form a *tert*-carbonium ion at the central bridgehead. Thus it is not surprising that *(24)* also produces the ether derivative *(25)* (X = OCH_3) on methanolysis.



2.3.3. Thermal Rearrangements

Aziridinium salts containing the ring carbon grouping $-CH_2-CR_2-$ undergo thermal rearrangements in the

[63] *N. J. Leonard, E. F. Kiefer,* and *L. E. Brady,* J. org. Chemistry *28*, 2850 (1963).

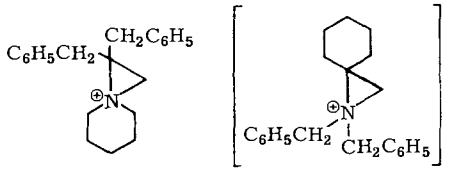


(A) (B)

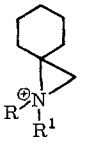
melt and in inert solvents to give iminium salts or a mixture of iminium and alkenylammonium salts [6, 28].

Thermal stability and product ratio depend markedly on the aziridinium structure. Work is in progress to delineate steric and electronic effects on the rearrangement.

At this stage, comparison of the stability of sterically similar salts *(26)* and *(27)* suggests that the dominant effect is electronic. While *(26)* is stable below its m.p. (139 °C), *(27)* is too labile to be isolated; reaction of the appropriate iminium salt with diazomethane gives only rearrangement products [28]. Increasing the number of *N*-benzyl substituents through the series



(26) *(27)*

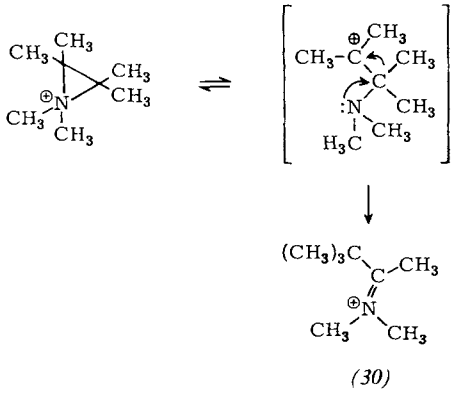


(28) R = R^1 = C_2H_5

(29) R = $CH_2C_6H_5$

R^1 = C_2H_5

(28), *(29)*, and *(27)* also increases product ratio *(B)*/*(A)* with values 25/75, 51/49, and 82/18, respectively [35]. A possible mechanism involves formation of



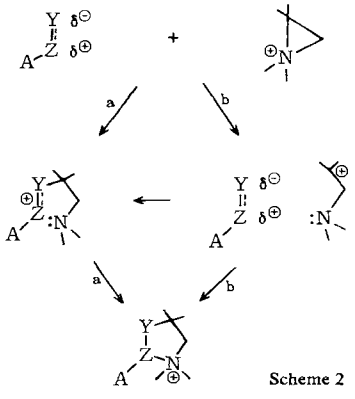
(30)

the more stable aminocarbonium ion followed by hydrogen migration to give products.

Also consistent with this mechanism is the rearrangement of hexamethylaziridinium perchlorate to give *(30)*, which can be interpreted as a Wagner-Meerwein methyl shift in the proposed intermediate [28].

2.3.4. Polar and Dipolar Additions

By considering the ring system as an aminocarbonium ion one can see the bifunctional nature of aziridinium ions and intuitively might expect additions to polar and dipolar species (Scheme 2).



Scheme 2

Here a three-membered ring is expanded to a five-membered ring, both bearing positive charges. This process has been conveniently written [27] as ③⊕ + 2→⑤⊕. This description is consistent with *Huisgen*'s [64] recent definitions in which a cycloaddition step is classified according to the number of new σ-bonds formed, with subdivisions determined by the number of ring members involved. An electronic description, on the other hand, awaits theoretical calculations similar to those reported for trimethylene and related 1,3-dipoles [65].

Whether the reaction is stepwise (path a) or concerted (path b) is a difficult question currently under discussion in the case of 1,3-dipolar cycloaddition [66]. Work on the kinetics and stereospecificity of the cycloaddition [67] represented in Scheme 2 should help in elucidating the mechanism. For reasons of clarity and ability to rationalize simultaneous solvolysis and thermal rearrangements, these ring expansions will be illustrated in terms of aminocarbonium ion intermediates, though it is hoped the reader will bear in mind the mechanistic ambiguities.

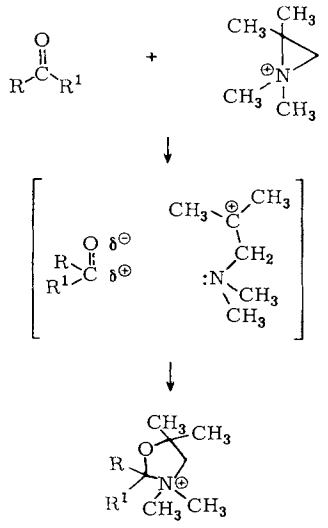
The first ③⊕ + 2→⑤⊕ expansions were observed with aldehydes [63] and ketones [27]. Structures of the oxazolidinium salt products were consistent with reaction

[64] *R. Huisgen*, Angew. Chem. *80*, 329 (1968); Angew. Chem. internat. Edit. *7*, 321 (1968).

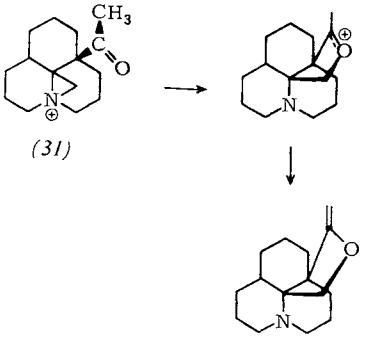
[65] *R. Hoffmann*, J. Amer. chem. Soc. *90*, 1475 (1968).

[66] a) *R. A. Firestone*, J. org. Chemistry *33*, 2285 (1968); b) *R. Huisgen*, *ibid. 33*, 2291 (1968).

[67] The definition of "cycloaddition" [64] includes both concerted and stepwise processes. In the present case, aziridinium ions are considered polar species since they bear a full positive charge even when ring-opened; "polar additions" are those in which the second species can be represented without formal charge separation, while "dipolar additions" are those in which this species requires charge separation in all its formal structures.



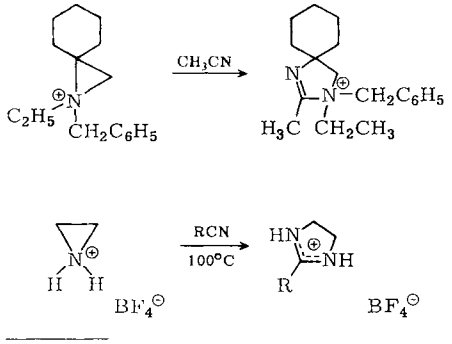
of the electronegative atom at the more stable carbonium ion center as shown. Generality was demonstrated by successful reaction of various aziridinium perchlorates with aromatic aldehydes, aryl and alkyl ketones, and cycloalkanones. If sterically prevented from 1,2-addition, a carbonyl group can function as a weak nucleophile [*(31)*→*(32)*][68,69].

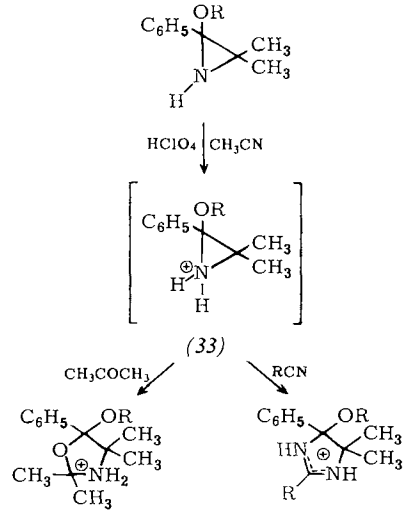


(31)

(32)

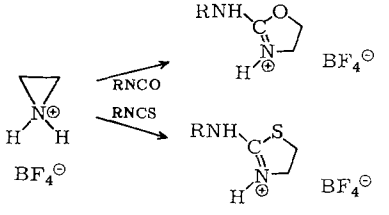
The same type of ring expansion occurs with nitriles and substituted[70] or unsubstituted aziridinium ions[71] to give imidazolium salts. Alkoxy ring substituents do not interfere with the expansion; thus the cation *(33)*, formed by protonation, can also undergo ring expansion with nitriles and ketones[72]. The same



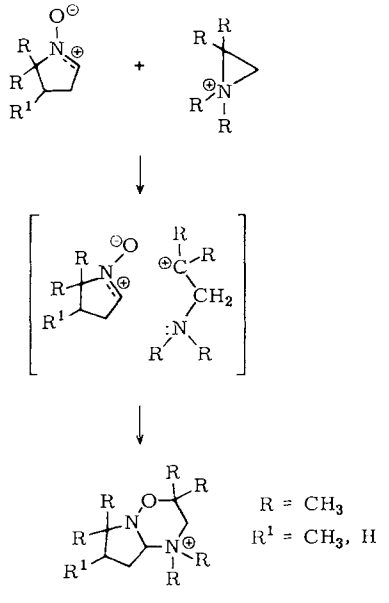


(33)

reaction conditions can cause analogous reactions with oxiranes, as previously observed in the presence of tin chloride[73].



Isocyanates and isothiocyanates also undergo 1,2-polar addition to aziridinium tetrafluoroborate[74] to give another type of ③⊕ + 2→⑤⊕ process.



(34)

[68] a) *G. Baddeley, E. K. Baylis, B. G. Heaton*, and *J. W. Rasburn*, Proc. chem. Soc. (London) *1961*, 451; b) *H. Wiener* and *R. A. Sneen*, J. Amer. chem. Soc. *85*, 2181 (1963); c) *B. Capon, M. J. Perkins*, and *C. W. Rees*: Organic Reaction Mechanisms. John Wiley and Sons, London 1965, p. 55.

[69] *C. K. Steinhardt*, Ph. D. Thesis, University of Illinois, 1963.

[70] *N. J. Leonard* and *L. E. Brady*, J. org. Chemistry *30*, 817 (1965).

[71] *E. Pfeil* and *U. Harder*, Angew. Chem. *77*, 505 (1965); Angew. Chem. internat. Edit. *4*, 518 (1965).

[72] *N. J. Leonard* and *B. Zwanenburg*, J. Amer. chem. Soc. *89*, 4456 (1967).

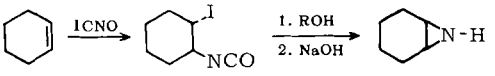
[73] *T. I. Temnikova* and *T. E. Zhesko*, Ž. obšč. Chim. *33*, 3436 (1965).

[74] *E. Pfeil* and *K. Milzner*, Angew. Chem. *78*, 677 (1966); Angew. Chem. internat. Edit. *5*, 667 (1966).

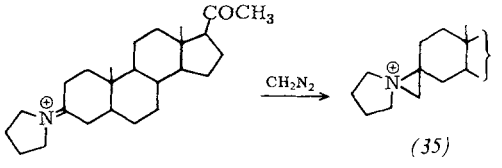
A 1,3-dipolar addition has been carried out[75] with aziridinium perchlorates and nitrones to give the novel heterocyclic system *(34)*. These reactions constitute a ③⊕ + 3→⑥⊕ conversion.

2.4. Synthetic Utility of Aziridinium Salts

Since the ready availability of aziridines is a decisive factor in this connection, the following synthesis starting from olefins should play an important role[76].



Ring expansions by solvolysis or by 1,2-polar and 1,3-dipolar additions can lead to complex heterocyclic ring systems in good yields. These ③⊕ + 2→⑤⊕ and ③⊕ + 3→⑥⊕ expansions parallel the extremely useful Diels-Alder synthesis of carbocyclic systems. The addition of diazomethane to iminium salts occurs so readily, even at low temperature, that side reactions with carbonyl groups do not interfere. Thus the steroidal aziridinium salt *(35)* was obtained in 70% yield[77].



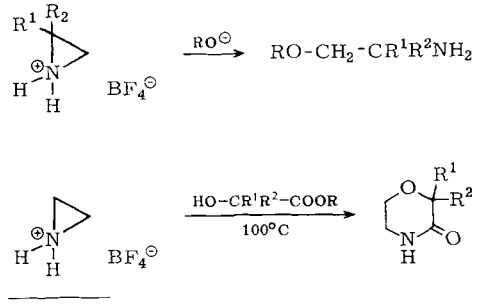
(35)

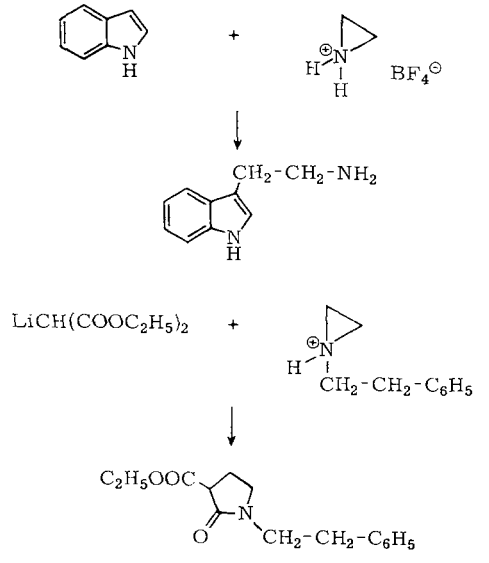
The proper combination of sequences involving enamines, iminium salts, and aziridinium ion reactions can be very useful in alkaloid synthesis. An example of direct displacement by hydride was reported in a β-benzomorphan synthesis[78].



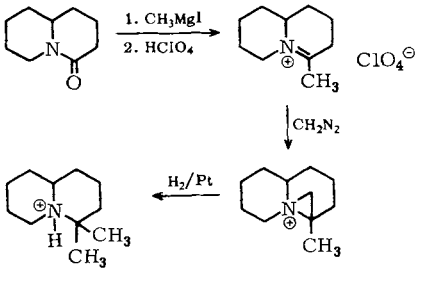
Amino ethers can be prepared by alkoxide displacement on aziridinium ions[55]. An extension of this reaction is the preparation of oxalactams by similar alkylation of hydroxy esters, with subsequent ring closure[1d]. Side reactions leading to linear polyamides limited yields to the 27–34% range.

C-Alkylation of indole by aziridinium ions gives tryptamine. With 2-methylindole, the 3-aminoethyl product was formed in 80–90% yield[1d]. Diethyl lithiomalonate reacts with *N*-(2-phenylethyl)aziridine only in the presence of an excess of malonic ester, which suggests reaction of an aziridinium ion[1e].





Hydrogenation causes reductive cleavage of a C–N⊕ aziridinium bond[26]. This reaction has been used as a synthetic route to introduce *gem*-dimethyl substitution α to nitrogen[79].



3. Azetidinium Salts

Although azetidinium salts are quite stable, their literature is not so extensive as that for aziridinium compounds since some are difficult to synthesize and they appear to have less biological activity[80]. Many of the syntheses and reactions are directly analogous to those described above for aziridinium salts.

The earliest example of an azetidinium salt was reported by *Gabriel*[81]. However, it was possible that the vigorous conditions used in its formation had caused dimerization. The original claim was proved valid by preparation of authentic, monomeric *(36)* under

[75] *N. J. Leonard, D. A. Durand,* and *F. Uchimaru,* J. org. Chemistry *32,* 3607 (1967).

[76] *A. Hassner, M. E. Lorber,* and *C. Heathcock,* J. org. Chemistry *32,* 540 (1967).

[77] *J. V. Paukstelis,* Ph.D. Thesis, University of Illinois, 1965.

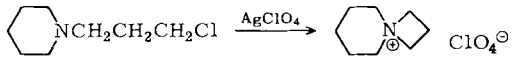
[78] *E. M. Fry,* J. org. Chemistry *30,* 2058 (1965).

[79] *N. J. Leonard* and *R. Lambert,* unpublished work.

[80] Ref. [11], p. 908.

[81] *S. Gabriel* and *R. Stelzner,* Ber. dtsch. chem. Ges. *29,* 2381 (1896).

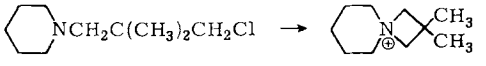
the action of silver perchlorate [82] and conversion of *Gabriel*'s chloride to the same salt.



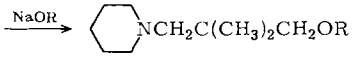
(36)

3.1. Azetidinium Salts as Reactive Intermediates

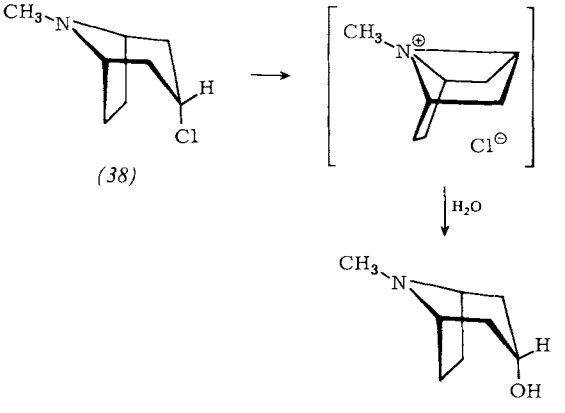
To explain an enhanced rate of substitution in the γ-chloroamine *(37)* relative to neopentyl chloride, *Wheatley* and *Cheney* postulated [83] reaction through the azetidinium ion.



(37)



Similarly an azetidinium ion intermediate was invoked [84] to account for retention of configuration in the solvolysis of tropanyl chloride *(38)*. The epimeric chloride underwent fragmentation with loss of chloride, as predicted by *Grob*'s stereoelectronic fragmentation rules [85].

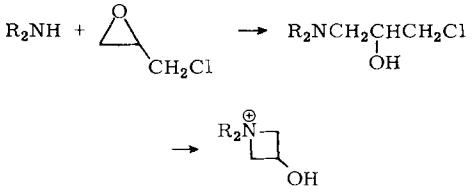


(38)

3.2. Synthesis of Azetidinium Salts

Direct alkylation of 1-alkylazetidines leads to isolable azetidinium salts. Precursors can be obtained by cyclization of secondary amines having a suitable leaving group in the γ-position or by reduction of β-lactams and malonimides [11].

The cyclization procedure has recently been extended to the synthesis of 3,3-disubstituted azetidinium salts [86] previously obtained by an indirect route [87]. A second mode of preparation is the direct cyclization of tertiary amines [11]; thus a monomeric [89] 3-hydroxyazetidinium chloride was synthesized from a secondary amine and epichlorohydrin [88].



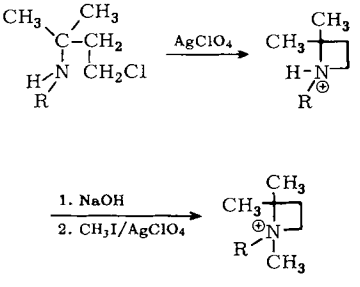
The main synthetic problem lies in the sluggishness of cyclization which permits side reactions such as fragmentation, elimination, and polymerization. In these competitive processes, the steric requirements of substituents are an important factor [90]. As illustrated for a sulfonamido anion, the conformation preceding cyclization is given by *(39)* while that for fragmentation is given by *(40)*. With this large *N*-substituent, form *(40)* is less important than for simple amines and



(39) *(40)*

cyclization is favored. Symmetrical *gem*-substitution on either C-2 or C-3 should have little effect on the rate of cyclization but should increase product stability [91]. *threo*-Substituents should have little effect on cyclization *vs.* fragmentation.

A modification of the cyclization procedure [82] for a primary chloride uses silver perchlorate. The first step is complete after one day at room temperature. Nearly



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[82] *N. J. Leonard* and *D. A. Durand*, J. org. Chemistry *33*, 1322 (1968).

[83] *W. B. Wheatley* and *L. C. Cheney*, J. Amer. chem. Soc. *74*, 1359 (1952).

[84] *S. Archer, M. R. Bell, T. R. Lewis, J. W. Schulenberg*, and *M. J. Unser*, J. Amer. chem. Soc. *80*, 4677 (1958).

[85] a) *C. A. Grob*, Experientia *13*, 126 (1957); b) *C. A. Grob*: Kekulé Symposium, Theoretical Organic Chemistry, Butterworth and Co., London 1959, p. 114.

[86] *A. G. Anderson* and *M. T. Wills*, J. org. Chemistry *33*, 2123 (1968).

[87] a) *E. Testa, L. Fontanella, L. Mariana*, and *G. F. Christiani*, Liebigs Ann. Chem. *633*, 56 (1960); b) *E. Testa, A. Bonati, G. Pagani*, and *E. Gatti, ibid. 647*, 92 (1961).

[88] a) *L. Niemilowicz*, Mh. Chem. *15*, 118 (1894); b) *B. Rothstein* and *K. Binovic*, C. R. hebd. Séances Acad. Sci. *236*, 1050 (1953).

[89] *J. H. Ross, D. Baker*, and *A. T. Coscia*, J. org. Chemistry *29*, 824 (1964).

[90] *W. R. Vaughan, R. S. Klonowski, R. S. McElhinney*, and *B. R. Millward*, J. org. Chemistry *26*, 138 (1961).

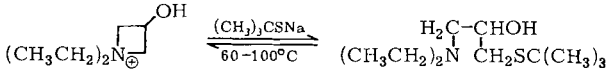
[91] For a general discussion of the *gem*-dimethyl effect, see a) *E. L. Eliel, N. L. Allinger, S. J. Angyal*, and *G. A. Morrison*: Conformational Analysis. Wiley, New York 1965, p. 191; b) *N. L. Allinger* and *V. Zalkow*, J. org. Chemistry *25*, 701 (1960), and references therein.

quantitative yields show that side reactions are eliminated at the low reaction temperature. This procedure has also been used to prepare bis(azetidinium) salts [92].

3.3. Reactions of Azetidinium Salts

3.3.1. Nucleophilic Ring Openings

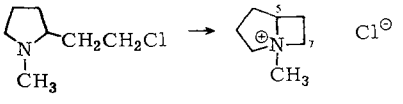
The reaction of monocyclic azetidinium salts represented by *(41)* with various nucleophiles [$(CH_3)_3CSNa$, R_2NH, R_3N, KOC_6H_5, KCN] has been investigated by *Gaertner* [93]. Although ring opening occurs readily in these cases, the chloride *(41)* does not react with refluxing methanol as do the aziridinium perchlorates.



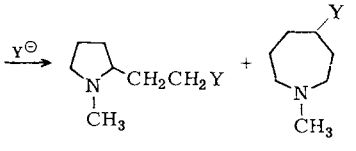
(41) *(42)*

It might be expected that the resultant tertiary γ-amino derivatives *(42)* could cyclize to the starting material, and this does happen with a compound of type *(42)* [Cl instead of $SC(CH_3)_3$]. Equilibrium constants for cyclization of the alcohols were *ca.* 50 times greater than for the corresponding acetates.

Nucleophilic ring openings occur in bicyclic systems as well, and can lead to a rearrangement [94] analogous to the chloromethylpyrrolidine-chloropiperidine system (see Section 2.2.2). Since the same product ratio was found starting from the γ-chloroamine *(43)* and

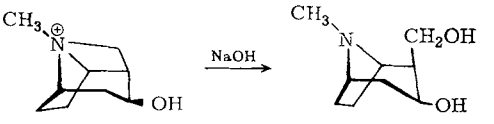


(43) *(44)*

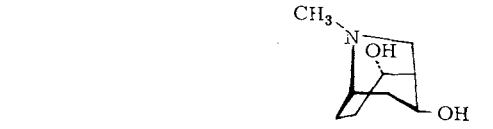


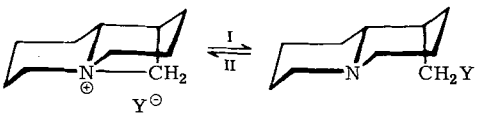
the independently synthesized *(44)*, it seems likely that *(43)* first undergoes an internal nucleophilic displacement to give the ion *(44)*. Reaction of $Y^{\ominus}$ at C-5 of *(44)* would then lead to ring expansion and at C-7 to direct substitution.

Similar ring opening displacements also occur in tricyclic systems such as *(45)* [95] and *(46)* [95–97]. In the latter case, a ring-chain isomerization was observed in which the product mixture depended on the nucleophile as indicated [96].



(45)

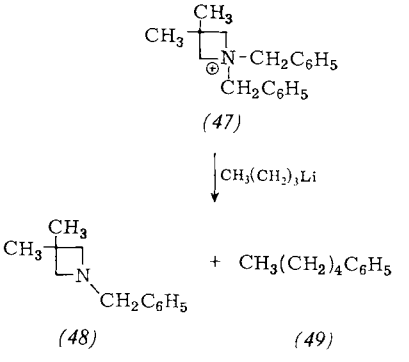




(46) I, Y = Br, I, CN, OCH_3
II, Y = OTs

A related process is dimerization and ultimately polymerization in which free azetidines act as nucleophiles. This reaction is not so important as in the aziridinium series, and while the *N,N*-dimethylazetidinium salt polymerizes fairly rapidly, the diethyl salt is relatively stable [98].

An exception to nucleophilic ring openings is the reaction of *(47)* with *n*-butyllithium at the benzylic position to give *(48)* and *(49)* along with rearrangement products [99].



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

3.3.2. Base-Catalyzed Eliminations and Rearrangements

Azetidinium salts containing α-methyl groups have been found [82, 100] to undergo an elimination reaction in contrast to the nucleophilic substitution observed in the bicyclic systems described above. Part of this difference may be due to facility of an E2 mechanism [101], since, as indicated for *(50)* [82] in Scheme 3, any of the six hydrogens of the methyl groups can lie

[92] *K. Morizawa et al.*, Japan. Pat. 4787 (March 16, 1966); Chem. Abstr. *65*, 730 (1966).

[93] *V. R. Gaertner*, J. org. Chemistry *33*, 523 (1968).

[94] *A. Ebnöther* and *E. Jucker*, Helv. chim. Acta *47*, 745 (1964).

[95] *G. Fodor, N. Mandava*, and *I. Weisz*, Tetrahedron *24*, 2357 (1968).

[96] *G. Fodor*, J. Amer. chem. Soc. *88*, 1040 (1966).

[97] *O. E. Edwards, G. Fodor*, and *L. Marion*, Canad. J. Chem. *44*, 13 (1966).

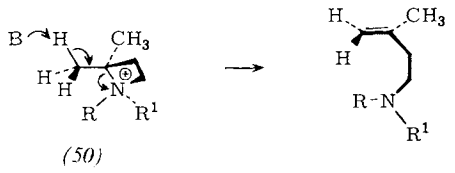
[98] *C. F. Gibbs* and *C. S. Marvel*, J. Amer. chem. Soc. *56*, 725 (1934); *57*, 1137 (1935).

[99] *A. G. Anderson* and *M. T. Wills*, J. org. Chemistry *32*, 3241 (1967).

[100] *M. Kohn* and *J. Giaconi*, Chem. Mh. *28*, 461 (1907); *M. Kohn* and *O. Morgenstern*, *ibid. 28*, 479 (1907).

[101] Other factors which are difficult to assess may be involved, such as those imposed by the rigid, strained bicyclic systems and the extent of other elimination mechanisms [102].

[102] *J. F. Bunnett*, Angew. Chem. *74*, 731 (1962); Angew. Chem. internat. Edit. *1*, 225 (1962).

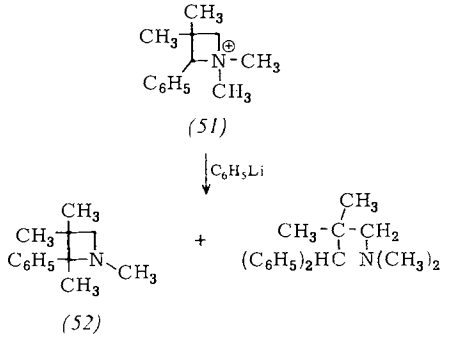


(50)

Scheme 3

in the *trans* coplanar arrangement of atoms required by this mechanism [102]. The similarity of ground and E2 transition state geometries, together with the inherent ring strain, may decrease the free energy of activation for elimination sufficiently so that no other processes can compete.

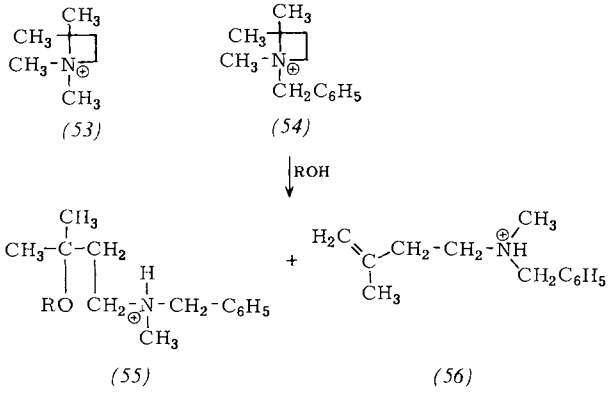
With a strong base such as phenyllithium or potassamide, ring opening of *(51)* occurs as the major reaction along with formation of a minor amount of a Stevens rearrangement product *(52)* [103]. It is possible that an ylide → ring-opened carbene mechanism is operative for this strained system.



(51) (52)

3.3.3. Reactions Proceeding *via* Aminocarbonium Ions

Azetidinium ions are less susceptible to S_N1-like ring openings than aziridinium salts, as illustrated by the complete failure of *(53)* to undergo solvolysis [82,104] or ring expansion [82], despite *gem*-dimethyl assistance to such reactions. The more reactive *N*-benzyl salt *(54)*, however, gave two products resulting from cleavage of the $N^{\oplus}$–C-2 bond [82]. This is particularly interesting in view of the lengthened C-2–N distance



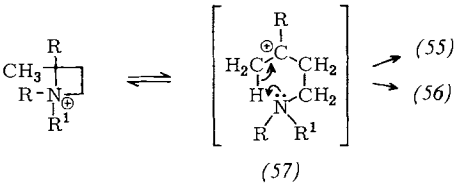
(53) (54) (55) (56)

[103] *A. G. Anderson* and *M. T. Wills*, J. org. Chemistry *33*, 536 (1968).

[104] Attempted methanolysis of a 3-hydroxyazetidinium salt was also unsuccessful [93].

(1.60 Å as determined by X-ray analysis [105]). Olefin *(56)*, formed initially about one-third as fast as *(55)*, was the sole product of attempted ring expansions with acetone or acetonitrile.

This reaction can be rationalized in terms of competitive S_N1 and E1 mechanisms involving the aminocarbonium ion intermediate *(57)*.

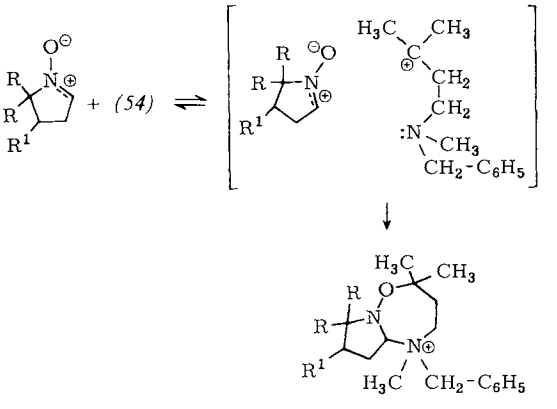


(57)

Kinetic control of product formation by a facile intramolecular hydrogen transfer could explain the absence of ring expansion or internal olefinic products. Alternatively the olefin may be formed by an E2 mechanism in which a catalytic amount of base transfers hydrogen from methyl to nitrogen.

3.3.4. Dipolar Additions

As mentioned above, azetidinium salts do not undergo 1,2-polar additions with acetone or acetonitrile. However, if the azetidinium $N^{\oplus}$–C bond is sufficiently reactive toward polar cleavage, as provided by the *N*-benzyl group in *(54)*, 1,3-dipolar addition with nitrones of the type ④$^{\oplus}$ + 3 → ⑦$^{+}$ can occur [82].



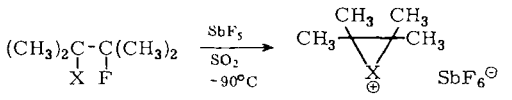
4. Other Heterocycles

Halonium ions have frequently been postulated as reaction intermediates [106]. Recent evidence suggests that these species may be stable in strong acid media [107]. A solution of *(57a)* in SbF_5–SO_2 shows only one NMR absorption peak, strongly suggestive of conversion into the symmetrical species *(58)*.

[105] *C. L. Moret* and *L. M. Trefonas*, J. heterocyclic Chem. *5*, 149 (1968).

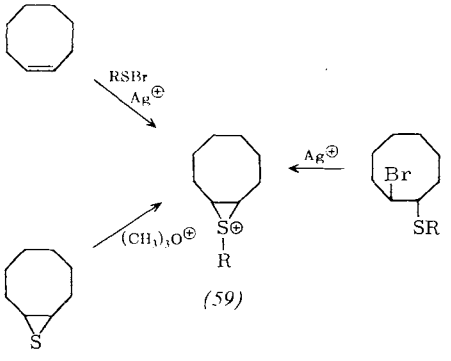
[106] *P. B. D. de la Mare* and *R. Bolton*: Electrophilic Additions to Unsaturated Systems. Elsevier, New York 1966, p. 86.

[107] *G. A. Olah* and *J. M. Bollinger*, J. Amer. chem. Soc. *89*, 4744 (1967); for a review see *G. A. Olah* and *C. U. Pittman, Jr.* in *V. Gold*: Advances in Physical Organic Chemistry. Academic Press, New York 1966, Vol. 4, p. 305.



(57a), X = Cl, Br, I *(58)*

Episulfonium picrylsulfonates derived from cyclooctene have been prepared by various methods[108]. As with aziridinium salts, unusual stability may result from fusion to a medium-sized ring. The reaction of dimethyl sulfide with *(59)* causes ring opening to *trans* product.

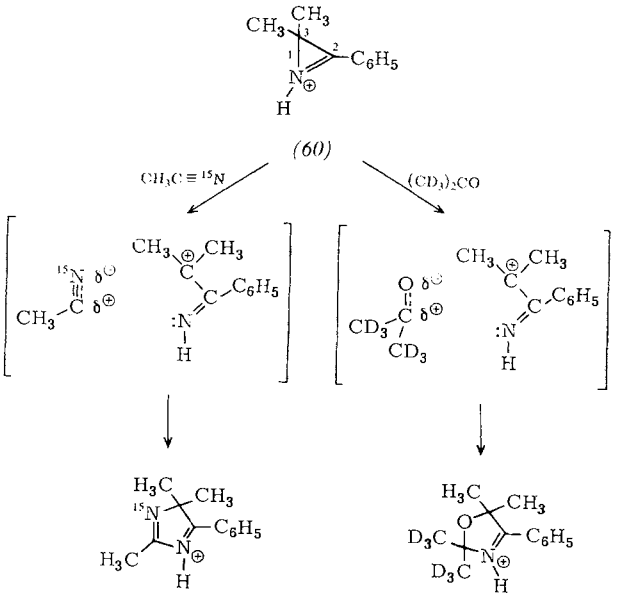


(59)

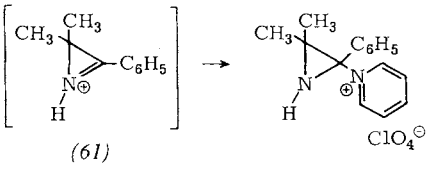
The azirinium perchlorate *(60)*, formed *in situ* with perchloric acid, undergoes 1,2-polar addition to acetone and nitriles[72]. As before, the question of the reaction sequence is unsettled, and only concerted-type processes are shown (Scheme 4).

Mechanistic ambiguities arising from molecular symmetry have been clarified by isotopic labeling experiments. Chemical degradation of products followed by NMR or mass spectral analysis showed the isotope distribution indicated in Scheme 4. These results require that in both cases reaction proceeds by $N^{\oplus}$–C-3 bond cleavage of the starting azirinium ion.

Unlike the case of aziridinium salts, nucleophiles can add to the unsaturated bond of the 1-azirinium cation, as observed in the reaction of the free azirine with pyridinium perchlorate[72]. With anilinium perchlorate[109] and with perchloric acid in methanol[72], the initially formed cation *(61)* undergoes 1,2-bond cleavage after addition of the nucleophile. It is probable that rearrangements of 1-azirines in the presence



Scheme 4



(61)

of acyl chlorides[110], acid anhydrides[111], and carboxylic acids[111] are also initiated by formation of azirinium cations.

Received: December 9, 1968 [A 725 IE]
German version: Angew. Chem. *81*, 953 (1969)

[108] a) *D. J. Pettitt* and *G. K. Helmkamp*, J. org. Chemistry *28*, 2932 (1963); b) *D. J. Pettitt* and *G. K. Helmkamp*, *ibid. 29*, 2702 (1964); c) *G. K. Helmkamp*, *B. A. Olsen*, and *D. J. Pettitt*, *ibid. 30*, 676 (1965).

[109] *N. J. Leonard*, *E. F. Muth*, and *V. Nair*, J. org. Chemistry *33*, 827 (1968).

[110] *F. W. Fowler* and *A. Hassner*, J. Amer. chem. Soc. *90*, 2875 (1968).

[111] *S. Sato*, *H. Kato*, and *M. Ohta*, Bull chem. Soc. Japan. *40*, 2938 (1967).

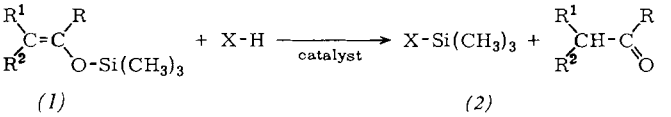
COMMUNICATIONS

Vinyloxytrimethylsilanes as Silylating Agents

By *M. Donike* and *L. Jaenicke*[*]

We have found that vinyloxytrimethylsilanes *(1)*[1,2] are suitable as silylating agents. The course of this group transfer reaction resembles that of chemical and of biological acylation and phosphorylation with enol esters.

In order to verify this hypothesis we investigated IR spectroscopically the reaction of *n*-butyl alcohol with excess of *(1a)*. No noticeable reaction takes place in the absence of catalysts. Addition of catalytic amounts of trimethylchlorosilane immediately induces a slightly exothermal reaction leading to the formation of *n*-butyl trimethylsilyl ether. Compounds *(1b)*, *(1e)*, and a mixture of *(1c)* and *(1d)* behave similarly.



(1) *(2)*

R, R^1 = $-(CH_2)_4-$, R^2 = H
R = R^1 = C_2H_5, R^2 = H
R = C_2H_5, R^1 = R^2 = H
R = R^1 = CH_3, R^2 = H
R = CH_3, R^1 = R^2 = H
X-H = R-OH, R-SH, $R-NH_2$, R-COOH

To establish which functional groups can be silylated with vinyloxytrimethylsilane we carried out reactions with typical silylable compounds and *(1e)* (see Table 1). Compound *(1e)*

Table 1. Reaction of 2-trimethylsiloxypropene *(1e)* with silylable compounds X—H [a].

X—H	Rel. Yield (%) [a]	X—H	Rel. Yield (%) [a]
n-Butanol	99	*N*-Methylacetamide	0
Stearyl alcohol	99	Mercaptoethanol	5
Palmitic acid	98	Propylene ethanol	52
Thiophenol	86	*n*-Butylamine	0 [b]
Phenol	96	Diethylamine	0
Hydroquinone	97	Phenylamine	40
Catechol	97	Ephedrine	0 [c]
Resorcinol	99		

[a] In each case 10 mg of X—H was dissolved (or suspended) in acetonitrile (1 ml) and treated with compound *(1e)* (0.4 ml) and trimethylchlorsilane (0.02 ml). Comparable suspensions were treated with *N*-methyl-*N*-trimethylsilyltrifluoroacetamide (0.42 ml). After 30 mins' heating at 80 °C the conversion was determined gas chromatographically and the yields calculated with reference to 100% conversion in the comparison suspension.

[b] Formation of a Schiff base.

[c] Formation of an oxazolidine.

was chosen because its volatility (b.p. 94 °C) makes it particularly suitable for use in gas chromatographic investigations (cf. Table 2). Moreover, *(1e)* is readily accessible by reaction of *N*-methyl-*N*-trimethylsilylacetamide[2] with dry acetone in a hydrocarbon in absence of moisture.

Table 2. Retention indices, according to *Kovats* [4], of silylating agents on 10% UCW 98 (methylvinylsilicone rubber).

Silylating agent	Retention index
Trimethylchlorosilane	560
2-Trimethylsiloxypropene *(1e)*	691
N-Methyl-*N*-trimethylsilyl-trifluoroacetamide	779
Hexamethyldisilazane	798
N,N-Diethyltrimethylsilylamine	806
N,N-Bis(trimethylsilyl)trifluoroacetamide	858
N-Methyl-*N*-trimethylsilylacetamide	908
O,N-Bis(trimethylsilyl)acetamide	888

Carboxyl, monofunctional aliphatic hydroxyl, and phenol groups react with *(1e)*, somewhat slowly compared with *N*-methyl-*N*-trimethylsilyltrifluoroacetamide[3], but nevertheless completely to give the trimethylsilyl esters or ethers *(2)*.

Vicinal functions, *e.g.* α-amino acids, 1,2-diols, and β-mercaptoalcohols lead to heterogeneous products. Primary amines condense to Schiff bases whereas secondary and tertiary amines do not react even after prolonged heating. Secondary α-hydroxy amines readily yield oxazolidines.

Results of previous investigations have shown that although *(1e)* is not so generally applicable as silylamides its high volatility nevertheless offers many advantages in chromatographic analysis, particularly in trace analysis, of lower carboxylic acids and alcohols.

Received: September 2, 1969 [Z 80 IE]
German version: Angew. Chem. *81*, 995 (1969)

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[1] *C. R. Krüger* and *E. G. Rochow*, J. organometallic Chem. *1*, 476 (1964); *R. Bourhis* and *E. Frainnet*, Bull. Soc. chim. France *1967*, 3552; *I. F. Lutsenko, Yu. I. Baukov, O. V. Dudukina*, and *E. N. Kramarova*, J. organometallic Chem. *11*, 35 (1968).

[2] *L. Birkofer* and *H. Dickopp*, Chem. Ber. *101*, 3579 (1968).

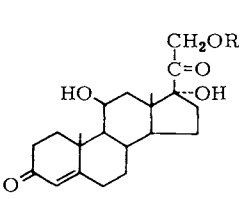
[3] *M. Donike*, J. Chromatogr. *42*, 103 (1969).

[4] *A. Wehrli* and *E. Kovats*, Helv. Chim. Acta *24*, 2709 (1959).

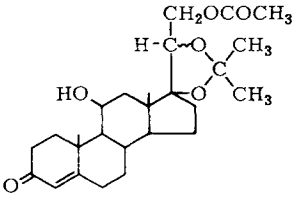
Effect of Crystalline Form on the Air-Oxidation of Steroidal 11β-ols to 11-ones

By *G. Brenner, F. E. Roberts, A. Hoinowski, J. Budavari, B. Powell, D. Hinkley*, and *E. Schoenewaldt*[*]

We have observed the spontaneous air-oxidation of crystalline hydrocortisone-21-*tert*-butylacetate *(1a)* to cortisone *tert*-butylacetate and have extended our study to encompass a variety of 11β-hydroxy-steroid-21-esters. A recent report[1] of a similar oxidation of crystalline *(2)* prompts preliminary publication of our results.



(1)



(2)

(1a), R = CO–CH_2–$C(CH_3)_3$
(1b), R = CO–$(CH_2)_4CH_3$
(1c), R = CO–$(CH_2)_{14}CH_3$
(1d), R = CO–$(CH_2)_2$-cyclo-C_5H_9
(1e), R = CO–$C(CH_3)_3$
(1f), R = CO–CH_3
(1g), R = CO–C_2H_5

Samples of crystalline *(1a)* stored for 1—2 years have been found to contain up to 40% of the readily isolated 11-ketonic cortisone TBA and a 15-year-old sample was found to have oxidized to the extent of 80%. Thin layer chromatograms, X-ray patterns, IR and NMR spectra showed that only starting material and oxidation product were present. The oxidation is easily duplicated in thermally accelerated tests and can be measured by NMR using the shift of the 18-methyl singlet from 9.04 τ (11β-ol) to 9.33 τ (11-one). The reaction requires molecular oxygen and produces water. It is accelerated by heat, greatly accelerated by free-radical initiators or by UV light, and is quenched by free-radical inhibitors. No impurity could be found responsible for the reaction.

Similar evidence of air-oxidation to the 11-ketone was found in old samples of *(1a)*—*(1d)* and, to a markedly lesser degree, prednisolone *tert*-butylacetate. In baffling contrast, 15—17 year-old samples of *(1e)*—*(1g)* and 9α-fluorohydrocortisone *tert*-butylacetate were completely free of 11-ketonic products nor could oxidation be induced in steroids of this group under the most drastic conditions of thermal and photolytic initiation in the solid state.

The finding that polymorphic modifications of hydrocortisone- and prednisolone *tert*-butylacetate could be prepared that were likewise inert to air-oxidation permits formulation of a generalization with predictive value relating oxidative-susceptibility to the type of crystalline form. Esters in this series are commonly encountered in one or more of three types of crystal form:

Type A: A form in which the crystallizing solvent(s) is held within the crystal in non-stoichiometric proportion and which can be completely desolvated in vacuum without change in X-ray pattern.

Type B: A stoichiometric solvate. Desolvation is accomplished only at elevated temperature and is accompanied by changes in the X-ray pattern.

Type C: A non-solvated form.

We find that all steroid esters subject to air-oxidation are of type *A*; all steroid esters resistant to oxidation are of types *B* or *C*.

To validate this generalization, type *C* crystals were prepared and found to be inert to photolytic oxidative conditions under which the *A* forms were extensively oxidized (see Table 1).

Table 1. Dependence of oxidation on crystal form. Thermal oxidation at 100 °C, photolytic oxidation at 50 °C

Steroid	Solvate	Type	Thermal oxidation		Photolytic oxidation
			Time (days)	Yield (%)	2.5 days, Yield (%)
(1a)	H_2O, C_2H_5OH	A	7	6–9	72
	—	C	7	0	0
(1b)	$(C_2H_5)_2O$	A	[a]		40
	—	C	2.5	0	0
(1d)	C_2H_5OH	A	[a]		66
	—	C	2.5	0	0
(1e)	1 C_2H_5OH	B	2.5	0	0
	—	C	2.5	0	0
(1f)	—	C	2.5	0	0
(1g) 9α-Fluoro-*(1a)*	—	C	2.5	0	—
	—	C	2.5	0	0
Predni-solone *tert*-butyl-acetate	H_2O	A	7	4–5	11
	1 C_2H_5OH	B	7	0	0
	—	C	7	0	0

[a] At 80 °C, conversion into Type C.

The air-oxidation of 11β-hydroxy steroids has also been demonstrated in solution (dimethylacetamide, 100 °C, 1600 psig air). Thus no chemical barrier to oxidation need be invoked for steroids stable in the crystalline state.

Received: September 8, 1969 [Z 82 IE]
German version: Angew. Chem. *81*, 1046 (1969)

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[1] *M. L. Lewbart*, Nature (London) *222*, 663 (1969).

Cycloadditions to 1,1-Dicyclopropylethylene[1]

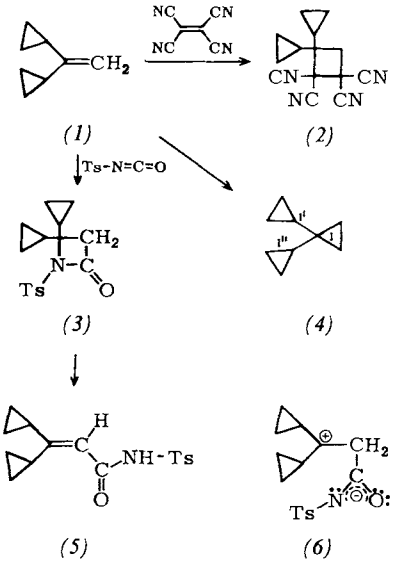
By *F. Effenberger* and *W. Podszun*[*]

While the stabilization of cationic centers by alpha cyclopropyl groups has been verified in many instances[2, 3], to the best of our knowledge nothing is known about the influence of cyclopropyl groups, as substituents, on the reaction mechanism of multiple bonds. The α-cyclopropylcarbonium ions[4] that may be formed are capable of rearrangement, thus providing additional information as to a polar or a more concerted mechanism of cycloaddition.

We have therefore investigated the reaction of 1,1-dicyclopropylethylene *(1)* with electrophiles. Reaction of *(1)* with tosyl isocyanate in ether at 0 °C leads to the formation of the β-lactam *(3)* (yield 50%, m.p. 93 °C; IR: $\nu_{C=O}$ = 1788 cm^{-1}). In boiling benzene, *(3)* rearranges to the acrylamide *(5)* (yield 100%, m.p. 98 °C; IR: $\nu_{C=O}$ = 1704 cm^{-1}, ν_{NH} = 3276 cm^{-1}) which is possible *via* the dipole *(6)* only. If the reaction of *(1)* with tosyl isocyanate is carried out at 20 °C, a mixture of *(3)* and *(5)* is formed.

Tetracyanoethylene reacts with *(1)* at 20 °C to give the cyclobutane derivative *(2)*. When the reactants are mixed in benzene the solution turns blood-red, indicating π-complex formation. Attempts at thermal isomerization of *(2)* into a substitution product corresponding to the amide *(5)* failed. On prolonged standing in [D_6]-DMSO, the intensity of the cyclopropyl proton signals decreases, possibly by rearrangement of a carbonium ion dipole corresponding to *(6)*.

The reactivity of compound *(1)* towards diphenylketene is much lower than towards tosyl isocyanate. Comparison with corresponding cycloadditions to enol ethers[5] shows that, relative to the R—O group (which exerts a greater mesomeric



effect), the cyclopropyl group favors cycloadditions *via* polar transition states over more concerted processes.

Simmons-Smith reaction [CH_2I_2, Zn(Cu)] with *(1)* affords the interesting compound 1,1-dicyclopropylcyclopropane *(4)* in moderate yields; *(4)* can be separated from the reaction mixture by gas chromatography [^{1}H-NMR: τ ≈ 8.95 (m/2H on $C^{1'}$ and $C^{1''}$); ≈9.8 (m/8H on $C^{2'}$, $C^{3'}$, $C^{2''}$, $C^{3''}$); 10.0 (s/4H on C^2 and C^3)].

Received: September 1, 1969 [Z 85 IE]
German version: Angew. Chem. *81*, 1046 (1969)

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

[2] *D. Bethell* and *V. Gold*: Carbonium Ions. Academic Press, New York 1967; *M. Hanack* and *H. J. Schneider*, Angew. Chem. *79*, 709 (1967); Angew. Chem. internat. Edit. *6*, 702 (1967); *N. C. Deno*, Progr. physic. org. Chem. *2*, 129 (1964).

[3] *S. A. Sherrod* and *R. G. Bergman*, J. Amer. chem. Soc. *91*, 2115 (1969); *M. Hanack* and *T. Bässler*, *ibid.* *91*, 2117 (1969).

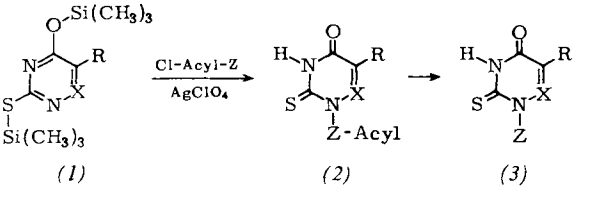
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A Simple New Synthesis of 2-Thiopyrimidine Nucleosides[**]

By *H. Vorbrüggen*, *P. Strehlke*, and *G. Schulz*[*]

2-Thiopyrimidine nucleosides have hitherto been available only by multistep syntheses[1]. Two recently published direct syntheses starting from 2-thiopyrimidine derivatives and acylated halo sugars using the mercury salt method[2] and the *Hilbert-Johnson* procedure[3] respectively prompt us to report a very simple general synthesis of 2-thiopyrimidine nucleosides and a 6-aza analog *via* the silyl modification of the *Hilbert-Johnson* method[4, 5].



(1) (2) (3)

	R	X	(2) Acylated halo sugar Cl-Acyl-Z	(2) Yield (%)	(2) M.p. (°C)	(2) $[\alpha]_D$ (°) [a]	(3) Yield (%)	(3) M.p. (°C)	(3) $[\alpha]_D$ (°) [b]	(3) H-1′ δ (ppm) J (Hz)	UV pH = 7 λmax (nm) (log ε)	UV pH 12 λmax (nm) (log ε)
(a)	H	CH	2,3,5-Tri-*O*-benzoyl-ribofuran-osyl chloride	71	—	−28	100	214–215	+39	6.70 [d] 2.5	218 (4.21) 275 (4.13)	239 (4.32) 271 (4.13)
(b)	C_2H_5	CH	2-Deoxy-3,5-di-*O*-*p*-toluoylribo-furanosyl chloride	81 [c] α	164–166	+6	53	81–83	+43	6.75 [e] $J_{AX} + J_{BX}$ = 9 Hz	221 (4.09) 274 (4.03)	240 (4.28) 264 (4.07) shoulder
				β	199–202	−82.5	75	187–188	+6.5	7.7 [f] $J_{AX} + J_{BX}$ = 12 Hz	220 (4.18) 278 (4.23)	242 (4.40) 265 (4.20) shoulder
(c)	H	N	2,3,5-Tri-*O*-benzoyl-ribofuran-osyl chloride	78	173	−35.5	87	197–198	−96.6	6.95 [d] 2.5	218 (4.13) 269 (4.26)	236 (4.14) 267 (4.30)

[a] $c = 0.5$ in $CHCl_3$. [b] $c = 0.5$ in H_2O. [c] Crude yields: crystalline α-anomer 35%, β-anomer 11.5%. [d] D_2O at 90 °C. [e] D_2O at 30 °C. [f] [D_5]-Pyridine at 30 °C.

Treating 2-thiouracils with hexamethyldisilazane in anhydrous dioxane gave the *O,S*-bis(trimethylsilyl) derivatives *(1)* in almost quantitative yield. These derivatives react with acylated halo sugars in anhydrous benzene containing one equivalent of silver perchlorate[6] at 25 °C [*(1a)* and *(1c)* 60 min; *(1b)* 30 min] to provide the acylated 2-thionucleosides *(2)*, usually in good yield. Saponification with 0.01–0.02 N $NaOCH_3$ in anhydrous methanol or methanolic ammonia leads finally to the free 2-thiopyrimidine nucleosides *(3a)* and *(3b)*, as well as the 6-aza analog *(3c)*[7], usually in excellent yield. Elemental analyses and physical data are in accord with structures *(2)* and *(3)*. In the case of tribenzoylribofuranosyl chloride, only the β-D-ribofuranosides were obtained. Their configuration was proved not only by their NMR data but in the case of *(3a)* also by oxidation with $NaOH/H_2O_2$[8], whereupon we isolated a 70% yield of crystalline uridine, which was identified by comparison of its IR spectrum (KBr) and thin-layer chromatogram with authentic material.

All the 2-thiouridines, when compared with the uridines, showed a characteristic deshielding of the 1′-H in the NMR spectrum of up to one δ unit[9].

Further applications of this new method, *e.g.* synthesis of 2-thiocytidines, are being investigated[10].

Received: September 18, 1968; revised: August 27, 1969 [Z 89a IE]
German version: Angew. Chem. *81*, 997 (1969)

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[**] Synthesis of Nucleosides, Part 1.

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[7] β-2-Thiothymidine [3′,5′-ditoluate, m.p. 205–207 °C; free nucleoside, m.p. 182–183 °C, $[\alpha]_D = +16°$ ($c = 0.5$ in methanol)] was prepared analogously.

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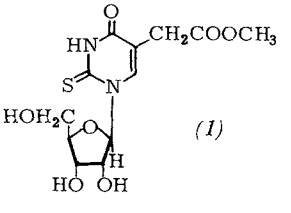
[10] Starting from the *N,S*-bis(trimethylsilyl) derivative of 2-thiocytosine, 2′,3′,5′-tribenzoyl-2-thiocytidine, m.p. 193–195 °C [3], was obtained in 75% yield.

Synthesis of Hall's Methyl 2-Thiouridine-5-acetate from Yeast-tRNA[1]

By *H. Vorbrüggen* and *P. Strehlke*[*]

Using our new method of preparing 2-thionucleosides[1] we have synthesized the methyl 2-thiouridine-5-acetate *(1)* recently isolated from yeast-tRNA by *Hall et al.*[2].

From diethyl 2-formylsuccinate, thiourea, and potassium carbonate in water we obtained ethyl 2-thiouracil-5-acetate, m.p. 185–187 °C, which with hexamethyldisilazane afforded the *O,S*-bis(trimethylsilyl) derivative in excellent yield. With tri-*O*-benzoyl-D-ribofuranosyl chloride and silver perchlorate in benzene (15 min, 24 °C) the silyl derivative gave a 78% yield of crystalline ethyl 2′,3′,5′-tri-*O*-benzoyl-2-thiouridine-5-acetate, m.p. 118–120 °C, $[\alpha]_D = -83°$ ($c = 0.5$ in $CHCl_3$). Hydrolysis and simultaneous transesterification with 0.02 N-sodium methoxide in anhydrous methanol (16 h, 24 °C) afforded a 74% yield of *Hall*'s methyl 2-thiouridine-5-acetate *(1)*, m.p. 195–196 °C (from 4 : 1 CH_3OH/H_2O), $[\alpha]_D = +19.8°$ ($c = 0.5$ in H_2O), $\delta_{H-1'} = 6.67$ ppm ($J = 2.5$ Hz at 90 °C in D_2O), which was shown to be identical with the natural product by m.p., UV and mass spectra, and thin-layer chromatography[3,4].



(1)

Received: September 18, 1969;
revised: August 27, 1969 [Z 89b IE]
German version: Angew. Chem. *81*, 998 (1969)

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[1] Synthesis of Nucleosides, Part 2. – Part 1: *H. Vorbrüggen, P. Strehlke*, and *G. Schulz*, Angew. Chem. *81*, 997 (1969); Angew. Chem. internat. Edit. *8*, 976 (1969).

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[3] We thank Prof. *Hall* for the comparison with the natural product by thin-layer chromatography. An independent synthesis of *(1)* is described by *R. H. Hall*, Canad. J. Biochem., in the press.

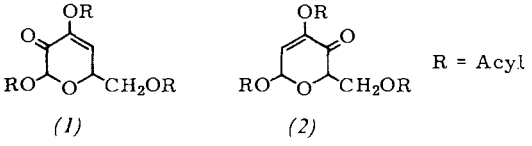
[4] Using *Ueda*'s method [5], ethyl 2',3',5'-tribenzoyl-2-thiouridine-5-acetate, m.p. 118–120 °C, can also be obtained, in 30% overall yield, by reaction of ethyl 2-(methylthio)-4-(trimethylsilyloxy)-5-pyrimidineacetate with tribenzoyl-D-ribofuranosyl chloride in acetonitrile in the presence of molecular sieves and subsequent treatment of the product with H_2S in pyridine.

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Intermediates in the Formation of γ-Pyrones from Hexose Derivatives: A Simple Synthesis of Kojic Acid and Hydroxymaltol

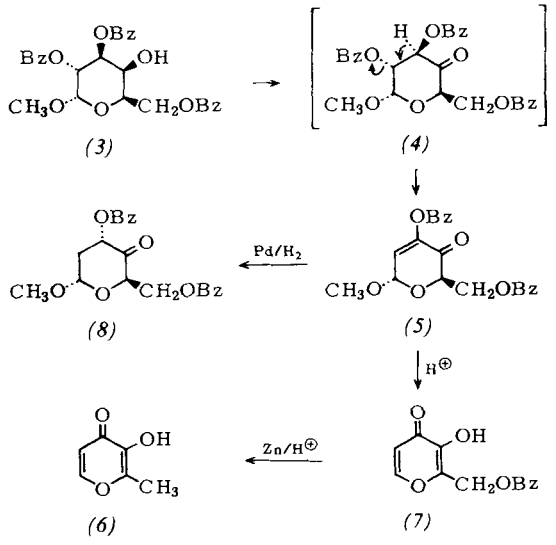
By *F. W. Lichtenthaler* and *P. Heidel*[*]

Sugar enolones of types *(1)* and *(2)* have been postulated as hypothetical intermediates in the formation of, respectively, kojic acid from acylated ald-2-uloses[1] and hydroxymaltol from the 3-*C*-formyllyxose portion of the antibiotic hydroxystreptomycin[2]. We have prepared enolones of these types in a simple manner, by oxidation of partially acylated aldopyranosides with dimethyl sulfoxide and acetic anhydride; their ready conversion into γ-pyrones supports the earlier mechanistic considerations and provides the simplest chemical synthesis to date of kojic acid and hydroxymaltol.



(1) *(2)*

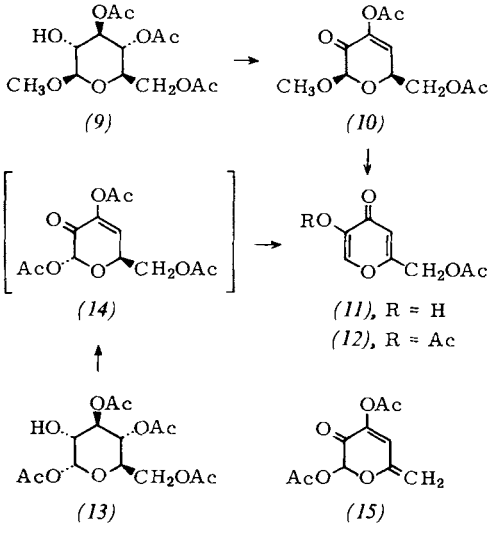
When methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside *(3)*[3] is oxidized by dimethyl sulfoxide-acetic anhydride, a new product[4] can be detected[6] already after 2 hours alongside *(3)* (approx. 70%) and the ketone *(4)*. The amount of the new product increases as the reaction proceeds and after 24 hours constitutes the sole reaction product (apart from benzoic acid). Working up gives needles, m.p. 127 to 128 °C, $[\alpha]_D^{25} = +70°$ ($CHCl_3$). Combustion analysis, the molecular weight determined by mass spectrometry, decoloration of bromine water and permanganate solution, and the isolation of benzoic acid (78% calc. on 1 equivalent) indicate that this is an unsaturated dibenzoate; failure to react with 2,4-dinitrophenylhydrazine, an enone *R*-band in the circular dichroism plot at 342 nm ($\Delta\varepsilon = -2.15$ in dioxane)[7], and the NMR data (4 Hz doublets for H^3 and H^2 at $\tau = 3.26$ and 4.58; ABC system for H^6 and C-6–CH_2 around $\tau = 5.2$ in $CDCl_3$) prove conclusively the presence of a conjugated enone, (2*S*, 6*R*)-4-benzoyloxy-6-(benzoyloxymethyl)-5,6-dihydro-2-methoxy-2*H*-pyran-5-one *(5)*. Thus oxidation of the free hydroxyl group in *(3)* is accompanied under the reaction conditions by an acid-catalyzed β-elimination of benzoic acid [*(4)* → *(5)*], which has analogies in the elimination under similar conditions of phosphoric acid from nucleotides[8] and of acetic or benzoic acid from acylated aldulosides[9].



(3) *(4)* *(5)* *(6)* *(7)* *(8)*

Hydrogenation over 10% palladium-charcoal in methanol-ethyl acetate (40 min) converts *(5)* quantitatively into methyl 3,6-di-*O*-benzoyl-2-deoxy-α-D-*erythro*-hexopyranoside *(8)*, which was characterized as a pure syrup by combustion analysis, by spectral data (νCO at 1740 and 1720 cm^{-1}, quartet for H^1 and H^3 at $\tau = 4.81$ and 4.12, respectively, with $J_{1,2} = 5.5$ and 7.0, as well as $J_{2,3} = 7.5$ and 13.0 Hz), and as 2,4-dinitrophenylhydrazone, needles, decomp. 191–193 °C. The enolone *(5)* is stable towards weak acids such as acetic acid; however, strong acids such as trifluoroacetic acid convert it, with spontaneous hydrolysis of the 2-methoxyl and 4-benzoyloxyl group[10], into the more stable γ-pyrone, 2-(benzoyloxymethyl)-3-hydroxy-4*H*-pyran-4-one *(7)*, m.p. 136–139 °C (89% yield); this structure followed unambiguously from the NMR data (OH singlet at $\tau = 0.49$, 5.5 Hz doublet for H^6 and H^5 at $\tau = 1.84$ and 3.55, CH_2 singlet at $\tau = 4.63$) and by conversion into maltol *(6)*[11] by zinc and hydrochloric acid[12].

As in the case of *(3)*, oxidation of methyl 3,4,6-tri-*O*-acetyl-β-D-glucopyranoside *(9)*[13] by dimethyl sulfoxide and acetic anhydride occurs with β-elimination of acetic acid from the 2-keto compound that is the primary product, leading thus to (2*S*, 6*R*)-4-acetoxy-2-(acetoxymethyl)-6-methoxy-5,6-dihydro-2*H*-pyran-5-one *(10)*, m.p. 139–142 °C, in 47% yield, and this is converted immediately on dissolution in trifluoroacetic acid into monoacetylkojic acid *(11)*[14], m.p. 135 to 136 °C, in 82% yield.



(9) *(10)* *(14)* *(11)*, R = H *(12)*, R = Ac *(13)* *(15)*

The enolone *(14)* expected on oxidation of 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside *(13)*[15] could, however, not be isolated. Owing to the greater lability of the 1-acetoxyl than of the 1-methoxyl group of *(10)*, the weakly acidic oxidation conditions suffice for formation of the γ-pyrone system; diacetylkojic acid *(12)*[14] results and is isolated in 74% yield. Accordingly, the product obtained by *Perlin* and co-workers[9b] on oxidation of *(13)* by DMSO–SO_3 and considered to be the conjugated 3,5-dienone *(15)* is more correctly formulated as *(12)*[16,17].

(2S,6R)-4-Benzoyloxy-6-(benzoyloxymethyl)-5,6-dihydro-2-methoxy-2H-pyran-5-one (5)

The glycoside *(3)* (3.0 g, 6.0 mmoles) in DMSO (20 ml) is treated with acetic anhydride (10 ml) and set aside at room temperature for 2 days, then stirred into ice-water. The oil that separates is taken up in chloroform, dried over Na_2SO_4, freed from solvent, and treated with methanol, whereupon it

crystallizes. Recrystallization from ethanol gives 1.2 g (52%) of *(5)* as colorless needles, m.p. 127–128 °C, $[\alpha]_D^{25} = +70°$ ($c = 1$ in $CHCl_3$).

Received: August 29, 1969 [Z 90 IE]
German version: Angew. Chem. *81*, 998 (1969)

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[5] *O. Gabriel*, Carbohydr. Res. *6*, 319 (1968).

[6] Thin-layer chromatography on silica gel HF_{254} (E. Merck AG., Darmstadt, Germany) with 50 : 1 benzene-2-propanol as eluent. Development by iodine vapor or spraying with 2% methanolic perchloric acid and warming at 100 °C.

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[16] Structure *(15)* is already refuted by previous NMR data [9b] (2H singlet for the methylene protons of an enol ether). These data agree with those for diacetylkojic acid except for one signal [singlet at $\tau = 2.95$ instead of $\tau = 3.52$ for H-3 in *(12)*].

[17] Note added in proof: The formation of diacetylkojic acid on dimethyl sulfoxide oxidation of *(13)* has also been demonstrated by *G. J. F. Chittenden* (personal communication and Carbohydrate Res., in press).

3-Nitro-2-azachromone (4*H*-1,2-Benzoxazin-4-one): Structure of the Presumed *p*-Nitrophenylnitroacetylene[1]

By *H. G. Viehe*, *V. Jäger*, and *F. Compernolle* [*]

After appearance of our communication on the synthesis of the first nitroacetylene[1] we learnt[2] that in 1903 *Wieland* and in 1960 *Novikov et al.* regarded a compound $C_8H_4N_2O_4$ *(1)*[3] as *p*-nitrophenylnitroacetylene *(2)* on the basis of elemental analysis and molecular-weight determination. We can confirm the formation of *(1)*; its chemical and physical properties can be brought into accord only with the structure *(3a)* of a 2-azachromone.

A melting point of about 140 °C without decomposition is, in our experience with nitroacetylenes, unthinkable for a compound such as *(2)*. The NMR spectrum of *(1)* shows four neighboring aromatic protons and, together with the analytical data, indicates a fused heterocycle.

In accord with formulation *(3a)*, compound *(1)* has in its IR spectrum strong CO and NO_2 absorption bands at 1676[4], 1550, and 1352 cm^{-1} and other strong bands at 1613, 1565, 1460, 1040, 813, and 771 cm^{-1}, but does not have the strong C≡C absorption characteristic of nitroacetylenes[1]. The UV spectrum of *(1)* in methanol has maxima at 242 nm (log ε = 3.90), 256.5 (3.83 shoulder), and 321.5 (3.76). In the mass spectrum, fragment ions appear at *m/e* = 192, 165, 146, 120, 118, 92, 90 (base peak), 64, and 63. The position of the metastable peaks proves the following degradation paths:

192 → 165 (−HCN)
192 → 146 (−NO_2) → 118 (−CO) → 90 (−CO)
and 146 → 90 (−2CO); 90 → 64 and 63 (−CN and −HCN, resp.)

Treatment of *(1)* with carbonyl reagents does not lead to corresponding derivatives; instead, treatment with phenylhydrazine in ethanol and a little acetic acid gives ethyl salicylate. Alkaline degradation with 2 N-KOH at room temperature affords salicylic acid. *(1)* reacts neither with concentrated sulfuric acid in the cold nor with 20% aqueous H_2SO_4 in THF under reflux, but with 90% H_2SO_4 at 100 °C affords 1,2-benzisoxazole-3-carboxylic acid[6].

Dilute alcoholic hydrochloric acid in THF at room temperature replaces the nitro group of *(1)* by Cl. This corresponds to a nucleophilic substitution and shows the relation to nitrolic acids $RC(NO_2)=NOH$, which are converted into hydroxamic acids by concentrated HCl[7].

These results leave *(3a)* and *(3b)* as the only possible formulations of *(1)* and the chlorine derivative, and this is confirmed by the mass spectrum of *(3b)*.

The compound $C_8H_4N_2O_4$ *(1)* designated as *p*-nitrophenylnitroacetylene is thus to be considered as a derivative of the barely known 4*H*-1,2-benzoxazin-4-ones (2-azachromones)[8].

Received: September 17, 1969 [Z 92 IE]
German version: Angew. Chem. *81*, 999 (1969)

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[1] Heterosubstituted Acetylenes, Part 27, and Nitroacetylenes, Part 2. – The paper by *V. Jäger* and *H. G. Viehe*, Angew. Chem. *81*, 259 (1969); Angew. Chem. internat. Edit. *8*, 273 (1969), is considered to be Part 1.

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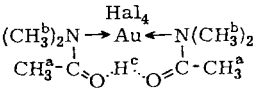
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Hydrogen Tetrahalogenobis(*N,N*-dimethylacetamide)aurates(III)

By *M. Ziegler, P. Barth,* and *H. Winkler* [*]

Addition of *N,N*-dimethylacetamide (DMA) to aqueous solutions (≧ 8%) of hydrogen tetrahalogenoaurates(III) affords less readily soluble, crystalline complexes: $H[AuCl_4(DMA)_2]$ *(1a)*, yellow, m.p. 66 °C; $H[AuBr_4(DMA)_2]$ *(1b)*, dark red, m.p. 79 °C. These adducts are not only soluble in water or alcohol, but, in contrast to the starting compounds $H[AuHal_4]$, they also dissolve extremely readily in aliphatic halogenohydrocarbons which can therefore be used for their extraction.

Elemental analysis and IR- and ^{1}H-NMR spectra show the new compounds to correspond to formula *(1)*.



(1)

Since no bands are registered above 3000 cm^{-1} in the IR spectrum, proton coordination at the nitrogen, as, for example, is found in the ammonium salt $[HN(C_4H_9)_3][AuCl_4]$ with νNH = 3150 cm^{-1} ($[DN(C_4H_9)_3][AuCl_4]$, νND = 2395 cm^{-1}), would appear unlikely. On the other hand, broadened bands (width up to 200 cm^{-1}) around 812 cm^{-1} would indicate hydrogen bonding of the kind —CO · · · H · · · OC— [1]. The formulation *(1)* is confirmed by the intensity ratio of the ^{1}H-NMR signals $H^a : H^b : H^c$ = 6 : 12 : 1 (H^c : acetamide = 1 : 2); the δH^c values ($CDCl_3$; TMS as external standard) of —17.45 [*(1a)*] and —17.05 ppm [*(1b)*] are extreme values within the range of diamagnetic shifts expected.

The exclusive decrease of the H^c values by competing proton exchange is indicative of solvent reactions of compound *(1)* with aliphatic halogenohydrocarbons, *e.g.*, CH_2Cl_2; a concomitant increase in δH(methylene) from —1.88 to about —10 ppm is also observed.

Received: September 15, 1969 [Z 96 IE]
German version: Angew. Chem. *81*, 1047 (1969)

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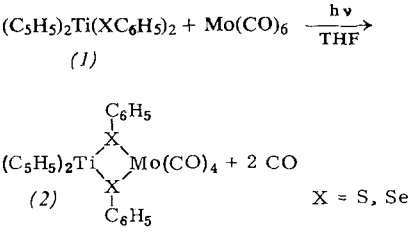
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Titanium-Molybdenum Complexes with Chalcogen Bridging Ligands

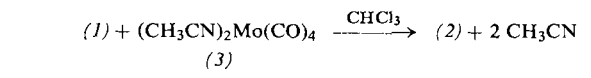
By *H. Köpf* and *K. H. Räthlein* [*]

Bi- and tri-nuclear germanium(or tin)-chromium complexes joined by sulfur bridging atoms have recently [1] been prepared by direct introduction of organometallic sulfides as ligands replacing CO in hexacarbonylchromium.

We have applied this synthetic method to organotitanium chalcogenides by treating the potentially bidentate ligands

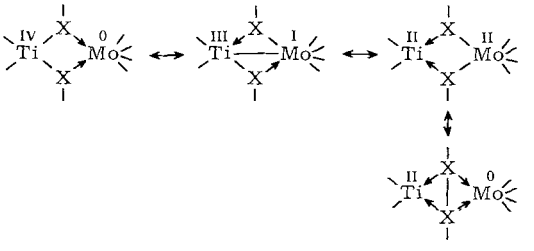


bis(phenylchalcogeno)bis(cyclopentadienyl)titanium(IV) *(1a)* (X = S) [2] and *(1b)* (X = Se) [3] with equimolar amounts of hexacarbonylmolybdenum in tetrahydrofuran under UV irradiation [4] for 3 hours at room temperature. This afforded the doubly bridged, binuclear complexes *(2a)* and *(2b)*, which, after concentration of the dark reaction solutions in a vacuum, were isolated as bluish-black crystals that were soluble in organic solvents, sensitive to air and solvolysis, yet thermally stable up to 200 °C in the absence of air. The complexes *(2)* from bis(acetonitrile)tetracarbonylmolybdenum(0) [5] *(3)* were formed particularly smoothly in chloroform without irradiation:



The IR spectra of *(2)* showed four CO stretching vibrations for the carbonyl skeleton of symmetry C_{2v} as well as the characteristic π-C_5H_5 and C_6H_5 bands. The molecular weight determined in benzene was in accord with the monomeric *cis*-structure *(2)* formulated.

The oxidation state of the metals concerned in the diamagnetic compounds *(2)* can no longer be stated unambiguously. Several limiting forms may participate in the ground state (non-bonding electron pairs and terminal ligands are omitted), viz:



In fact the τC_5H_5 values in the ^{1}H-NMR spectra indicate for the complexes *(2)* a considerably greater shielding of the cyclopentadienyl protons in comparison with *(1)*. This is not in accord with the decrease in the electron density on titanium that is to be expected from an increase in the donor function of the chalcogen atoms X to molybdenum [6], but it can be readily explained as due to electron back-donation from molybdenum and/or a chalcogen-dichalcogen redox system to the unoccupied ψ_0-orbital of Ti^{IV} [7]. The increase in the mobility of the electrons in the TiX_2Mo ring follows also from the bathochromic shift in the visible absorption from reddish-violet (539 nm; in chloroform) for *(1a)* to blue (also 618 nm) for *(2a)*.

Bis(cyclopentadienyl)diphenoxotitanium(IV) *(1c)* (X = O) [9] reacts with hexacarbonylmolybdenum or *(3)* under analogous conditions but instead of giving *(2c)* it splits off two further CO groups and affords the yellow, relatively stable, trinuclear tetrasubstitution product *cis*-$[(C_5H_5)_2Ti(OC_6H_5)_2]_2Mo(CO)_2$ *(4)*. The *cis*-structure of *(4)* (symmetry C_2) follows from the appearance of two IR frequencies in the carbonyl region and two ^{1}H-NMR signals of equal intensity that can be assigned to two pairs of C_5H_5 groups in different surroundings. The pale red color of the solutions, unchanged from that of *(1c)*, and the position of the τC_5H_5 values for *(4)* indicate that in this case mesomerism is not important. The effect of mesomerism on the ground state thus increases from O to Se, the limiting structure with diphenyldichalcogenide bridges acquiring additional weight in the same series.

Di(μ-phenylthio)bis(cyclopentadienyl)titaniumtetracarbonylmolybdenum (2a)

A solution of *(1a)* (396 mg, 1 mmole) in chloroform (20 ml) is added dropwise within 30 minutes to a stirred suspension of *(3)* (290 mg, 1 mmole) in chloroform (10 ml) under nitrogen. The red solution becomes deep blue. After 2 hours'

further stirring and filtration most of the solvent is removed in a vacuum. The bluish-black leaflets precipitated are washed with a little cold chloroform and dried in a vacuum. After dissolution in, and recovery from, chloroform the yield is 51% (310 mg). *(2b)* (66%, 460 mg) is obtained analogously from *(1b)* (1 mmole, 490 mg); and *(1c)* (364 mg, 1 mmole) affords *(4)* (260 mg, 59%), a yellow powder, on dissolution of the crude product in carbon disulfide, concentration, and rubbing of the residue with methanol.

Compound X =	τC_5H_5 [a] (ppm)	νCO (cm^{-1})	γCH [b] (cm^{-1})	γCH [c] (cm^{-1})
(1a), S	4.00		828	747 700 692
(2a), S	4.52	2020 1920 1900 1880	827	746 698 690
(1b), Se	4.01		824	735 694
(2b), Se	4.63	2010 1910 1890 1870	825	740 690
(1c), O	3.69		863 818	750 697
(4), O	3.63 3.56	1950 1900	875 810	760 694

[a] Singlet, measured for saturated solutions in CS_2 with TMS as external standard. [b] C_5H_5 group. [c] C_6H_5 group.

Received: September 26, 1969 [Z 99 IE]
German version: Angew. Chem. *81*, 1000 (1969)

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[7] Cf. *H. Köpf*, Z. Naturforsch. *23b*, 1531 (1968). If the Ti in *(2)* is replaced by Mo, the mesomerism is blocked by the already occupied ψ_0-orbital on Mo^{IV}. Correspondingly, $(C_5H_5)_2Mo(SC_6H_5)_2$ and $Mo(CO)_6$ give the trisubstituted carbonyl $(C_5H_5)_2Mo(SC_6H_5)_2Mo(CO)_3$, in which, by a reversal, the cyclopentadienylmetal acts as donor to the carbonylmetal [8].

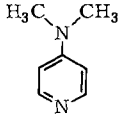
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N,N-Dimethyl-4-pyridinamine, a Very Effective Acylation Catalyst

By *W. Steglich* and *G. Höfle* [*]

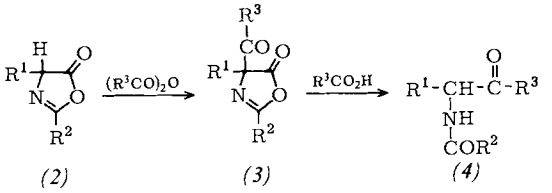
We have found that *N,N*-dimethyl-4-pyridinamine *(1)* [1], alone or mixed with triethylamine, is a superlative acylation catalyst, much superior to pyridine [2].



(1)

O-Acylations: Acylation of tertiary alcohols is considered to be difficult [3]. For example, *tert*-butyl alcohol and 1-methyl-1-cyclohexanol are not acylated by acetic anhydride and pyridine [4]. Yet acetylation in the presence of an equivalent amount of *(1)* is complete after 10 hours at room temperature (NMR kinetics). For preparative purposes it suffices to add catalytic amounts of *(1)* and to bind the acid formed by triethylamine. [Example: 1-Methyl-1-cyclohexanol (11.4 g, 0.1 mole), acetic anhydride (20 ml, 0.21 mole), triethylamine (20 ml, 0.15 mole), and *(1)* (0.5 g, 4.1 mmoles); after 14 hours at room temperature 86% of acetate; analogously, 60% of *tert*-butyl acetate. The amounts of acetate formed by pyridine and/or triethylamine are less than 5%.]

C-Acylations: The Dakin-West reaction [5] was chosen as example, its most important step being the pyridine-catalyzed acylation of the 5-oxazolone *(2)* to the 4-acyl-5-oxazolone *(3)* [6,7].



(2) *(3)* *(4)*

(a), $R^1 = R^3 = CH_3$, $R^2 = C_6H_5$
(b), $R^1 = C_6H_5$, $R^2 = R^3 = CH_3$

Here *(1)* accelerates this reaction much more than pyridine does. For example, acetylation of *(2a)* to *(3a)* with pyridine requires about 6 hours [7], but with 0.05 part of *(1)* only 3 minutes are needed. At the same time the decarboxylative ring fission is greatly accelerated, so that the Dakin-West reaction can be carried out at room temperature.

Analogously to *(4a)* (see below), 2-phenylglycine afforded *N*-(1-phenylacetonyl)acetamide *(4b)* in good yield after 13 hours' stirring. Further, conversion of oxazolones into *(4)* by carboxylic acids [7,8] is effected smoothly at room temperature under catalysis by *(1)*; for example, *(2a)* (0.97 g, 5.55 mmoles), glacial acetic acid (0.32 ml, 5.55 mmoles), and *(1)* (40 mg, 0.33 mmole) in methylene chloride give 73% (0.80 g) of *(4a)* after one day.

N-(1-Methylacetonyl)benzamide (4a)

N-Benzoylalanine (3.9 g, 20 mmoles) and *(1)* (0.1 g, 0.82 mmole) are stirred with acetic anhydride (4 ml, 42 mmoles) and triethylamine (4 ml, 0.29 mmole). Lively evolution of CO_2 and slight warming occur. After 30 min glacial acetic acid (30 ml) is added, then the solution is set aside for 30 min, concentrated in a vacuum, shaken with 2 N NaOH, and extracted with ether. Shaking the ethereal phase with 1 N-HCl, drying, and evaporation gives 78% (3.0 g) of *(4a)*, m.p. 63 °C (m.p. in [9] is 69 °C).

Received: August 28, 1969 [Z 100 IE]
German version: Angew. Chem. *81*, 1001 (1969)

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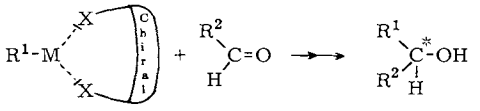
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Asymmetric Solvent Catalysis; *N,N,N′,N′*-Tetramethyl-2,3-dimethoxy-1,4-butanediamine, a New Chiral Medium

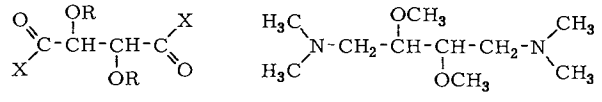
By *D. Seebach, H. Dörr, B. Bastani,* and *V. Ehrig* [*]

Chiral bifunctional [1] ethers [2] (2,3-dimethoxybutane) and amines [3] (sparteine) can be used forasymmetric syntheses [4] of, *e.g.*, alcohols *(2)* from aldehydes and organometallic reagents (asymmetric catalysis by coordination bonding).



(1), M = Li, Mg *(2)*
X = OR, NR_2

Experiments so far have been done with a ratio (*r*) of chelating agent to metal derivative of $r = 1$ in an inert solvent (benzene or hexane); the optical yield (*p*) reached a maximum of 6% with M = Li [3]. We have found that *p* can be raised appreciably if the asymmetric addend is not only the complexing agent ($r = 1$) but also the solvent (r = up to 20). As



(3a), X = OC_2H_5, R = H DAB
(3b), X = $N(CH_3)_2$, R = H
(3c), X = $N(CH_3)_2$, R = CH_3

chiral medium [5] we used *N,N,N′,N′*-tetramethyl-2,3-dimethoxy-1,4-butanediamine (DAB), which is readily obtained from diethyl tartrate *(3a)*.

Table 1. Optical yields *p* obtained on addition of butyllithium to benzaldehyde, leading to 1-phenyl-1-pentanol [a], in DAB-pentane (20 mmolar batches; aldehyde added after dilution with pentane). Also, for comparison, the same reaction in ether and in presence of (−)-sparteine [b] and (−)-2,3-dimethoxybutane (DMB) [c].

No.	Temp. (°C)	DAB/BuLi (*r*)	Pentane/DAB (vol.) approx.	*p* (%)
1	0	2	6	8.5
2	− 78	0.25	60	6.2
3	− 78	0.5	30	8.5
4	− 78	1	13	9.5
5	− 78	2	6	14.8
6	− 78	2.5	5	15.2
7	− 78	3	4	15.6
8	− 78	4	2.5	15.2
9	− 78	8	1.2	20.2
10	− 78	15	0.5	20.6
11	−120	2	8	22.3
12	−120	4	2.6	25.0
13	−130	9	1.2	33.0
			Ether/DAB	
14	− 78	2	5	12.5
		Sparteine/BuLi	Hexane/ Sparteine	
15	− 70	1	11	5.8 [3]
16	− 78	3	4.5	13.3
		DMB/BuLi	Hexane/DMB	
17	− 78	3	10	3.9

[a] (+)-DAB, (−)-sparteine, and (−)-DMB led in all cases to (+)-alcohol of (*R*) configuration. As value for the optically pure carbinol we took $[\alpha]_D = 17.5°$ (homogeneous) or $[\alpha]_D = 31.3°$ ($c = 13$ in C_6H_6) [8]

[b] $[\alpha]_D = 5.62°$ (homogeneous).

[c] $[\alpha]_D = 3.71°$ (homogeneous), from (+)-tartaric acid.

Conversion into the diamide *(3b)* [$NH(CH_3)_2$—CH_3OH; m.p. 184.2–185.0 °C; $[\alpha]_D = 42.7°$ ($c = 3.0$ in C_2H_5OH)], esterification to give *(3c)* [$(CH_3)_2SO_4$, NaH—THF; m.p. 63.2–63.5 °C; $[\alpha]_D = 115.7°$ ($c = 3.1$ in C_6H_6)], and reduction ($LiAlH_4$—THF) affords a 65% overall yield of (*S,S*)-(+)-DAB from natural (+)-tartaric acid and of (*R,R*)-(−)-DAB from (−)-tartaric acid [b.p. 62–63 °C/3 torr; $n_D^{20} = 1.4343$; $d^{20} = 0.896$; $[\alpha]_D = 14.65°$ (homogeneous); dipicrate, m.p. 151.2–152.0 °C, $[\alpha]_D = 20.5°$ ($c = 3.5$ in $(CH_3)_2CO$)] [6].

Nos. 2–10 in Table 1 show that the optical yield on addition of butyllithium to benzaldehyde increases with increasing content of DAB in the medium up to $r = 2$, then remains constant up to $r = 4$, and with $r = 8$ increases again; on cooling down to −130 °C (compare nos. 1, 5, and 11, nos. 8 and 12, and nos. 9 and 13) we obtained values of *p* up to 33% [7].

DAB solidifies to a glass at about −30 °C but can be stirred at very low temperatures if small amounts of pentane are added (column 4 of Table 1); mixtures with butyllithium are clear and homogeneous.

The optical yield decreases only slightly if ether is used for dilution instead of pentane (Table 1, nos. 14 and 5).

Table 2. Optical yields *p* on addition of organometallic compounds to carbonyl compounds in the presence of (+)-DAB (solvent: pentane for RLi, ether for Mg derivatives).

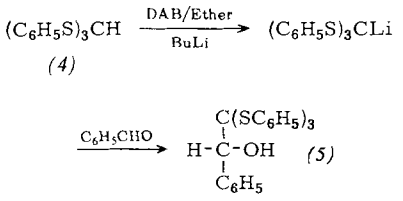
Carbonyl compound	R-metal	Temp. (°C)	DAB/ R-metal	$[\alpha]_D$ (*c*, solv.) [a]	*p* (%)
C_6H_5—CHO	$CH_3Li/LiBr$ (Ether)	−100	3	−0.76 (16, CH_3OH)	1.7
CH_3—CHO	BuLi (Hexane)	−120	2	+1.6 (4, C_2H_5OH)	14
C_2H_5—CHO	BuLi (Hexane)	−120	2	+1.6 (10, C_2H_5OH)	19
$(CH_3)_2CH$—CHO	BuLi (Hexane)	−120	2	+6.1 (5, C_2H_5OH)	22
C_6H_5—CHO	$(CH_3)_2CHLi$ (Hexane)	−120	4	+6.6 (7.5, Ether)	14
C_4H_9—CHO	C_6H_5Li (Benzene/ Ether)	− 78	2	+2.4 (13, C_6H_6)	7.8
$(C_6H_5)_2CH$—CHO	C_6H_5Li (Benzene/ Ether)	− 78	3	−11.1 (9, C_2H_5OH)	10
$CH_3COC_2H_5$	C_6H_5Li (Benzene/ Ether)	− 78	3	+0.6 (−)	3.3
C_6H_5—CHO	*n*-C_4H_9MgI	− 78	3	−2.0 (13, C_6H_6)	6.5
C_6H_5—CHO	$(n\text{-}C_4H_9)_2Mg$	− 78	2	−2.5 (7, C_6H_5)	8

[a] For rotations of optically pure products see [8b, 10].

Table 2 gives further examples comprising other carbonyl and other organometallic compounds. Optically active compounds result in all these cases. The optical yields vary greatly; from the absolute configurations of the favored antipodes produced it appears that there is no single mechanism concerned [9].

Asymmetrically solvated lithium derivatives besides those shown in Table 2 can be obtained by metalation with butyllithium in DAB-hexane or -ether. For instance, when butyllithium is added to the orthotrithioformic ester *(4)* [11] in ether-(+)-DAB [ratio DAB: (4) = 4 : 1] at −78 °C, an insoluble mass is formed on the wall of the flask but this redissolves on subsequent additon of benzaldehyde. The (*R*)-mandelic acid derivative *(5)* [12], $[\alpha]_D = +23°$ ($c = 5$ in CH_2Cl_2), is formed in 91% yield.

Experimental (see Table 1, no. 13): (+)-DAB (20 ml, 90 mmoles) and pentane (20 ml) under argon at −80 °C are treated with butyllithium (10 mmoles; 2.7 M in hexane) and stirred with a mechanical Teflon overhead stirrer. The pentane bath is caused to solidify (−130 °C) by addition of liquid nitrogen. The contents of the flask assume the consistency of honey. Benzaldehyde (10 mmoles) in pentane (5 ml)



is then added during 5 min, this causing formation of a precipitate. After the addition, the mixture sometimes soldifies and cannot be stirred. It is allowed to warm slowly, at −50 °C it is treated with water (2 ml), then acidified by addition of 17% HCl with cooling and transferred in pentane to a separatory funnel. The aqueous phase is extracted with pentane. The pentane phases are united, washed with dilute HCl, $NaHCO_3$ solution, and water, and dried over Na_2SO_4. Distillation affords 1-phenyl-1-pentanol (1.21 g, 74%;pure on gas chromatography), b.p. 81 °C/0.8 torr, $[\alpha]_D = +5.74°$ (homogeneous), $[\alpha]_{365} = +17.75°$. To regenerate the DAB (90%, with no loss of activity) the hydrochloric acid solutions are collected, saturated with KOH, and extracted continuously with ether or benzene.

Received: September 15, 1969 [Z 101a IE]
German version: Angew. Chem. *81*, 1002 (1969)

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[5] An excess of sparteine also increases *p* (Table 1, nos. 15 and 16), but this amine is less effective than DAB for other Li derivatives.

[6] The sign of rotation of all the products is the same as that of the tartaric acid used. The DAB picrate rotates in the opposite direction; all the numerical values, including the rotations, were the same within experimental error in the two series.

[7] This corresponds to a 66% yield of one antipode, which, to our knowledge, is the highest value so far recorded for an asymmetric solvent-catalysis of an irreversible [2b] reaction.

[8] a) *P. A. Levene* and *L. A. Mikeska*, J. biol. Chemistry *97*, 379 (1932); b) *R. MacLeod, F. J. Welch*, and *H. S. Mosher*, J. Amer. chem. Soc. *82*, 876 (1960).

[9] We consider mechanistic conclusions as yet unjustifiable; it seems that compounds LiR (a) that form precipitates with DAB [R = CH_3, C_6H_5, and $(C_6H_5S)_3C$] and (b) that give homogeneous solutions [R = C_4H_9 and $(CH_3)_2CH$] add preferentially to opposite sides of the carbonyl compound. The optical yields are distinctly higher in group (b).

[10] *A. W. Ingersoll*, Org. Reactions *2*, 376 (1944) and literature cited therein; *J. Collins, W. A. Bonner*, and *L. T. Lester*, J. Amer. chem. Soc. *81*, 460 (1959).

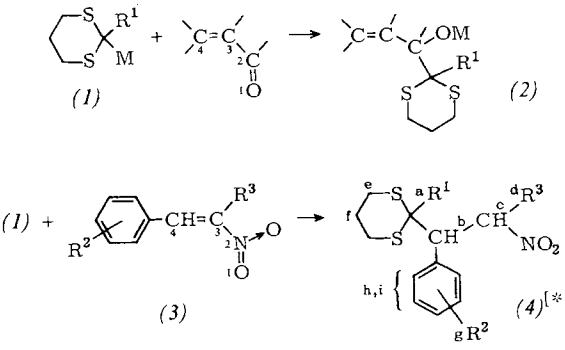
[11] *D. Seebach*, Angew. Chem. *79*, 468 (1967); Angew. Chem. internat. Edit. *6*, 442 (1967).

[12] The optical yield could not be determined since the hydrolysis [11] leading to (*R*)-(−)mandelic acid was accompanied by partial racemization.

1,4-Addition of 2-Lithio-1,3-dithianes to Substituted ω-Nitrostyrenes

By *D. Seebach* and *H. F. Leitz* [*]

Metalated 1,3-dithianes *(1)* [M = Li, Mg, Mg/Cu^I, Zn, or Cd], which have proved their value as nucleophilic acylating agents[1], add to α,β-unsaturated carbonyl compounds exclusively at the 1,2-positions (*i.e.*, to the C=O group), giving compounds *(2)* [1b,2].



	R^1	R^2	R^3	*(4)* [3] Yield (%)[a]	M.p. (°C)
(a)	H	4-CH_3O	H	25	89.6–91.0
(b)	H	2,5-$(CH_3O)_2$-4-CH_3	H	90	143.1–144.2
(c)	H	4-CH_3O	CH_3	50	132.8–134.2
(d)	H	2,5-$(CH_3O)_2$-4-CH_3	CH_3	70	155.0–156.1
(e)	CH_3	4-CH_3O	H	25	81.0–82.0
(f)	C_6H_5	4-CH_3O	H	90	93.1–94.2
(g)	C_6H_5	2,5-$(CH_3O)_2$	H	72	138.2–139.2

[a] Yields are not optimal in all cases.

We have now found that 1,4-addition occurs if the nitrostyrenes *(3)* are added slowly to the 2-lithio-1,3-dithianes *(1)* (both in THF at −78 °C); after hydrolysis we isolated the 2-(2-nitroalkyl)-1,3-dithianes *(4)*. The structure of products *(4)* [3] was established chemically (elemental analysis, preparation of optically active *(4)* [4] and reduction to primary amines) and by spectroscopy; the IR spectrum contains no C=N, b–H, or N–H bands. ^{1}H-NMR data [3] (in $CDCl_3$, TMS as internal std., 60 MHz) were as follows for two examples: *(4a)*, τ = 2.78 and 3.14 ($H^{h,i}$/2d), J_{hi} = 8.5 Hz; τ = 4.92 (H^c/dd), J_{cd} = 13 Hz, J_{bc} = 5.5 Hz; τ = 5.28 (H^d/dd), J_{bd} = 9 Hz; τ = 5.72 (H^a/d), J_{ab} = 7.5 Hz; τ = 6.14 (H^b/ddd); τ = 6.22 (3 H^g/s); τ = 7.2 (4 H^e/br. m); τ = 8.4 (2 H^f/br. m). *(4c)*, τ = 4.76 (H^c/dq), J_{bc} = 9 Hz, J_{cd} = 6.5 Hz; τ = 5.52 (H^a/d), J_{ab} = 6 Hz; τ = 6.58 (H^b/dd); τ = 8.35 (3 H^d/d); other signals as for *(4a)*.

We consider the 1,4-addition unusual for the following reasons: (1) Nitrostyrenes, like other oxidizing agents, could lead to radical dimerization of lithiodithianes [1b]; (2) high yields on 1,4-addition to nitroolefins have been obtained only with strongly CH-acidic compounds [5a]; (3) with Mg-, Zn-, and Cd-alkyl and -aryl compounds, competing 1,2-addition reduces the yields [5b]; and (4) organolithium compounds in particular favor 1,2-addition to α,β-unsaturated electrophiles, which would lead to hydroxylamines in the present case [5c].

Received: September 15, 1969 [Z 101b IE]
German version: Angew. Chem. *81*, 1047 (1969)

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[**] The small letters in this formula are labels for the protons.

[1] a) *D. Seebach*, Angew. Chem. *81*, 690 (1969); Angew. Chem. internat. Edit. *8*, 639 (1969); b) Synthesis *1*, 17 (1969).

[2] Acrylonitrile is polymerized by lithiodithianes.

[3] Two diastereoisomers can be detected (NMR) in the crude adducts to nitropropenes *(3)* (R = CH_3); the data given here all refer to the form isolated by the purification procedure (recrystallization, chromatography on Al_2O_3 or SiO_2).

[4] Cf. *D. Seebach, H. Dörr, B. Bastani*, and *V. Ehrig*, Angew. Chem. *81*, 1002 (1969); Angew. Chem. internat. Edit. *8*, 982 (1969).

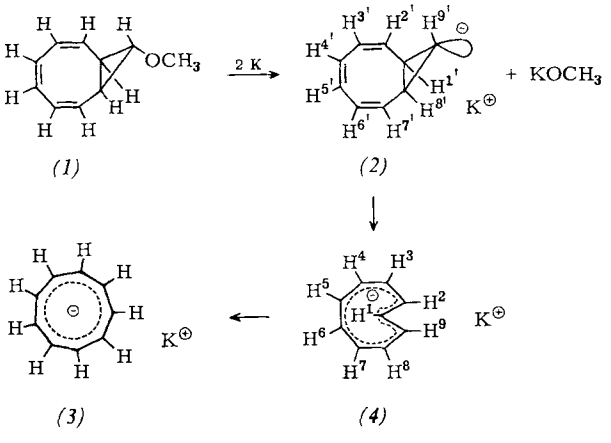
[5] a) *V. V. Perekalin et al.*, Usp. Chim. *24*, 613 (1955) [review]; Doklady Akad. Nauk SSSR *112*, 441 (1957); *A. S. Polyanskaya*, Uch. Zap. Leningr. Gos. Ped. Inst. *160*, Pt. 1, 53 (1959); Chem. Abstr. *50*, 159 (1959); *51*, 13866 (1960); *57*, 16590 (1962); *H. Feuer* and *R. Miller*, J. org. Chemistry *26*, 1349 (1961); *E. B. Hodge*, US-Pat. 3024232 (1962); Chem. Abstr. *57*, 11046 (1962); b) *E. P. Kohler* and *J. F. Stone*, J. Amer. chem. Soc. *52*, 761 (1930); *G. D. Buckley* and *E. Ellery*, J. chem. Soc. (London) *1947*, 1494, 1497; Brit. Pat. 571804 (1945); Chem. Abstr. *41*, P 4508; *J. Michel* and *E. Henry-Basch*, C. R. hebd. Séances Acad. Sci. *C 262*, 1274 (1966); c) *P. Buck* and *G. Köbrich*, Tetrahedron Letters *1967*, 1563.

trans,cis,cis,cis-Cyclononatetraenyl Anion, a New Aromatic 10 π System

By *G. Boche*, *D. Martens*, and *W. Danzer*[*]

Woodward and *Hoffmann*[1] predicted that thermal ring opening of the cyclopropyl anion to the allyl anion would proceed in a conrotatory fashion. *Huisgen et al.*[2] have been able to detect the expected thermal conrotation and photochemical disrotation in the isoelectronic aziridine/azomethine ylide system.

Katz and *Garratt*[3] have prepared potassium *cis,cis,cis,cis*-cyclononatetraenide *(3)* in essentially quantitative yield[4] by reaction of *anti*-9-methoxy-*cis*-bicyclo[6.1.0]nona-2,4,6-triene *(1)* with potassium in tetrahydrofuran. Orbital symmetry considerations[1,5] would, however, suggest that the cyclopropyl anion *(2)* undergoes conrotatory ring opening to give potassium *trans,cis,cis,cis*-cyclononatetraenide *(4)*.



(1) *(2)* *(3)* *(4)*

We have, therefore, reinvestigated the course of the reaction in [D_8]-THF at −40 °C by NMR spectroscopy and, after complete consumption of *(1)*[6], a spectrum was obtained that indicates the presence of only 4 ± 2% of *(3)* (sharp signal at τ = 2.87). The chemical shifts observed clearly indicate that the remaining signals cannot be assigned to the potassium cyclopropanide compound *(2)* but to the aromatic potassium *trans,cis,cis,cis*-cyclononatetraenide *(4)*: The six protons H^3—H^8 absorb between τ = 3.0 and 3.6; the signal due to H^2 and H^9 appears as a broadened doublet (J = 15 Hz) centered at τ = 2.73, and H^1 absorbs as a triplet at τ = 13.52 (J = 15 Hz).

As, for example, in the case of the aromatic annulenes[7], the delocalization of the π electrons in *(4)* in an external magnetic field gives rise to a ring current which shifts the NMR signals of the protons situated outside the ring (H^2—H^9) downfield, and that of the inner proton H^1 upfield[8]. If *(2)* were present, six olefinic protons ($H^{2'}$—$H^{7'}$) and three cyclopropyl-anion protons[9] ($H^{1'}$, $H^{8'}$, $H^{9'}$) would be observed. The ring opening *(2)*→*(4)*[10], which is fast even at −40 °C, profits from formation of the 10π aromatic compound *(4)*. On the other hand, ring opening does not occur at a measurable rate in the aziridine/azomethine ylide system until the temperature has been raised to 100 °C[2a]. None of the isolable cyclopropyl anions is known to undergo ring opening[1,5,9].

Potassium *trans,cis,cis,cis*-cyclononatetraenide *(4)* can be stored for days at −40 °C in a closed vessel. However, conversion to the all-*cis* compound *(3)* takes place when the reaction mixture is stirred at room temperature.

Received: September 19, 1969 [Z 102 IE]
German version: Angew. Chem. *81*, 1003 (1969)

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[2] a) *R. Huisgen*, *W. Scheer*, *G. Szeimies*, and *H. Huber*, Tetrahedron Letters *1966*, 397; b) *R. Huisgen*, *W. Scheer*, and *H. Huber*, J. Amer. chem. Soc. *89*, 1753 (1967); c) *R. Huisgen*, *W. Scheer*, and *H. Mäder*, Angew. Chem. *81*, 619 (1969); Angew. Chem. internat. Edit. *8*, 602 (1969); d) *R. Huisgen*, *W.Scheer*, *H. Mäder*, and *E. Brunn*, Angew. Chem. *81*, 621 (1969); Angew. Chem. internat. Edit. *8*, 604 (1969); e) *R. Huisgen* and *H.Mäder*, Angew. Chem. *81*, 621 (1969); Angew. Chem. internat. Edit. *8*, 604 (1969).

[3] *T. J. Katz* and *P. J. Garratt*, J. Amer. chem. Soc. *85*, 2852 (1963); *86*, 5194 (1964).

[4] After allowing the temperature of the reaction mixture to rise from −78 to +25 °C within 12 h, *Katz* and *Garrat* observed only the sharp absorption signal of the all-*cis* compound *(3)* at τ = 2.96 (alongside the signals due to the solvent) in the NMR spectrum.

[5] *H. C. Longuet-Higgins* and *E. W. Abrahamson*, J. Amer. chem. Soc. *87*, 2045 (1965).

[6] The reaction time, which depends on the rate of stirring, is 3–6 h at −40 °C

[7] For a review, see: *F. Sondheimer*, *I. C. Calder*, *J. A. Elix*, *Y. Gaoni*, *P. J. Garratt*, *K. Grohmann*, *G. di Maio*, *J. Mayer*, *M. V. Sargent*, and *R. Wolowsky*, Spec. Publ. No. 21 (Chem. Soc., London),p. 75.

[8] *J. A. Pople* and *K. G. Untch*, J. Amer. chem. Soc. *88*, 4811 (1966).

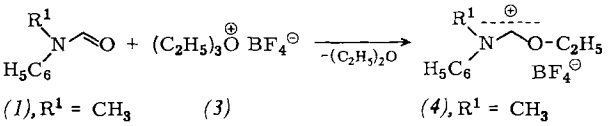
[9] For the NMR spectrum of cyclopropyllithium see: *D. Seyferth* and *H. M. Cohen*, J. organometallic Chem. *1*, 15 (1963/64).

[10] *(2)* could not be detected by NMR spectroscopy.

C–N Fission of *O*-Alkylated Formamides[1,2]

By *H. G. Nordmann* and *F. Kröhnke*[*]

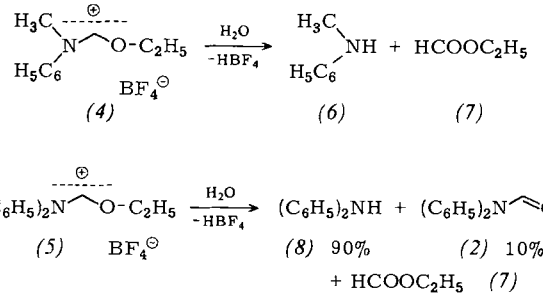
We have prepared the *O*-alkylated formamides ethoxy-*N*-(methylanilino)- *(4)* and ethoxy-*N*,*N*-(diphenylamino)-methylium tetrafluoroborate *(5)* by alkylation of *N*-methylformanilide *(1)* and diphenylformamide *(2)*, respectively, with triethyloxonium tetrafluoroborate *(3)*[3,4].



(1), R^1 = CH_3 *(3)* *(4)*, R^1 = CH_3
(2), R^1 = C_6H_5 *(5)*, R^1 = C_6H_5

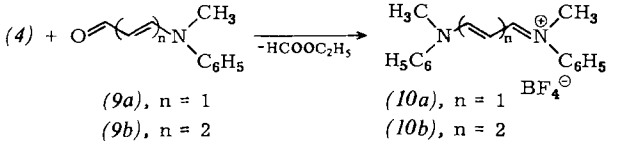
These products *(4)* and *(5)* are crystalline substances that are relatively insensitive to atmospheric moisture and can be recrystallized from acetonitrile-ether. Their structure has been proved by analyses and NMR spectra. A characteristic feature is that introduction of the positive charge shifts the formyl-H signals from 8.27 to 8.48 ppm [*(1)*→*(4)*] and from 8.55 to 8.82 ppm [*(2)*→*(5)*] (δ values; in $CDCl_3$; TMS as internal standard).

(4) reacts with an excess of water at room temperature to give *N*-methylaniline *(6)* and ethyl formate *(7)* almost quantitatively; but, in this reaction, *(5)* gives diphenylamine *(8)* (90%), diphenylformamide *(2)* (10%), and ethyl formate



(7) (analysis by NMR spectroscopy and gas chromatography).

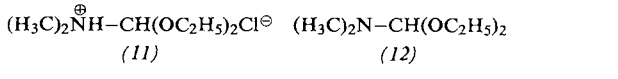
At room temperature in methylene chloride the salts *(4)* and *(5)* transfer the amino group almost quantitatively to vinylogous amides *(9)* and similar carbonyl compounds. *E.g.*, the symmetrical vinylogous amidinium salts *(10)* can be prepared in this way.



(9a), n = 1 *(10a)*, n = 1
(9b), n = 2 *(10b)*, n = 2

The above results accord with the ready hydrolytic fission of the C—N bond in *O*-alkylated and *O*-acylated vinylogous amides and in the vinylogous formimidoyl chlorides. This C—N fission is the basis for formation of symmetrical amidinium salts from vinylogous amides in an alkylating or acylating medium (the "symmetry reaction"), as well as for the synthesis of β-chlorovinyl aldehydes [2].

Analogously, dimethylformamide diethyl acetal hydrochloride *(11)* suffers hydrolysis of the C—N bond by *Meerwein*'s method [4], giving the hydrochloride of the leaving amine quantitatively. However, *Bredereck* [5] found that dimethylformamide diethyl acetal *(12)* [which on dissociation in an inert solvent gives an *O*-alkylated formamide similar to *(4)* and *(5)*] undergoes mainly C—O fission on hydrolysis, *i.e.*, dealkylation to dimethylformamide.



(11) *(12)*

Ethoxy-N-(methylanilino)methylium tetrafluoroborate (4)

(3) (19 g, 100 mmoles) is treated with *(1)* (14.86 g, 110 mmoles = 13.50 ml) with exclusion of moisture and ice-cooling, and the mixture is stirred at room temperature. *(4)* crystallizes within 30 min from the ether layer (ice-cooling). The product is filtered off and washed with dry ether until colorless and dry. It must be kept in a desiccator over P_2O_5. Yield: 25.1 g (100%). For purification, *(4)* is dissolved in dry acetonitrile at room temperature, treated with active charcoal, and precipitated with anhydrous ether at 0 °C [2 ml of acetonitrile/10 ml of ether/1 g of *(4)*], forming colorless, narrow leaflets, m.p. 104—106 °C (unsharp; in a sealed tube). *(5)* is prepared analogously, forming colorless rods, m.p. 92—94 °C (unsharp).

N-Methyl-[3-(N'-methylanilino)propenylidene]anilinium tetrafluoroborate (10a)

(4) (2.51 g, 10 mmoles) is dissolved in anhydrous methylene chloride (10 ml) and treated with *(9a)* (1.61 g, 10 mmoles), and the mixture is stirred at room temperature for 2 hours with exclusion of moisture. The orange solution obtained is cooled in ice and treated with ether (50 ml) whilst being rubbed. The yellow *(10a)* crystallizes and is collected and washed with ether (yield 3.10 g, 92%). For purification it is dissolved in acetonitrile at room temperature and treated with ether with rubbing until a permanent turbidity is produced [6 ml of acetonitrile/100 ml of ether/1 g of *(10a)*]. Lemon yellow rods, m.p. 149—151 °C, are obtained.

Received: August 25, 1969 [Z 103 IE]
German version: Angew. Chem. *81*, 1004 (1969)

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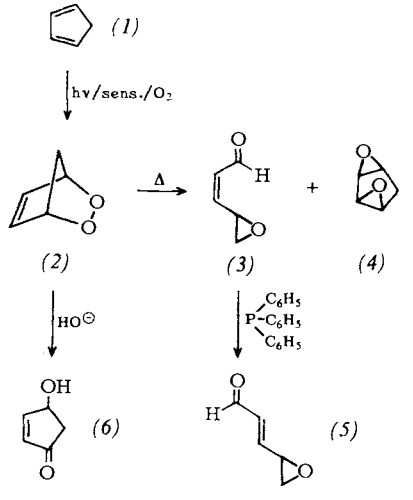
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A New Peroxide Rearrangement: *cis*-4,5-Epoxy-2-pentenal from 1,4-Epidioxy-2-cyclopentene

By *K. H. Schulte-Elte, B. Willhalm*, and *G. Ohloff* [*]

1,4-Epidioxy-2-cyclopentene *(2)* is formed by 1,4-addition of singlet oxygen to cyclopentadiene *(1)* and can be isolated at —100 °C [1]. In an attempt to prepare *(2)* by dye-sensitized photo-oxidation of *(1)* in alcoholic solution and in presence



of polymerization inhibitors at temperatures above 0 °C we obtained, surprisingly, the hitherto unknown compound *cis*-4,5-epoxy-2-pentenal *(3)* in 58% yield [b.p. 35 °C/0.1 torr; $n_D^{20} = 1.4933$; $d_4^{20} = 1.04$; IR: 762, 1635 cm^{-1} (*cis*-CH=CH—); 1675, 2730, 2850 cm^{-1} (—CHO); NMR (CCl_4 + $CDCl_3$/TMS): 9.92 ppm (1H/m, —CHO); 6.1 ppm (2H/m, *cis*-CH=CH—); 4.17 ppm (1H/m, oxiranyl proton); 3.12 and 2.71 ppm (2H/2 × 2d, oxiranyl protons, J = 4.5 and 5.5, and 2.3 and 5.5 Hz resp.)]. *cis*-1,2,3,4-Diepoxycyclopentane *(4)* [2] (7%) and polymeric compounds (30%) were formed at the same time.

1-Hydroxy-2-cyclopenten-4-one *(6)* (b.p. 70 °C/0.1 torr; $n_D^{20} = 1.4882$; $d_4^{20} = 1.02$), which was previously obtained [1] as an isomerization product from *(2)*, was not formed in this reaction. In alkaline alcoholic solution [3], however, it was formed in 20% (maximum) yield. The prerequisites for the preparation of *(6)*, therefore, are that the synthesis is carried out rapidly, at or below room temperature, and at a pH of 8—10.

In the presence of triphenylphosphine, compound *(3)*, which is stable in the pure state, rearranges almost quantitatively at room temperature to the *trans* isomer *(5)* [b.p. 36 °C/0.1 torr; $n_D^{20} = 1.4931$; $d_4^{20} = 1.08$; IR: 923, 972, 1638 cm^{-1}

(*trans*-CH=CH); 1680, 2720, 2810 cm^{-1} (—CHO); NMR (CCl_4 + $CDCl_3$/TMS): 9.46 ppm (1 H/m, —CHO); 6.41 ppm (2 H/m, *trans*-CH=CH—); 3.53 ppm (1 H/m, oxiranyl proton); 3.06 and 2.70 ppm (2 H/2 × 2d, oxiranyl protons, J = 4.5 and 5.5, and 2.3 and 5.5 Hz resp.)].

As dienophiles, compounds *(3)* and *(5)* exhibit about the same reactivity as crotonaldehyde. Thus the adduct from 2,3-dimethylbutadiene can be obtained in 82% yield merely by heating the components in benzene. Heating *(3)* and *(5)* in dilute hydrochloric acid leads to smooth formation of furfuryl alcohol, while their reduction with $NaBH_4$ in ethanol yields a mixture of *trans*-2-pentene-1,4-diol (b.p. 127 °C/ 12 torr; n_D^{20} = 1.4740; d_4^{20} = 1.02) and *trans*-2-pentene-1,5-diol (b.p. 132 °C/12 torr; n_D^{20} = 1.4712; d_4^{20} = 1.038) in a ratio of 3:1.

The purely thermal isomerization of *(2)* to *(3)* represents a new type of rearrangement of peroxides of the 3,6-dihydro-1,2-dioxin[4,5] or 1,2-dioxolane type[6]. This smooth rearrangement, which is not influenced by solvents or radical inhibitors, is presumably an electrocyclic four-center reaction. Alkyl derivatives of 1,4-epidioxy-2-cyclopentene can isomerize in a similar way[7].

Received: October 14, 1969 [Z 104 IE]
German version: Angew. Chem. *81*, 1045 (1969)

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[1] *G. O. Schenck* and *E. D. Dunlap*, Angew. Chem. *68*, 248 (1956).

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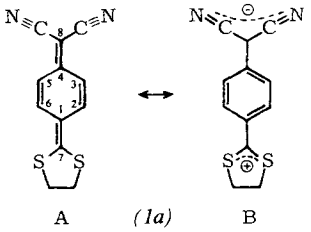
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Azaquinodimethanes[1]

By *H.-U. Wagner* and *R. Gompper*[*]

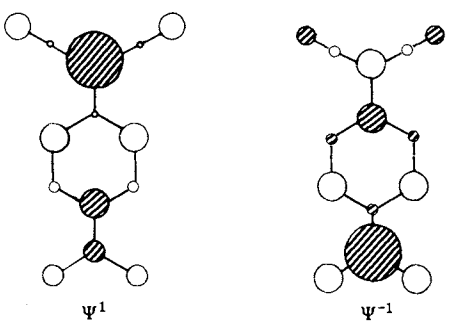
The "push-pull" substituted quinodimethanes of type *(1)* are characterized by intense, longwave absorption bands in the visible region[2]. According to the simple HMO model these bands correspond to an electron transition from the highest occupied molecular orbital, Ψ^1, to the lowest unoccupied orbital, Ψ^{-1}. This transition is polarized in the direction of



A *(1a)* B

the two-fold axis of the molecule and associated with a charge shift from the dicyanomethylene to the dimercaptomethylene[3]. The polarization is also reversed at positions 2 and 3: During the transition from Ψ^1 to Ψ^{-1} the electron density at position 2 increases, whereas at position 3 it decreases (Fig. 1).

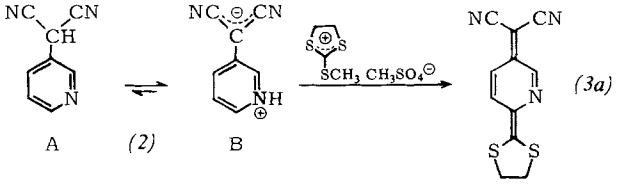
It is to be expected, therefore, that when the carbon is replaced by the more electronegative nitrogen, the Ψ^1 level is lowered much more than the Ψ^{-1} level. The lower energy difference should be characterized by a bathochromic shift of the longwave band. The converse is true for position 3.



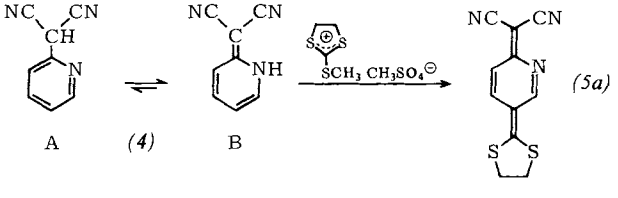
Ψ^1 Ψ^{-1}

Fig. 1. Molecular orbital diagrams. The diameters of the circles correspond to the linear combination coefficients. HMO parameters: h_N = 0.8, h_S = 1.0, k_{C-CN} = 0.8, k_{C-S} = 0.7, $k_{C=N}$ = 1.8. The shading denotes negative sign. The ethylene bridge in the dithiolane ring is not considered in the π process.

The desired azaquinodimethanes of types *(3)* and *(5)* can be prepared from the pyridylmalonodinitriles *(2)* and *(4)* respectively and a dithiolanylium salt [cf. the synthesis of *(1a)*[4,5]].

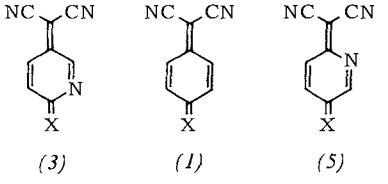


A *(2)* B *(3a)*



A *(4)* B *(5a)*

The pyridylmalonodinitriles *(2)* and *(4)* were synthesized from the corresponding acetonitriles by direct introduction of cyano group using cyanates (cf. the cyanation of malonodinitrile[6]). According to the IR spectra, compounds *(2)* and *(4)* (solid in KBr) are present in the tautomeric forms B. Both compounds exhibit intense NH bands at 3150—3100 cm^{-1} and very strong cyanide bands (*(2)* at 2190 and 2140, *(4)* at 2200 and 2170 cm^{-1}). These doubly split cyanide bands, which are also found in the spectra of *(1a)* and the azaquinodimethanes mentioned in Table 1, are characteristic of strongly conjugated dicyanomethylene groups (cf.[4]). The high melting points [*(2)* at 246—248 °C, *(4)* at 245—250 °C; cf. phenylmalonodinitrile, m.p. 68 °C] are indicative of highly polar compounds.



(3) *(1)* *(5)*

(a), X =  *(b)*, X = 

(c), X =  *(d)*, X = 

(e), X = 

Table 1. Longwave bands of azaquinodimethanes of types *(3)* and *(5)*, and of quinodimethanes of type *(1)* [a].

	(3) λ (nm)	*(1)* λ (nm)	*(5)* λ (nm)
(a)	610 [b]	590	585 [b]
	560	555	540
	520	510	505
(b)	675	660	640
	620	610	590
	575		555
(c)	665	640	635
	610	585	580
	565	545	540
(d)	770	700	670
	720		645
(e)	760	750	710
	690		670
	640		

[a] Measured in chloroform. The solubility is so low that a determination of the extinction was considered inpracticable. The bands generally show pronounced partial vibration bands. The figures quoted denote the maxima of the individual parts of the bands.
[b] Log ε about 4.7.

The reactions of *(2)* and *(4)* with 2-methylthio-1,3-dithiolanyl methyl sulfate are carried out in boiling pyridine under reflux. The azaquinodimethanes *(3a)* and *(5a)* precipitate from the hot solution as bluish-black, very fine needle-like crystals. The azaquinodimethanes *(3b)*–*(3e)* and *(5b)*–*(5e)* (see Table 1) are prepared in an analogous manner. The structures of the new compounds were determined by elemental analysis, and IR and UV spectroscopy.

As shown in Table 1, aza substitution in position 2 leads to the expected bathochromic shift — in position 3 to a hypsochromic shift. According to the HMO models for quinodimethanes containing a π-cyclic donor X, the shifts in these systems should be slightly greater in magnitude than in *(3a)* and *(5a)*. Since, however, the position of the maxima depends largely on the shape of the bands, and the 0–0 transition cannot be determined unequivocally, these fine differences cannot be interpreted quantitatively. All systems exhibit weakly negative solvatochromism (longwave bands: λ_{CHCl_3}–λ_{CH_3CN} about 10–30 nm). According to *Förster*[7] this points to a diminution of the polarity on electron excitation, *i.e.* the non-polar resonance structure A makes a greater contribution to the excited state than to the ground state. The HMO model also shows that the overall polarity of the molecule is lowered by transition of an electron to the oppositely polarized molecular orbital Ψ^{*-1} [8].

Received: September 22, 1969 [Z 105 IE]
German version: Angew. Chem. *81*, 1004 (1969)

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[1] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Bayerische Akademie der Wissenschaften (Leibniz-Rechenzentrum München).

[2] *R. Gompper* and *H.-U. Wagner*, Tetrahedron Letters *1968*, 165.

[3] According to our own SCF-CI calculations, the contribution of this electronic configuration to the lowest excited singlet states exceeds 96%.

[4] *R. Gompper, H.-U. Wagner*, and *E. Kutter*, Chem. Ber. *101*, 4123 (1968).

[5] *R. Gompper, E. Kutter*, and *H.-U. Wagner*, Angew. Chem. *78*, 545 (1966); Angew. Chem. internat. Edit. *5*, 517 (1966).

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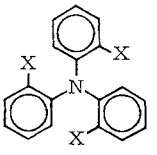
[7] *Th. Förster*, Z. Elektrochem. angew. physik. Chem. *45*, 548 (1939); *47*, 52 (1941); Z. physik. Chem. *47*, 245 (1940).

[8] According to SCF–CI calculations, the lowest excited singlet state has a considerably lower dipole moment than the ground state.

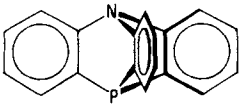
Azaphosphatriptycene[**]

By *D. Hellwinkel* and *W. Schenk*[*]

In an extension of our work on organic derivatives of main-group elements in higher coordination states, which owe their marked stability to the bidentate 2,2′-biphenylylene group[1], we set about preparing compounds of this type containing tridentate ligands. Since 2,2′,2″-triiodotriphenylmethane and 1,1,1-tris(2-iodophenyl)ethane[2] have hitherto proved preparable only in insufficient yields we resorted to tris(*o*-bromophenyl)amine *(1a)* as starting material, this compound being formed in 50–54% yield, m.p. 185.5 to 186 °C, on reaction of bis(*o*-bromophenyl)amine[3] with *o*-dibromobenzene, potassium carbonate, and copper bronze.



(1a), X = Br
(1b), X = Li



(2)

Tris(*o*-lithiophenyl)amine *(1b)*, which is prepared from *(1a)* and *n*-butyllithium and is sparingly soluble in ether, reacts with triphenyl phosphite in ether/THF to give colorless crystals of azaphosphatriptycene *(2)*, m.p. 255–255.5 °C, in 30% yield.

The relatively high proportion of doubly and trebly charged ions is particularly conspicuous in the mass spectrum of *(2)* (Table 1); such ions have also been observed in the mass spectrum of triptycene itself[4].

Table 1. Molecular ions and most important fragment ions of *(2)* (singly, doubly, and trebly charged ions are listed under one another together with their relative intensities).

M	M − H	M − 2H	M − 3H	M − 4H
273	272	271	270	269
(67%)	(100%)	(4%)	(9.3%)	(1.6%)
$136^1/_2$	136	$135^1/_2$	135	$134^1/_2$
(10%)	(10%)	(7.8%)	(10.5%)	(2.1%)
91	$90^2/_3$	$90^1/_3$	—	$89^2/_3$
(0.2%)	(0.1%)	(0.1%)		(0.1%)

The ^{31}P-NMR signal of *(2)* appears at an astonishingly high field strength: $\delta^{31}P$ = +80 ppm ($CHCl_3$); +79 ppm (THF) (85% H_3PO_4 as external standard)[5]. This suggests that the lone pair on phosphorus has a high s character and therefore that the CPC bond angle must be in the region of 90°[6]. Such a value, *i.e.* 93°, is also calculated from the formulas developed by *Parks*[7], which correlate bond angles, chemical shift of the phosphorus, and differences in electronegativity for the participating atoms in tertiary phosphines. The second value of 104.5° obtained on solution of the resulting quadratic equation can be neglected as implausible[2].

Interestingly, the UV spectrum of *(2)* (ethanol): λ_{max} = 216.5 nm (log ε = 4.31); shoulder at 245 nm (log ε = 3.35); ($CHCl_3$): λ_{max} = 247.5 nm (log ε = 3.57), shoulder at 279 nm (log ε = 2.94) shows little resemblance to that of azatriptycene[8].

Reaction of *(2)* with methyl iodide in a bomb tube affords *P*-methylazaphosphoniatriptycene iodide : decomposition point 279–285 °C; τ = 6.68 (CH_3), J_{HCP} = 15.6 Hz; $\delta^{31}P$ = +4.75 ppm (CF_3COOH). In this compound the phosphorus is more strongly shielded than in triphenylmethylphosphonium iodide (τ = 7.19 (CH_3); J_{HCP} = 13.6 Hz; $\delta^{31}P$ = −19.4 ppm), whereas the methyl protons absorb at lower field strength. This is again compatible with the concept that the Pσ orbital bonded to the methyl group possesses relatively high s character which leads to an electron density that is

higher than normal (pure sp^3 valence) on phosphorus and lower on the methyl group.

Reaction of *(2)* with bromine and subsequent hydrolysis gives the *P*-oxide: decomposition point 300—301 °C, ν P=O = 1250 cm^{-1}; λ_{max} = 220.5 nm (log ε = 3.98), shoulder at 238 nm (log ε = 3.67) (ethanol).

Compounds of type *(2)* [9] are of interest with regard to higher valencies of the bridgehead atoms, since it is possible that unusual molecular geometries can be realized with the aid of the rigid nitrilo-2,2′,2″-triphenyl system.

Received: October 6, 1969 [Z 106 IE]
German version: Angew. Chem. *81*, 1049 (1969)

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

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[8] *G. Wittig* and *G. Steinhoff*, Liebigs Ann. Chem. *676*, 21 (1964).

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[3]-Catenanes[1] [**]

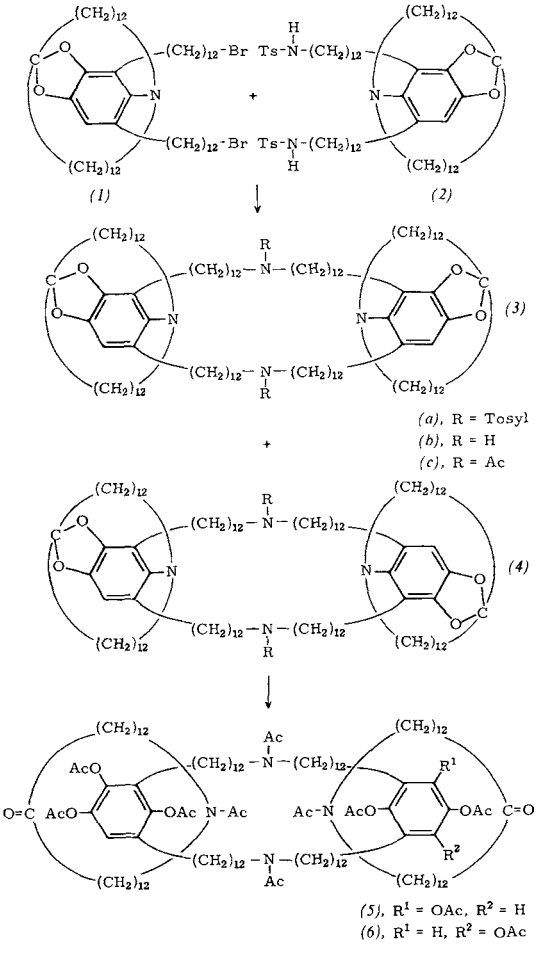
By *G. Schill* and *C. Zürcher* [*]

We have prepared catenanes from three rings joined after the manner of links in a chain by an extension of the principle of the directed synthesis [2].

Reaction of the diansa-dibromo compound *(1)* [3] with *p*-toluenesulfonamide in the presence of sodium hydride in anhydrous dimethylformamide [4] yields the ditosyl derivative *(2)* in 74% yield. Subsequent cyclization of *(2)* with *(1)* in the molar ratio 1 : 1 in anhydrous dimethylformamide [5] at 100 to 120 °C in highly diluted solution with potassium carbonate [6] affords a 38% yield of a mixture of the *cis-trans* isomeric cyclization products *(3a)* and *(4a)* which cannot be separated by thin-layer chromatography. On removal of the tosyl groups by reaction with sodium in anhydrous butanol [7] to form *(3b)* and *(4b)* and subsequent acetylation with pyridine/acetic anhydride we obtained a mixture of the [3]-pre-catena compounds *(3c)* and *(4c)*.

The mass spectrum [8] of *(3c)* + *(4c)* contains the molecular ion as base peak at *m/e* 1720 and a peak due to the doubly charged molecular ion at *m/e* 860 having an exceptionally high relative intensity of 91%. (The isotopic peaks at *m/e* 1721 and 860.5, whose intensities exceed those of the peaks at 1720 and 860, are neglected.) The spectrum exhibits a remarkably low degree of fragmentation. Although groups of peaks occur at intervals of 14 mass units, as in the spectra of saturated long-chain hydrocarbons, the relative intensity of the highest peak is only 20%. Other di- and tri-ansa compounds have also been observed to behave similarly.

The chemical bonds between the doubly-bridged systems are broken in a manner similar to that used in earlier experiments [2]. We isolated a 32% yield (calculated with respect to *(3c)* and *(4c)*) of a mixture of the two [3]-catena compounds



(5) and *(6)* as a colorless oil that appears homogeneous on thin-layer chromatography.

The results of elemental analysis, the IR spectrum (CO frequencies of the phenolic acetyl groups at 1780 cm^{-1}, of the keto groups at 1720 cm^{-1}, of the *N*-acetyl groups at 1650 cm^{-1}), and the molecular weight as determined by vapor pressure osmometry are in agreement with the structures given for *(5)* and *(6)*.

The NMR spectrum (in $CDCl_3$, TMS as internal standard) shows the following signals: τ = 3.03 (aryl protons); τ = 6.78 ($-CH_2-N-$ protons); τ = 7.68, 7.71, 7.76 (*O*-acetyl protons); shoulder at τ = 7.64 (benzylic and $-CH_2-\overset{\overset{O}{\|}}{C}-$ protons.

Received: October 6, 1969 [Z 107 IE]
German version: Angew. Chem. *81*, 996 (1969)

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

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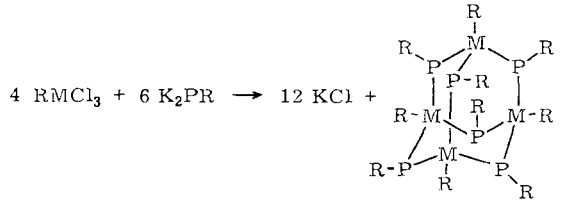
[8] The mass-spectrometric investigations were carried out by Dr. *W. Vetter*, Hoffmann La Roche AG, Basel (Switzerland).

Organometal-Substituted Phosphines having a Cage-Like Structure[**]

By *H. Schumann* and *H. Benda*[*]

Di- and trifunctional organometal halides react with phosphine, alkali-metal phosphides, or alkali-metal organophosphides to give not only polymeric but also oligomeric organometallophosphines having a cage-like structure. Thus we recently reported on the synthesis of *closo*-tetrakis(phenylstannylphosphine)[1].

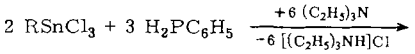
If a benzene solution of phenyltrichlorosilane or phenyltrichlorogermane and a suspension of dipotassium phenylphosphide in monoglyme/ether are simultaneously added under argon to a 2 : 1 mixture of diethyl ether/monoglyme, a *ca.* 60% yield of colorless *closo*-tetrakis(phenylsilyl)hexakis(phenylphosphine) *(1)* or pale-yellow *closo*-tetrakis(phenylgermyl)hexakis(phenylphosphine) *(2)* is obtained alongside potassium chloride and small amounts of insoluble polymers.

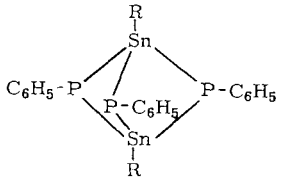


(1), R = C_6H_5, M = Si
(2), R = C_6H_5, M = Ge

The crystals of *(1)* and *(2)* are soluble in benzene, sensitive to oxygen, and decompose, without melting, above 125 °C with blistering; their homogeneity was established by thin-layer chromatography[2]. Complete elemental analyses, the cryoscopically determined molecular weight, and the IR spectra [*(1)*: νSi—P at 406, 348, and 326 cm^{-1}; *(2)*: νGe—P at 390, 334, and 309 cm^{-1}] confirm the adamantane-type structure, which has also been found for the corresponding organosilyl[3], organogermyl[4], and organostannyl[5] sulfides.

By contrast, the reaction of butyl- or phenyl-trichlorostannane with phenylphosphine in the presence of triethylamine affords a *ca.* 25% yield of benzene-soluble *closo*-bis(butylstannyl)tris(phenylphosphine) *(3)* or *closo*-bis(phenylstannyl)tris(phenylphosphine) *(4)*, together with polymeric products.





(3), R = n-C_4H_9
(4), R = C_6H_5

The colorless compounds *(3)* and *(4)* are sensitive to air and melt at 89—91 °C (decomp.) and 133—135 °C, respectively. The trigonal-bipyramidal structure is in accord with the cryoscopically determined molecular weights, the results of elemental analyses, the ^{31}P-NMR spectra[6] [*(3)* shows a singlet at +5.2 ppm], as well as the IR spectra[7] [νSn—P at 375, 328, 305 (*(3)*), and 362, 320, 296 cm^{-1} (*(4)*)].

Procedure:

(1) and *(2)*: Phenyltrichlorosilane (4.2 g, 0.02 mole) or phenyltrichlorogermane (5.1 g, 0.02 mole) is dissolved in benzene; one third of the solution is transferred, together with ether (60 ml) and monoglyme (30 ml), to a three-necked flask that has been flushed out with dry argon. The remaining two thirds of the solution is then added dropwise and simultaneously with a suspension of dipotassium phenylphosphide (0.03 mole) in monoglyme (50 ml), over a period of 4h with stirring. After six hours' stirring, half of the solvent is removed under reduced pressure, the solution is filtered, and the filtrate is concentrated until it becomes oily. Repeated extraction with petroleum ether and methylcyclohexane, dissolution in benzene, and fractional precipitation with pentane/methylcyclohexane affords almost pure crystals, which can be recrystallized from toluene/methylcyclohexane.

(3) and *(4)*: Solutions of butyltrichlorostannane (5.7 g, 0.02 mole) or phenyltrichlorostannane (6.0 g, 0.02 mole), phenylphosphine (3.3 g, 0.03 mole), and triethylamine (6.1 g, 0.06 mole) in benzene are simultaneously added dropwise at the same rate to benzene (150 ml) under dry argon. The resulting precipitate is removed after six hours' stirring. On fractional precipitation with pentane/methylcyclohexane, the clear concentrated benzene solution yields a product that proves pure on thin-layer chromatography.

Received: October 15, 1969 [Z 113 IE]
German version: Angew. Chem. *81*, 1049 (1969)

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to Dr. *G. Engelhardt*, Berlin-Adlershof, for recording the ^{31}P-NMR spectra.

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[6] 10% solution in benzene, 85% H_3PO_4 as external reference.

[7] Nujol mull, capillary.

Rotational Isomerism of N^2-Methyl-N^2-phenylthioformohydrazide[1]

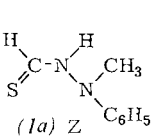
By *W. Walter* and *H. Weiss*[*]

A number of N^2,N^2-dialkylthioformohydrazides exhibit betaine-thioacyl tautomerism[2,3]. In the case of N^2,N^2-diethylthioformohydrazide it was assumed[3] that an additional rotational isomerism (E—Z isomerism) occurs in solutions of thioacyl tautomers, as is generally observed in thioamides[1]. We report here on N^2-methyl-N^2-phenylthioformohydrazide *(1)*, which does not form a betaine and permits direct observation of the rotational isomerism. The compound crystallizes in two forms having different melting points and exhibiting different IR- and UV spectra.

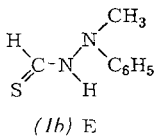
In carbon tetrachloride an equilibrium is rapidly set up between *(1a)* and *(1b)* [about 10% *(1a)*: 90% *(1b)*]. Nevertheless, the bands could be assigned to the two isomers by comparison with those of the rotational isomers of thioamides[4].

Since rapid isomerization occurs in solution the signals of both forms, *i.e.* of *(1a)* and *(1b)*, appears in the ^{1}H-NMR spectrum. In $CDCl_3$ the formyl proton of the E form *(1b)* couples with the N—H proton to give an AB system. The coupling constant is of the same order of magnitude as in N^2,N^2-diethylthioformohydrazide[3] and in thioamides[5],

and thus confirms the assignment given. A coupling with the formyl proton of *(1a)* was not observed. Deuteration eliminated the coupling in *(1b)*. The ratio of isomers is also about 9 : 1 under NMR conditions. The lower value of the NH stretching vibration of *(1b)* in KBr indicates the presence of a cyclic dimer, which can be formed from *(1b)* but not from *(1a)* [5].



(1a) Z



(1b) E

	(1a) Z	*(1b)* E
M.p.	114—115 °C	86—87 °C
IR (KBr) (ν-NH)	3270 cm^{-1}	3120 cm^{-1}
in CCl_4 $<10^{-3}$ M (ν-NH)	3322 cm^{-1}	3300 cm^{-1}
UV ($CHCl_3$) λ_{max}	252 nm	275 nm
ε_{max}	8.2×10^3	3.6×10^3
^{1}H-NMR —NH	τ = 1.09	AB J_{AB} = 12 Hz, τ_A = 1.10
—CH (in $CDCl_3$)	τ = 0.62	AB J_{AB} = 12 Hz, τ_B = 0.57
D—N—CH	τ = 0.65	τ = 0.60

The isomerization can be followed by IR spectroscopy. The rate constants for equilibrium and the free activation enthalpies of *(1b)* for equilibrium starting from *(1b)* of 4.9×10^{-3} s^{-1} ($\Delta G^{\neq}$ = 21.0 ± 0.2 kcal/mole) and from *(1a)* of 4.9×10^{-4} s^{-1} ($\Delta G^{\neq}$ = 22.4 ± 0.2 kcal/mole) were determined on the basis of a first order reaction. The values for secondary thioformamides [5] are of the same oder of magnitude, but somewhat higher.

N^2-Methyl-N^2-phenylthioformohydrazide (1)

A solution of *N*-methyl-*N*-phenylhydrazine (0.05 mole) in triethylamine (30 ml) is added dropwise and slowly with vigorous stirring to a solution of *O*-ethyl thioformate (0.5 mole) in triethylamine (15 ml); the reactants are kept ice cold during the addition and the reaction mixture is stirred for a further hour. The solvent is then removed by means of a rotatory evaporator and the residual oil is treated with petroleum ether. A crude crystalline product precipitates (yield 91%). Recrystallization from nitromethane yields *(1a)* as broad yellow crystals (m.p. 114—115 °C). *(1a)* is dissolved in an excess of chloroform and allowed to stand at room temperature for five hours. After removal of solvent in a rotatory evaporator, the crude product is recrystallized from nitromethane. Compound *(1b)* is obtained as colorless needles, m.p. 86—87 °C. The melt crystallizes at 90—95 °C and melts once again at 113—114 °C, *i.e.* when *(1b)* has once again rearranged to *(1a)*.

Received: October 6, 1969 [Z 108 IE]
German version: Angew. Chem. *81*, 1050 (1969)

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X-Ray Structure Analysis and Absolute Configuration of (+)-1-*m*-Bromobenzoyl-4-methylazetidin-2-one

By *E. F. Paulus, D. Kobelt*, and *H. Jensen* [*]

The enantiomers of optically active β-lactams can be obtained by separation from their racemic mixtures [1]. Thus, *rac*-4-methylazetidin-2-one, m.p. –12.4 °C, yields enantiomers having m.p. +26.7 °C and $[\alpha]_D^{21}$ = + or –8.22° (melt). On hydrolysis the levorotatory form is converted into (*S*)-(+)-β-aminobutyric acid [2]; the (*S*)-configuration can therefore be ascribed to the (–)-4-methylazetidinone [3]. While carrying out an X-ray determination of the steric features of the β-lactam ring we attempted a confirmation of the absolute configuration at the same time.

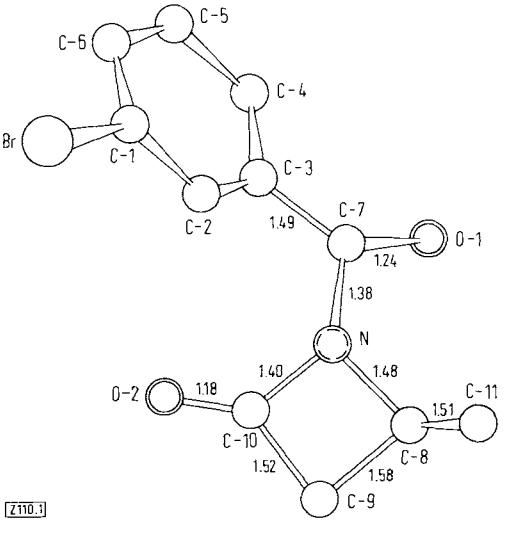
In order to do this it was necessary to introduce an anomalously scattering atom (for $Mo_{K\alpha}$ rays) into the molecule. This was achieved by acylation of (–)-4-methylazetidinone with *m*-bromobenzoyl chloride in ethyldiisopropylamine. (+)-1-*m*-Bromobenzoyl-4-methylazetidin-2-one, m.p. 88 °C, $[\alpha]_D^{22}$ = +255.0° (*c* = 3 g/100 ml; methanol), crystallizes in the space group $P2_12_12_1$ with *a* = 11.86 ± 0.01, *b* = 9.41 ± 0.01, *c* = 9.80 ± 0.01 Å; *Z* = 4; $d_{x\text{-ray}}$ = 1.63, d_{exp} = 1.61 g/cm³ (suspension method).

The intensities of the X-ray reflections were measured with a single-crystal diffractometer [7]. Of the 1834 reflections recorded, 643 had a statistical error of measurement of <10%, 505 an error of between 10 and 50%; these 1148 reflections were used in the structural analysis.

The heavy atom method was used for the determination of the phases for a Fourier synthesis of the electron density. A complication encountered was that the *x*-coordinate of the bromine atom was about 0.5. In the first Fourier synthesis, therefore, both molecular configurations appeared at the same time.

The atomic parameters of both configurations were refined by the method of least squares (full matrix). The *R*-factor ($R = [(\Sigma w(|F_o| - |F_c|)^2) / (\Sigma w |F_o|^2)]^{1/2}$ for the (*S*)-configuration is 6.05% and for the (*R*)-configuration 7.49%. According to *Hamilton* [4], the probability for the (*S*)-configuration is greater than 99.9%. The difference between the *R*-factors of both configurations is therefore unusually great [4,5]. Thus the (*S*)-configuration is proved by X-ray analysis.

The figure shows a projection of the molecule on the "best" plane of the β-lactam ring. The nitrogen of the four-membered ring is only 0.08 Å above the C(7)—C(8)—C(10) plane, thus indicating that the N—C(7) bond is turned about 7.7° out of the N—C(8)—C(10) plane. The planes N—C(9)—C(10) and N—C(8)—C(9) are at an angle of 2.1°. This slight deviation of the four-membered ring from planarity is near the limit of significance (average standard deviation of bond angles: 0.8°).



Z110.1

The "best" plane through C(3)—C(7)—O(1)—N is at an angle of 18° to the β-lactam ring, and at an angle of 41° to the benzene ring. The lactam ring and benzene ring are inclined at an angle of 56° to each other.

The deviation of the molecule from the favorable planar resonance form appears to be due to steric factors. The hydrogen atom on C(2) approaches to within 2.75 Å of O(2), that on C(4) to within 2.71 Å of O(1); on the other hand the sum of the van der Waals radii in both cases is 2.7 Å.

A few characteristic bond lengths (in Å) are given in the Figure (average standard deviation: 0.015 Å). Particularly striking is the large distance between C(8) and C(9), which has also been observed in another β-lactam[6]. The C(10)—O(2) distance is unusually small for a carbon-oxygen double bond; this is also apparent from the carbonyl stretching vibration at 5.62 μm.

Received: October 2, 1969 [Z 110 IE]
German version: Angew. Chem. *81*, 1048 (1969)

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[*] Dr. E. F. Paulus, Dipl.-Math. D. Kobelt, and Dr. H. Jensen
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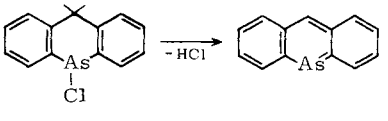
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9-Arsaanthracene[**]

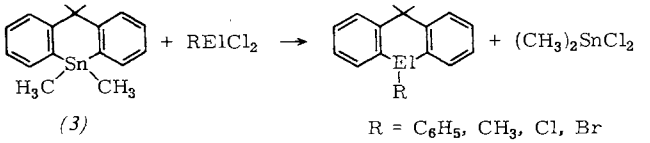
By *P. Jutzi* and *K. Deuchert*[*]

Compounds con taining an arsenic-carbon (p—p)π bond ought not to be particularly stable because of unfavorable orbital overlapping; hence, the recent synthesis of arsamethinecyanines[1] serves as the only unequivocal evidence for the existence of this type of bonding, even though (As_{4p}—C_{2p})π bonds had already been formulated in the 1920's[2,3]. 9-Arsaanthracene *(1)* ought to be formed by intramolecular loss of HCl from 9-chloro-9,10-dihydro-9-arsaanthracene *(2)*.



(2) *(1)*

Derivatives of dihydroanthracene having elements of the fifth main group as substituents in position 9 can generally be prepared by reaction of 9,9-dimethyl-9,10-dihydro-9-stannanthracene[4] *(3)* with element halides[5].



(3)

R = C_6H_5, CH_3, Cl, Br
El = P, As, Sb

Compound *(2)* can be prepared in this way in yields of up to 75%; a stoichiometric mixture of *(3)* and $AsCl_3$ is heated with stirring for 3 hours at 120 °C, $(CH_3)_2SnCl_2$ is sublimed off under vacuum (oil pump), and *(2)* is recovered and purified by distillation (m.p. 96 °C, b.p. 140 °C/0.03 torr).

Attempts were made to eliminate HCl from *(2)* by reaction with *tert*-butyllithium, triethylamine, and 1,5-diazabicyclo-[5.4.0]undec-5-ene[6] *(4)* in cyclohexane, benzene, and tetrahydrofuran; the characteristic electron excitation spectrum of each of the deep-yellow colored solutions was taken as a measure of the presence of *(1)*. According to our observations the most favorable conditions for reaction of *(2)* with *(4)* are achieved in THF saturated with argon. A solution of *(4)* (0.82 g) in THF (10 ml) is added dropwise and slowly to an ice-cold solution of *(2)* (1.49 g) in THF (90 ml); the reaction mixture immediately becomes cloudy and turns yellow in color. Reaction is complete within one hour. The precipitate (1.5 g), which contains the hydrochloride of *(4)* and polymers, is removed by filtration. The filtrate exhibits the spectrum shown in the diagram.

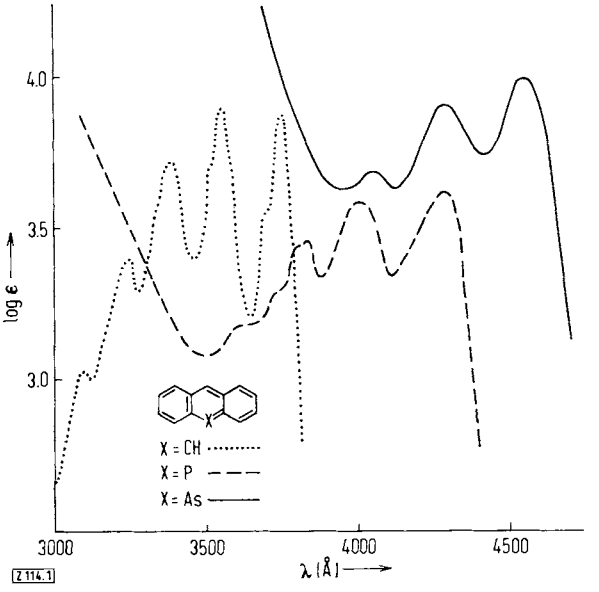
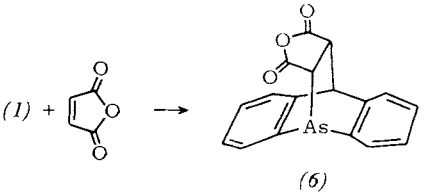


Fig. 1. UV spectra of anthracene (in cyclohexane), 9-phosphaanthracene *(5)* (in toluene), and 9-arsaanthracene *(1)* (in THF)[**]. The heights of the curves for *(5)* and *(1)* are in arbitrary units.

Comparison of the UV spectra of 9-phosphaanthracene[7] *(5)* and *(1)* reveals an almost superimposable structure of the absorption bands, the surprisingly large bathochromic shift in the spectrum of *(1)* (longwave absorption at λ = 454 nm) is possibly due to the low electronegativity of the heteroatom (χ_P = 2.5; χ_{As} = 2.1[8]). Furthermore, the relative intensities and spacing of the absorption maxima in the spectra of *(1)* and *(5)* are very similar to the ^1L_a band of anthracene.

We have not, as yet, been able to isolate compound *(1)*, which, like its phosphorous analog *(5)*[7], also proves to be unstable; polymerization occurs, with foaming, on removal of the solvents. The stability in solution is strongly solvent dependent (THF > benzene > cyclohexane). Decomposition takes place in the presence of oxygen or HCl. The yellow solution immediately decolorizes on addition of maleic anhydride, the Diels Alder adduct *(6)*, m.p. 248 °C, being formed in 70% yield. The structure of *(6)* follows from ebullioscopic determination of molecular weight, IR and ^{1}H-NMR spectroscopy, and elemental analysis.



(6)

The elimination of the HCl from *(2)* can be verified under mass spectrometric conditions: The stable ion $(1)^+$ (m/e = 240, I = 80%; corresponding metastable ion at m/e = 210) is formed in a one-step fragmentation from the molecular ion (m/e = 276, I = 20%). The occurrence of the doubly positively charged 9-arsaanthracene ion ($m/2e$ = 120) is characteristic of aromatic compounds.

Received: November 3, 1969 [Z 114a IE]
German version: Angew. Chem. *81*, 1051 (1969)

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[**] This work was supported by the Deutsche Forschungsgemeinschaft. Cf. also *H. Vermeer* and *F. Bickelhaupt*, Angew. Chem. *81*, 1052 (1969); Angew. Chem. internat. Edit. *8*, 992 (1969).

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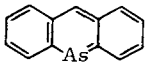
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Dibenz[*b,e*]arsenine (9-Arsaanthracene)[**]

By *H. Vermeer* and *F. Bickelhaupt*[*]

Tricyclic aromatic compounds containing arsenic as heteroatom have already been the subject of many reports[1,2]. However, the suggested structures of these molecules have remained somewhat doubtful, firstly because of inadequate structural proof and secondly because of their unusual properties compared with those of their phosphorous analogs[3]. We have, therefore, tried to prepare dibenz[*b,e*]arsenine (9-arsaanthracene) *(1)* as an authentic member of this type of compound by elimination of HCl from 5-chloro-5,10-dihydrodibenz[*b,e*]arsenine (9-chloro-9,10-dihydro-9-arsaanthracene) *(2)*[4,5]. The UV system of *(2)* does not contain an absorption maximum between 290 and 700 nm so that the arsonium chloride structure discussed by *Gump* and *Stoltzenberg*[4] can be ruled out.



(1)

In the mass spectrum[6] of *(2)* there are signals due to the ions $(2)^+$ (m/e = 278, 1.9%; m/e = 276, 5.6%), $(1)^+$ (m/e = 240, 92.9%), fluorene$^+$ (m/e = 166, 100%), fluorenyl$^+$ (m/e = 165, 92.9%), and $(1)^{2+}$ ($m/2e$ = 120, 15.7%). The transitions $(2)^+ \rightarrow (1)^+$ (*Jennings'* method[7]) and $(1)^+ \rightarrow$fluorenyl$^+$ (metastable ion at m/e = 113.5, calc. 113.54) take place in one step. In contrast to the analogous ion of dibenzo[*b,e*]phosphorin [$(3)^+$][3], the aromatic ion $(1)^+$ does not give the strongest peak.

Solutions of *(2)* (*ca.* 100 mg) in toluene, ether, or dimethylformamide (*ca.* 10 ml) immediately turn yellow on addition of a suitable base (triethylamine or 1,5-diazabicyclo[5.4.0]-undec-5-ene (DBU); 5—15% excess) and (except in dimethylformamide) a precipitate is formed (consisting mainly of the hydrochloride of the base; yield 85—95%).

The formation of *(1)* was deduced from the characteristic UV spectrum[**], which corresponded to the spectra of anthracene and *(3)*; as expected the long-wavelength maximum of *(1)* is shifted bathochromically with respect to that of *(3)*.

Not surprisingly, *(1)* is less stable than *(3)*; the UV absorption of the dissolved compound disappeared during the isolation, *e.g.* on evaporating the solution at room temperature. The yield is highest (*ca.* 8%[8]) in the system dimethylformamide/DBU but the stability is the lowest (decrease in extinction at 451 nm to about 30% in 20 min). This instability of *(1)* increases the doubt surrounding the validity of the structure suggested for the arsenic compounds mentioned above.

Received: November 7, 1969 [Z 114b IE]
German version: Angew. Chem. *81*, 1052 (1969)

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[**] Cf. also *P. Jutzi* and *K. Deuchert*, Angew. Chem. *81*, 1052 (1959); Angew. Chem. internat. Edit. *8*, 991 (1959).

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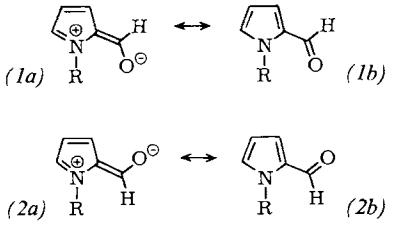
[8] Using the known extinction coefficients of anthracene, of the meso phenyl derivatives of anthracene and *(3)*, and of arsamethinecyanine [9] the following values were obtained by extrapolation: for *(1)*: $\varepsilon_{451} = 4000$; for *(3)*: $\varepsilon_{429} = 5500$.

[9] *G. Märkl* and *F. Lieb*, Tetrahedron Letters *1967*, 3489.

Conformational Studies in Pyrrole Chemistry

By *R. A. Jones* [*]

Extensive participation of the zwitterionic limiting forms *(1a)* and *(2a)* in the structure of 2-formylpyrrole hinders rotation about the C—C bond between the formyl group and the pyrrole ring, so that two conformers can exist.



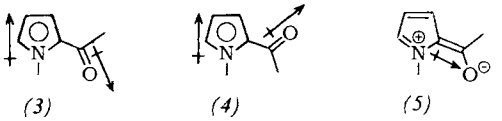
(1a) *(1b)*

(2a) *(2b)*

A study [1] of the dipole moment of 2-formylpyrrole [*(1)* or *(2)*, R = H] showed that the conformer *(1)* is the more stable. Further indications were obtained from IR [2] and NMR studies [3]. The NMR spectra show that the formyl-proton couples with the proton on C-5 [4]. Application of the zigzag rule [5,6] indicates the predominance of structure *(1)*. Coupling with the proton on C-4 was not observed.

Spectroscopic comparison of the 1-alkyl-2-formylpyrroles [7] [*(1)* or *(2)*, R = CH_3, C_2H_5, iso-C_3H_7, *tert*-C_4H_9] shows that the predominating conformation remains unchanged through the series in spite of the increasing size of the alkyl group. The IR and UV spectra can be interpreted only if the carbonyl group is twisted slightly out of the plane of the pyrrole ring. The effect of this twist on the coupling constants between the formyl-proton and the proton on C-5 is not known [6], but a diminution of this constant is to be expected. Since there is no coupling between the formyl-proton and the proton on C-4 it must be concluded that 1-butyl-2-formylpyrrole also exists in form *(1)*.

These results can be explained by dipole-dipole interaction [*(3)* and *(4)*]. This would lead to the energy content of system *(3)* being less than that of system *(4)*. Studies of the dipole

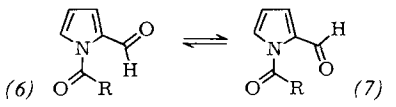


(3) *(4)* *(5)*

moment show that the "resonance moment" *(5)* is also important, but exact values are not available [8].

The formyl group of 1-formylpyrrole can rotate freely at 40 °C [9].

Spectroscopic examination of 1-ethoxycarbonyl-2-formylpyrrole and 1-acetyl-2-formylpyrrole shows that an equilibrium exists between *(6)* and *(7)*, the conformers *(6)* predominating to the extent of 70%, and assumption of dipole-dipole interaction is in agreement with these results.



(6) *(7)*

Lecture at Marburg (Germany), September 4, 1969 [VB 213 IE]
German version: Angew. Chem. *81*, 1006 (1969)

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SELECTED ABSTRACTS

The preparation of transition metal complexes by simultaneous condensation of vaporized atoms of the elements Cr, Fe, Co, and Ni with an excess of ligand has been achieved in good yields in gram quantities by *P. L. Timms*. Thus Cr, Fe, Co, and Ni react with PF_3 to give $Cr(PF_3)_6$, $Fe(PF_3)_5$, along with $(PF_3)_3Fe(PF_2)_2Fe(PF_3)_3$, $Co_2(PF_3)_8$, and $Ni(PF_3)_4$. Co-condensation of Cr and benzene gives a 60% yield of dibenzenechromium, that of Fe and Ni with cyclopentadiene gives ferrocene and π-cyclopentadienyl-π-cyclopentenylnickel. Fe and benzene yield a highly reactive product which explodes at temperatures above −50 °C and which affords cyclohexane in the presence of H_2, and ferrocene in the presence of cyclopentadiene. / Chem. Commun. *1969*, 1033 / —HB. [Rd 103 IE]

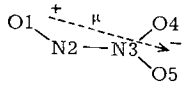
The fluorescence and phosphorescence of biacetyl in the gas phase at low pressures has been studied by *C. S. Parmenter* and *H. M. Poland* with a view to gaining information about the kinetics of the singlet-triplet transition. The quantum yields of both kinds of emission were independent of pressure between 0.1 and 40 torr on excitation with light of the wavelength 4358 Å; it therefore follows that, under these conditions, collisions play no part in the transition to the triplet system. The phosphorescence quantum yield decreased below 0.1 torr; it was shown that this is extensively or exclusively due to radiationless deactivation of triplet molecules by collision with the walls. Those excited singlet molecules that are not deactivated by fluorescence all undergo transition to the triplet state, the rate constant amounting to 10^{-8} s^{-1}; direct radiationless deactivation of the excited singlet to the ground state can be neglected. / J. chem. Physics *51*, 1551 (1969) / —Hz. [Rd 105 IE]

The ESR spectrum of the acetonyl radical $CH_3-CO-\dot{C}H_2$ has been investigated by *G. Golde, K. Möbius*, and *W. Kaminski*. The radical was generated by photolysis of an aqueous solution of acetone to which H_2O_2 had been added. The temperature dependence of the ESR spectrum shows that the rotation of the $\dot{C}H_2$ group about the C—C bond is hindered: analysis of the spectrum at various temperatures afforded the

Arrhenius parameters $E_a = 9.4 \pm 0.5$ kcal/mole and $\log k = 12.9 \pm 0.3$ for this rotational movement. This result can be interpreted in terms of a certain degree of delocalization of the spin density of the radical electron over the rest of the molecule. / Z. Naturforsch. *24a*, 1214 (1969) / —Hz.

[Rd 106 IE]

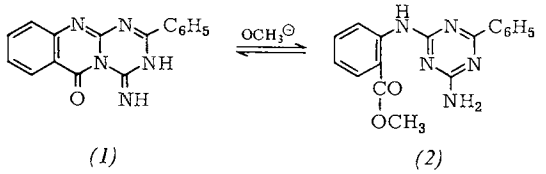
The molecular geometry of dinitrogen trioxide has been determined by *A. H. Brittain, A. P. Cox*, and *R. L. Kuczkowski* from the microwave spectrum. The main difficulty encountered in the measurements was that N_2O_3 is 99.5% dissociated to NO and NO_2 at the pressures (10^{-2} to 10^{-1} torr) used in microwave spectroscopy, even at temperatures as low as —78 °C. The spectra of N_2O_3 containing certain percentages of ^{15}N and ^{18}O yield the following data: N2—N3 = 1.864 Å; N2—O1 = 1.142 Å; N3—O4 = 1.202 Å; N3—O5 = 1.217 Å; O1—N2—N3 = 105.1 °; O4—N3—N2 = 112.7 °;



O5—N3—N2 = 117.5 °. The molecule is planar; the frequency of the twisting vibration about N2—N3 is 124 ± 25 cm^{-1}. The dipole moment amounts to 2.12 D and acts in a direction at 9.1 ° to N2—N3; the negative end of the dipole lies at the nitro group. / Trans. Faraday Soc. *65*, 1963 (1969) / —Hz.

[Rd 109 IE]

The triazino[2,1-*b*]quinazoline system has been synthesized for the first time by *J. T. Shaw* and *J. Ballentine*. The acid-catalyzed cyclization of K dicyanobenzamidine with methyl anthranilate (refluxed in anhydrous methanol in the presence of pyridine and benzenesulfonic acid) yields compound *(1)*, a derivative of the new ring system, m.p. 342—343 °C (DMF).

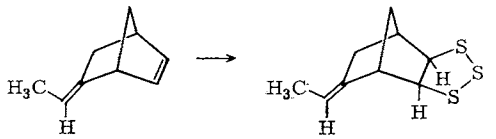


(1) *(2)*

Compound *(1)* is cleaved by $NaOCH_3$ to the ester *(2)*, which regenerates *(1)* when heated to a temperature in excess of its melting point. Several tautomers of *(1)* are possible. The NH and the phenyl group could be exchanged. / Chem. Commun. *1969*, 1040 / —Ma.

[Rd 111 IE]

A selective, stereospecific insertion of sulfur into olefins such as norbornene has been described by *T. C. Shields* and *A. N. Kurtz*. If sulfur is activated by NH_3 or aniline in the presence of an amide such as DMF as promotor and subsequently heated to 110 °C with norbornene, 5-ethylidenenorbornene



(1) *(2)*

(1), or similar compounds, *exo*-3,4,5-trithiatricyclo[5.2.1.$0^{2,6}$]-decane or the 8-ethylidene derivative *(2)* is obtained in 86 or 71% yield. Up to 99% DMSO or an excess of amide can serve as solvent. The addition occurs exclusively at the double bond of the ring. / J. Amer. chem. Soc. *91*, 5415 (1969) / —Ma.

[Rd 112 IE]

New luminescence experiments on azulene are the subject of a report by *P. M. Rentzepis*. Azulene and its derivatives occupy a special place among all organic compounds owing to the fact that under normal conditions they only fluoresce from the second excited singlet state. Excitation with extremely short laser pulses (several 10^{-12} s) has now revealed emission from the first excited singlet state S_1 (maximum at about 750 nm) and the lowest triplet state T_1 (maximum at about 1100 nm). The fluorescence from S_1 has a decay time less than 10^{-10} s and a quantum yield of about 10^{-7}. Phosphorescence from T_1 could only be observed at 77 °K with a decay time of 10^{-6} s. / Chem. Physics Letters *3*, 717 (1969) / —Hz.

[Rd 117 IE]

BOOK REVIEWS

Die Nomenklatur in der organischen Chemie (The Nomenclature of Organic Chemistry). By *W. Holland*. Verlag Harri Deutsch — Zurich-Frankfurt/M. 1969. 1st Edit., 190 pp., stitched, DM 34.80.

As stated in the introductory remarks, the author set himself the task, not merely of giving the nomenclature rules current today, but also of describing the older usages. The book does indeed contain numerous references to previous proposals for, and usages in, nomenclature, so that the original literature can still be understood by the reader. However, as a guide and help in the formation of names for organic compounds — and that is what it should be — the book cannot be unreservedly recommended because of the various contradictions it contains. For instance, on p. 46 methoxycarbonyl is correctly recommended in place of the older designation carbomethoxy, yet on p. 36 only carbobenzoxy (with the abbreviation Cbo) is given for the amino acid protecting group and not benzyloxycarbonyl (with the abbreviation Z). In the explanation of the ring fusion principle on pages 87—88 the instruction is recorded whereby the parent compound shall chosen to be as large as possible and the anneland as small as possible, but a contradiction to this is met on page 89 where in the explanation of numbering round the outer ring the example naphth[2.1-*a*]anthracene should correctly be named benzo[*b*]chrysene [RRI 6379]. And the list of such contradictions could be considerably extended. Also it is not evident why in the tables aromatic compounds are drawn sometimes with and sometimes without double bonds.

Ilse Spaeth [NB 837 IE]

Kunststoff-Handbuch, Band IV: Polyolefine (Plastics Handbook, Vol. 4: Polyolefins). Edited by *R. Vieweg, A. Schley*, and *A. Schwarz*. Carl Hanser Verlag, München 1969. 1st Edit., xxi + 976 pp., 795 illustrations, 106 tables, linen DM 270.—; on subscr. to the complete work (12 vol.) DM 216.—.

The rate of production of polyolefins has grown faster than that of any other thermoplastic, so that appearance of the present volume[1] should receive a warm general welcome,

[1] Cf. Angew. Chem. *81*, 542 (1969); Angew. Chem. internat. Edit. *8*, 468 (1969).

especially as the expanding area of application of polyolefins is in particular need of a review volume such as this.

The book is divided into the main sections Preparation, Properties, Fabrication, and Application of Polyolefins. It treats mainly the polymers of ethylene, propene, and isobutene; diolefins and mixed polymers of ethylene and propene, and of ethylene and vinyl acetate, leading to elastomers, are mentioned only marginally, and these should perhaps be treated in greater detail in the next edition because their importance is increasing.

The Ziegler low-pressure polymerization process, polymers obtained by that process, and modified polyolefins have ample space devoted to them, but the low-pressure polymerization process developed by Phillips Petroleum, and the high-pressure polymerization of ethylene by which most polyethylene is produced, are perhaps treated too briefly. The preparation of olefins themselves will not necessarily be looked for in a plastics Handbook.

The polymerization of ethylene and propene by means of Ziegler catalysts is presented in great detail, yet intelligibly and clearly, and this permits rapid and successful orientation even though there is unfortunately no reference later than 1960. The part dealing with the properties of polyethylene contains a wealth of material on the structure, on the thermal, mechanical, and electrical properties, and on the behavior towards chemical reagents. Detailed tables make it easier to find individual facts. The chapter on fabrication is very successful, presenting in full all the important methods of working polyolefins, such as extrusion, injection molding, calendering, powder sintering, and flame spraying, as well as procedures for dealing with semimanufactured material, each supported by good illustrations.

The largest part of the book is rightly devoted to application of polyolefins. This very properly recognizes the changes introduced by polyolefins in the most varied fields, *e. g.* packaging, building, agriculture, craft and vehicle construction, plant construction, and the household.

High praise should be awarded to the editors for their having engaged first-class experts for the individual sections; these authors have provided the reader with an excellent presentation in word and picture. In an area in a state of such dynamic development it is tolerable that there are small gaps here and there; for instance, it would have been good to be told something about methylpentene polymers (TPX) and about production of foams from polyolefins. The book contains a large number of references and good tables and indexes, and it can be warmly recommended to all who are interested in polyolefins, both for their study and for rapid information.

O. Horn [NB 839 IE]

Index Pharmacorum. Synonyma, Struktur und Wirkung der organisch-chemischen Arzneistoffe (Synonyms, Structure, and Action of Organic Drugs). By *H. Ippen.* Published on behalf of the Deutsche Forschungsgemeinschaft. Georg Thieme Verlag, Stuttgart, 1968. xxviii + 693 pp., bound, DM 130.—.

A problem familiar to all whose work concerns drugs is the fact that identical medications are often on sale in different countries with different trademarks, and the same substance may even be available under several protected trade names in one country, with the result that the unequivocal identification of a medication is extremely difficult. Added to this is the difficulty that by using trade names in scientific publications, one runs the risk of conflict with commercial interests. The chemical nomenclature for drugs, on the other hand, is often too clumsy and not readily understood by the non-chemist. Non-protected free names have therefore been introduced. Thus, in the USA there arose the "Generic Names", in England the "Approved Names", in Scandinavia the "Nordiske Farmakope-Naevn", in France the "Dénominations Communes", to which were added, after 1950, the "International Non-Proprietary Names" of the World Health Organization. None of these drug nomenclature systems, however, is anywhere near complete and their use in scientific publications is haphazard. The identification of a drug from its name consequently requires many aids, which are not available everywhere, and is often very time-consuming.

On behalf of the Deutsche Forschungsgemeinschaft, therefore, *H. Ippen* undertook to collect, in dictionary form, all defined organic substances that are, or have been, used as curative agents or as aids in the treatment, diagnosis, or investigation of illness. The following information is given for each one:

1. The non-protected name(s), with special indication of the names recommended or suggested by the World Health Organization.

2. The chemical designation of the compound according to the Beilstein and the "Chemical Abstracts" systems;

3. Officinal names insofar as they form part of the "Pharmakopoea Internationalis", the "Deutsche Arzneibuch", the "British Pharmacopoeia", or the "Pharmacopeia of the United States";

4. Trade names with the name of the firm holding the trademark;

5. Action and indications (only for some of the substances and only in keyword form);

6. The structural and molecular formulas.

The drugs are arranged either according to the organ system chiefly affected or according to indications. The arrangement within these groups has been determined mainly by chemical considerations. In addition to this very clear division of the book, two indexes (indications and substance groups, as well as a comprehensive 100 page index of synonyms) make the use of the work easier.

One can scarcely imagine the pains the author must have taken in compiling this dictionary, not only in bringing the wealth of information together, but also in checking its reliability. Whoever uses this book however, — the pharmacist, the pharmaceutical chemist, the pharmacologist, or the doctor — will thank the author for his trouble, for here is an aid as useful as it is long overdue. Not only will it be welcomed by information scientists, but its usefulness will also be put to the proof daily by practising doctors and dispensing pharmacists.

H. Grünewald [NB 842 IE]

Comprehensive Biochemistry. Edited by *M. Florkin* and *E. H. Stotz.* Vol. 23: Cytochemistry. Elsevier Publishing Company, Amsterdam-New York-London 1968. 1st Edit., xii + 167 pp., 32 illustr., 21 tables, bound Dfl. 35.—.

A cell surrounded by a membrane is composed of a nucleolus and cytoplasm in which can be detected cell compartments also separated by membranes of various types. This general type of structure is found in different but exact forms in microorganisms, plants, and animals. The physiological cell functions and the molecular processes characteristic of physicochemical regulation and biological control of the individual organelles are bound to complex highly organized structures; in this book they are collected in a section "Chemical Biology" that applies to all the molecular units and functions treated in the earlier sections.

Once more, competent authors have combined a review of the literature with their own observations and present a very valuable and useful reference work for the various features of structure and function of the cell. Each section deals with isolation, morphology, chemical composition, biochemical function, and enzymology, individual sections referring to the cell nucleus (*G. Siebert*), the nucleolus (*H. Busch*), lysosomes (*A. L. Tappel*), animal (*R. Coleman* and *J. B. Finean*) and bacterial cell membranes (*M. R. Salton*). Chapters are 30—40 pages in length and contain the literature up to the middle of 1966; in some cases appendices are provided covering further results up to the date of closure of the vol-

ume, showing the rapid development in this area of physiological biochemistry — there are as many references from the last year as from all previous years. The material is provided not only in the text but also impressively by good electron-optical illustrations and intelligible tables. The problems of the structure of membranes and the possibility of artefact formation are reported critically; current views on the homogeneity of membranes and on passive and active transport mechanisms are discussed with clarity. Thus this volume of "Comprehensive Biochemistry"[1] is an essential and welcome review of the biological-chemical requirements of dynamic biochemistry and is an important member within the general plan of this excellent series.

L. Jaenicke [NB 829 IE]

Quantitative Problems in the Biochemical Sciences. By *R. Montgomery* and *C. A. Swanson*. W. H. Freeman and Co., San Francisco-London 1969. 1st Edit., xiii + 308 pp., 51 illustr., 33 tables, bound 24 s.

Biochemistry ceased long ago to be a descriptive and qualitative science which the exact-thinking chemist regarded sceptically. On the contrary, it now makes full demands on the application of physicochemical procedures and ideas and is beyond doubt the most exact branch of biology. Moreover, the student who turns to biochemistry cannot learn too soon that the living organism does not play fast and loose with entropy; and he must not shy away from equipping himself with the necessary mathematical ability if he is to obtain more than a smell of physical chemistry; he needs to be in a position to formulate his observations mathematically, to discuss his experimental results in physical terms, and to evaluate meaningful reaction parameters; in short, to apply and make full use of the *modus operandi* of fundamental physical chemistry.

Unfortunately there are not nearly enough physical chemists with sufficient biological knowledge — and still fewer who will take the trouble — to provide courses or books that enable the student to train himself in the necessary experimental and mental work. The book under review here attempts to fill that gap. The approach used is didactically sound and full allowance is made for any missing elementary knowledge; so it begins with exercises in calculating exponentials and logarithms, discussing curves and equations, and dimensional analysis. There follow stoichiometric calculations, problems in the physics of solutions, chemical equilibria, hydrogen ion concentration and buffers, redox potentials, chemical energetics and kinetics, bringing in the most fundamental parts of enzyme kinetics (the Michaelis-Menten equation is discussed in different connections in three places, but without cross-references). The concluding chapters are more analytical and procedural: spectrophotometry and radiochemistry.

Each chapter begins with a short introduction that suffices to explain the methods of calculation involved; but a textbook of physical chemistry is needed for a deeper understanding of the problems set. Some examples are first worked out in full, then new problems are set whose solutions are given in an Appendix, and finally problems from experimental biochemistry are put up for discussion, with literature references but without a solution's being provided; answering these last problems without recourse to the cited paper demands thought, critical ability, and experience, as well as a good textbook of biochemistry, but these exercises are exceptionally stimulating for those with the necessary application and interest.

The book is excellently suited for seminars that follow courses or lectures if guidance from a person with some experience is available. For personal use alone it requires more character than is commonly met. *L. Jaenicke* [NB 828 IE]

[1] Cf. Angew. Chem. *80*, 974 (1968); Angew. Chem. internat. Edit. *7*, 901 (1968).

Clinical Pharmacology. By *M. Shepherd*, *M. Lader*, and *R. Rodnight*. In the series "Modern Medicine". The English University Press, Ltd., London 1968. 1st Edit., xi + 306 pp., bound 50s.

A psychiatrist, a pharmacologist, and a biochemist have undertaken to present a scientific field that has fundamentally changed both the treatment of mental patients and the outward appearance of mental hospitals during the past 15 years. The three authors have apparently collaborated in writing the individual chapters of this monograph, much to the benefit of its uniform quality.

In the first part methods are described for evaluating the clinical usefulness of psychotropic drugs by both animal and human experiments. Then the individual drugs are discussed in regard to their absorption, distribution within the organism, metabolism, pharmacology proper, effect on behavior, clinical effects, and side effects. Following a brief treatment of sedatives and hypnotics as well as central stimulants of longstanding use, and of lithium, which has come into widespread use in the treatment of mania during recent years, the comprehensive chapter deals with tranquilizers, especially phenothiazine derivatives, *Rauwolfia* alkaloids, and butyrophenone derivatives. Among the drugs with antidepressant action preferential consideration is given to the monoamine oxidase inhibitors while the tricyclic compounds of the imipramine type having far greater clinical importance are treated much more briefly.

Other chapters deal with recent developments in the field of sedatives and hypnotics, stimulants, and anti-Parkinson drugs. Chemicals producing psychosis-like states are also briefly considered, *i.e.* lysergic acid diethylamide (LSD 25) and mescaline, the concept of psychotomimetic drugs also being defined. A long chapter is devoted to the biochemical effects of psychotropic drugs and current hypotheses in this field are mentioned. Finally the ways along which psychopharmacological research should develop in the future are discussed.

The present book is notable for the authors' strict adherence to proven facts; though giving due consideration to all the hypotheses so abundant in this field the authors refrain from committing themselves to any particular one. Almost 1300 references, mostly to the English literature, open the reader's way into the field of psychopharmacology.

From the title of this work one may get the impression that the book is a clinical work addressed mainly to the clinician. This is not the case; not only does the book contain the information the clinician should know when administering these drugs, but it is also so clearly written and readily intelligible as to enable even the educated layman to familiarize himself with the whole field of psychopharmacology without any difficulty. It may be considered an irony of fate that the first mention of chlorpromazine, the compound that practically brought psychopharmacology into being, refers to an incorrect structural formula. *G. Quadbeck* [NB 830 IE]

Photoluminescence of Solutions. By *C. A. Parker*. Elsevier Publishing Co., Amsterdam-London-New York 1968. 1st Edit., xvi + 544 pp., 188 illustrations, 53 tables, bound Dfl. 85.—.

Unlike absorption spectrophotometry, emission methods in the field of molecular spectroscopy are far from having become a general tool in the analytical laboratory. This is clearly due to the greater experimental demands of the latter, particularly in respect of quantitative results. Although the recording of Raman spectra will become possible for a wide circle of interested chemists by application of lasers, the possible applications of fluorescence and phosphorescence spectroscopy have as yet been rarely exploited. The present book will help to remedy the situation.

The book is divided into the following chapters: 1, Basic Principles and Definitions (68 pages). The fundamentals of fluorescence and phosphorescence, polarization phenomena

and scattering effects are described. 2, Kinetics of Photoluminescence (58 pages). The important aspects of excitation and quenching processes are treated, as well as delayed fluorescence. 3, Apparatus and Experimental Methods (174 pages). In this chapter the author gives an excellent and full description of the technique necessary for measurement of luminescence. Each component of the luminescence spectrometer is described in detail. In the part dealing with methods, the main emphasis is placed on measurement of the light beam, correction of luminescence spectra and measurement of lifetime and quantum yield. 4, Special Topics and Applications (93 pages). Here the author has selected problems with which he is familiar, such as intersystem crossing efficiency, protolytic reactions in the excited state, excimers, and delayed fluorescence; but solvent effects and applications of polarization measurements are treated only briefly. 5, Application to Analytical Chemistry (105 pages). The use of luminescence methods in determination of molecular structure are described, also qualitative and quantitative investigation of organic and inorganic compounds and of the elements alone and in admixture. The book closes with a list of references and a detailed keyword index.

According to the foreword, the book is intended to fulfil a double purpose: first, to teach students the fundamentals and, secondly, to serve the specialist as a reference book. The second aim seems to be met in chapters 3—5. The author's great experience makes itself felt in the description of methods and apparatus; for instance, correction of emission and excitation spectra, not yet generally applied, are described in detail. However, when reading the results of luminescence spectroscopy recorded in the book one must not expect a review of the present state of knowledge, for the author has intentionally confined himself to his own specialist partial field.

As an introduction to the fundamentals the book can be recommended only subject to restrictions. That the author has refrained from quantum-chemical considerations is no disadvantage in principle, since specialist books exist in that area. This has, however, been taken too far, so that some fundamentals, such as the Frank-Condon principle cannot be clearly presented. A number of quantum-chemical ideas, such as charge-transfer state, nodal plane, and transition moment, are used without exact explanation. Further, the way in which certain basic relations are presented is open to a series of objections; for instance, polarization effects and the relation of lifetime to quantum yield are very sketchily explained; also more space should have been devoted to the solvent effect when treating the "Luminescence of Solutions".

The good points of the book are undoubtedly the sections on apparatus and methods. As a monograph it fills a gap in this respect, and it can be very warmly recommended to chemists, biochemists, and others interested in the application of luminescence spectroscopy. *H. Stegemeyer* [NB 835 IE]

Principles of Organometallic Chemistry. By *G. E. Coates, M. L. H. Green, P. Powell,* and *K. Wade.* Methuen & Co. Ltd., London 1968. 1st Edit., x + 259 pp., numerous illustrations, bound 38 s.

This is an abbreviated presentation of the principles of the organometallic chemistry of metals of the main and subgroups, based on the two-volume third edition of the same authors' "Organometallic Compounds".

In this abbreviation the authors wished above all to provide students with easy access to this rapidly developing branch of chemistry. The authors have been extremely successful in limiting themselves to the most important matters; they often use skillfully chosen figures to replace much text, though it is also good that the cost of preparation of some of the key compounds is also discussed. The relation of theory and physical studies (in particular X-ray structure studies) is well done. The book is very carefully and clearly printed. Because of its low price every student of chemistry can afford it. *P. Heimbach* [NB 840 IE]

Lehrbuch der Physikalischen Chemie – in elementarer Darstellung (Textbook of Elementary Physical Chemistry). By *J. Eggert, I. Hock,* and *G.-M. Schwab.* S. Hirzel Verlag, Stuttgart 1968. 9th revised Edition, 935 pp., 248 figures, 125 tables, bound DM 72.—.

The size of the present 9th edition of *J. Eggert*'s Textbook of Physical Chemistry differs only slightly from that of the 8th edition, which was published in 1960. The division into nine chapters has also been retained: "Principles of the Atomistic and Energetic Approach"; "Atoms"; "Molecules"; "Aggregation States"; "Chemical Thermodynamics"; "Electrochemistry"; "Colloid Chemistry"; "Chemical Kinetics"; and "Photochemistry". Nevertheless, substantial portions of the book have been completely revised and brought up to date. For instance, the section on the wave-mechanical theory of nonpolar bonding in the chapter on "Molecules" has been enlarged, and a section has been added on electron spin resonance, nuclear magnetic resonance, and the Mössbauer effect. The reworking and expansion of the chapter on "Aggregation States", in particular of the section on solids, also deserves mention. The main subjects dealt with here are methods of structure determination, ligand field theory, and the structure of organic substances. The chapter on "Chemical Thermodynamics" has been to some extent rearranged into a clearer and more logical form. One finds a highly interesting – and important – concession to current events in the changes and additions introduced in the sections on "Production of Extreme Temperatures" and "Thermodynamics of Space Flight". Apart from these more extensive changes from the 8th edition, the authors have introduced a large number of improvements in the interest of a concise and up-to-date presentation of the facts.

In the Preface the authors pose the question whether the field of physical chemistry still constitutes a scientifically homogeneous entity, or whether it has already broken up into independent parts roughly corresponding to the individual chapters of the book. The reviewer is in complete agreement with the authors when they suggest that the teaching profession should not split up the subject in this way but should continue to present physical chemistry as an entity for as long as possible; after all, an understanding of one of its constituent fields very often throws light on the principles of others.

In a comprehensive textbook of physical chemistry the treatment accorded to each individual subject should of course reflect the importance of that subject. On that score the book lays itself open to criticism. In a number of the chapters the reader is confronted with such a mass of detail that there is a danger of its obscuring his appreciation of the whole. On the other hand, at least a brief introduction to statistical thermodynamics, and certainly a more detailed treatment of wave mechanics, would have been welcome. This would admittedly have involved a departure from the somewhat elementary mathematical treatment, chosen in accordance with the intention professed in the title. However, in view of the importance that bonding theory now has for both organic and inorganic chemists, a student will in any case have to be taught enough of the mathematical treatment to enable him to go on to the specialized literature without undue difficulty. The same comment applies to the chapter on "Chemical Thermodynamics".

The constantly recurring problem of whether a course in physical chemistry should begin with a discussion of thermodynamics or the structure of matter is skilfully resolved by first presenting an elementary description of the ideas and procedures of thermodynamics, the kinetic theory of gases, and quantum mechanics. The subsequent treatment of the atom, the molecule, and aggregation states can be built up in the first place on information already familiar, on experience, and on intuition. Thus the somewhat more abstract thermodynamics is postponed till the second half of the book.

The very fact of the publication of the 9th edition of a work that first appeared 42 years ago testifies to its usefulness to the chemistry student. The beginner especially will be greatly

helped by the elementary approach, the detailed descriptions and explanations of the fundamental laws, and the formulas and diagrams. The copious marginal notes help toward an understanding of the relationships between the laws and also make it easier to find a particular explanation.

The print, the illustrations, and the tables are a model of clarity, and the overall presentation is outstandingly good.

G. Wedler [NB 843 IE]

Principles of Organic Synthesis. By *R. O. C. Norman*. Methuen & Co. Ltd., London 1968. 1st Edit. xiii + 722 pp., numerous illustrations and tables, bound £ 5.5.0.

The author sets out to provide the student who already posesses a basic knowledge of organic chemistry with all he needs to know for planning and carrying out organic syntheses. The book consists of two parts:

The first contains several chapters dealing with physical organic chemistry; for example, chemical thermodynamics, molecular structures, chemical kinetics, and reaction mechanisms, as well as a chapter on stereochemistry.

The second, appreciably larger part of the book deals with organic chemistry proper, and is arranged according to reaction type. It has chapters on formation of carbon-carbon bonds with organometallic reagents, formation of aliphatic carbon-carbon bonds by base-catalyzed condensations, formation of aliphatic carbon-carbon bonds by acid-catalyzed condensations, formation of aliphatic carbon-carbon bonds by four-center reactions, formation of carbon-nitrogen bonds, electrophilic aromatic substitutions, aromatic diazonium salts, molecular rearrangements, free-radical reactions, oxidations, reductions, syntheses of heterocyclic compounds, syntheses of natural products.

The selection and arrangement of the material in both parts of the book are very sound. It is particularly commendable that, despite a strict limitation of the material, all the important reactions have been included. The numerous structural formulas included in the text contribute substantially to the readability and take into account the reaction mechanisms. The book's usefulness is enhanced by the references to review literature and the sets of questions given at the end of each chapter. It must be said, however, that the bibliography might have been more comprehensive.

This book will be welcomed both by advanced students and by industrial chemists. A point that has puzzled the reviewer is the choice of title. With regard to its content the book differs little from other modern textbooks of organic chemistry that are subdivided according to reaction type, rather than according to the class of substance.

H. Stetter [NB 846 IE]

Analogcomputer in Chemie und Biologie. Eine Einführung. (Analog Computers in Chemistry and Biology. An Introduction.) By *H. Röpke* and *J. Riemann*. Springer-Verlag, Berlin-Heidelberg-New York 1969. 1st Edit., vii, 184 pp., 198 figs., bound DM 38.—.

Following an introduction to the mathematical treatment of problems in reaction kinetics, the authors outline the mode of operation of operational-amplifier analog computers. Simple examples are used to explain the construction of analog computer circuits. Computing circuits are given for 47 model examples, and the results obtained with them are shown. The last section deals with the use of analog computers for special problems, mainly from the authors' own field. A comprehensive bibliography on the kinetics of chemical reactions and the principles and applications of analog computers completes the book.

The authors deliberately concentrate on application problems, and the sections on the basic construction of analog computers (Sections 6 and 7) are accordingly kept very short. It would in fact have been preferable, from the point of view of chemists and biologists, to go into greater detail here to enable the book to fulfill its purpose as an introduction to analog computer techniques. It would not have taken much more space to derive the working equations of the adder and of the integrator in order to allow the reader to obtain a clear understanding of the basic procedure and to apply it correctly to the other parts of the computer.

Frequent use is made of symbols whose meaning is not defined, *e.g.* symbols for operational amplifiers with other inputs besides the direct input. The discussions of Figure 32, 38, 40, and 42 are incomprehensible for this reason. In other circuits (adder, integrator, potentiometer), the symbols should have been placed immediately adjacent to the circuit, and not in a summarizing table that appears only many pages later.

The numerous model examples, which make up two thirds of the book, are excellently chosen to give a clear grasp of the method of operation and to encourage its application to other kinetic problems. The book is therefore a valuable aid to anyone who is interested in the use of analog computers.

H.-D. Försterling [NB 847 IE]

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Editorial office: Ziegelhäuser Landstrasse 35, 6900 Heidelberg 1, Germany, Telephone 4 50 75, Telex 46 1855 kemia d, Cable address: Chemieredaktion Heidelberg.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie GmbH. (Presidents *Jürgen Kreuzhage* and *Hans Schermer*), Pappelallee 3, 6940 Weinheim/Bergstr., Germany, and Academic Press Inc. (President *Walter J. Johnson*), 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 *W. Thiel*), 6940 Weinheim/Bergstr., Pappelallee 3, Germany, Telephone Weinheim (06201) 3635, Telex 46 55 16 vchwh.

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